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Committee Secretary
Senate Standing Committees on Community Affairs
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Parliament House
Canberra ACT 2600
Australia

Inquiry into The Regulatory Standards for the Approval of Medical Devices

Submission to the Senate Standing Committee on Community Affairs

This submission is provided to address the first of the terms of reference of the inquiry:

> *(a) the role of the Therapeutic Goods Administration in regulating the quality of devices available in Australia;*

The Committee is thanked for the opportunity to provide this submission. I would welcome any request to appear before the Committee to answer questions on the content of this submission.

Yours sincerely

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About the Author

Prof. Arthur Brandwood is Founder and Chief Executive Officer of Brandwood: Biomedical, a Sydney based Technical and Regulatory Compliance Advisory firm, with operations in global medical device markets.

Prof. Brandwood has worked as Senior Officer at TGA, where he served as Director of Postmarket compliance, Director of the Biomaterials and Engineering Laboratories and Director of Device Registration and Assessment. He has spent his entire career in medical devices, commencing in product research and development and for the past 11 years has provided regulatory advice to a wide range of clients. These range from start ups including spin outs from Universities and CSIRO to several of the world's top 5 medical device and pharmaceutical multinationals. Currently he is Chair of National Advisory Committee of AusMedtech. He has previously held full time academic positions in the UK and in Australia and is currently visiting Professor in Biomedical Engineering at the University of Sydney where he lectures on medical devices regulation.

From this very broad based expertise Prof. Brandwood brings a perspective on the global context of regulation in Australia and options for development of a more effective and efficient Australian regulatory system.

Current Regulation of Medical Devices in Australia

TGA has regulated medical devices for approximately 20 years, with the current "European Style" regulatory system having operated for almost 9 years – since 2002.

Regulation in Australia must be placed into a context of a global industry. Australia constitutes approximately 1.5% of the global market in medical devices and imports the great majority of those used. This is especially the case for high risk devices, with orthopaedic implants being almost exclusively sourced from overseas.

Almost without exception such imported devices have been subject to prior assessment in overseas markets and in particular have been awarded a CE mark following European assessment.

TGA's current regulatory arrangements approve the great majority of medical devices based on unilateral acceptance by TGA of CE certification (from any Notified Body), plus review of certain summary documentation for higher risk products, effectively with no technical assessment or factory inspection.

TGA direct assessment is applied to only a very small number of imported high risk devices and to all Australian manufactured devices, apart from the lowest risk Class I devices.

The current Australian system is heavily based on the European framework, although with significant differences in implementation which impact heavily on the effectiveness of Australian regulation of medical devices. It is therefore instructive to compare the current situations in Europe and Australia.

European Regulatory Framework

The European system is built around technical standards and assessment processes which are essentially identical to those used in Australia. However the European system divides the administration of regulation into two parts:

1. ***Notified Bodies*** conduct premarket assessments of manufacturers and issue CE certifications resulting in the so-called "CE marking" of medical devices. . These are almost always private sector organisations.
2. ***Competent Authorities*** accredit and supervise the Notified Bodies. These are almost always national government departments or agencies. Competent Authorities are also responsible for the approval and audit of clinical trials and for postmarket monitoring of the safety of approved devices in the marketplace.

These arrangements provide safeguards in the form of independent supervision of the integrity and competence of Notified Bodies and direct government control of clinical trials and of postmarket monitoring of safety.

There are approximately 80 Notified Bodies of varying sizes. The larger Notified Bodies are very capable, well resourced organisations with histories in product certification exceeding 125 years. Examples include:

- TUV Rheinland, founded in 1872 and headquartered in Cologne, employs more than 13,800 people in over 490 locations in 61 countries.
- Intertek (25,000 employees) which has as its origins as the Electrical Testing Laboratories (ETL) founded by Thomas Edison in 1896.
- TUV Sud, founded 1866, and headquartered in Munich is active in over 60 locations, with over 11,000 employees.
- BSi was the first national Standards body in the world when founded as the Engineering Standards committee in London in 1901; it now has 2,600 personnel.

- Kema, founded in 1927, employs more than 1,700 professionals globally with offices and representatives in more than 20 countries
- DEKRA, founded in 1925, has over 20,000 employees.
- SGS (formerly Société Générale de Surveillance) founded in 1878 has more than 64,000 employees in over 1,250 offices and laboratories around the world.
- Bureau Veritas, founded in Antwerp in 1828 has 47,000 employees in 1000 offices and laboratories located in 140 countries.
- Underwriters Laboratories (UL), founded in 1894 has over 7,000 employees and operates 64 separate laboratory, testing and certification facilities serving customers in 98 countries.

Of course notified bodies operate across multiple industries and not all of their resources are involved in medical devices. The precise numbers of medical device experts employed is not public information, however informal advice obtained from several of the larger Notified Bodies indicates that each employs many hundreds of experts in the field, giving a combined resource of several thousand medical device expert assessors amongst this top tier group.

Notified Bodies tend to evolve specialist strengths – e.g. BSi has particular expertise in biological origin devices, UL and Intertek have great strength in electrical safety testing and TUV Sud has particular expertise in cardiovascular implant devices.

The larger Notified Bodies are truly global, operating in multiple jurisdictions and most will be accredited as medical device third party assessors in the regulatory systems of Canada, Japan and the US (all of which allow some extent of third party assessment of medical devices) as well their assessments being recognised in emerging markets as varied as Russia, Singapore and Saudi Arabia.

From time to time concerns are raised about the variable quality of European Notified Bodies. The growth of the European Community has led to the establishment of a large number of smaller Notified Bodies in Eastern and Southern Europe, where there is much less capacity for national government oversight. A CE mark issued by any Notified Body is valid throughout Europe and there have been justifiable concerns about opportunities for forum shopping by manufacturers.

However it is notable that in the recently published findings of the European Commission's consultations on the proposed "Recast" of the Medical Devices Directives, there were no calls for any substantive change to the regulatory framework. Rather the commission highlighted a need for the strengthening of national supervisory arrangements of Notified Bodies along with increased requirements for clinical evaluation and for postmarket monitoring.

Australian Regulatory Framework

In contrast to Europe, in Australia the functions of both Notified Body and Competent Authority are combined within TGA, which is not subject to any external systematic review of technical competence or accreditation.

TGA Capabilities

TGA has a staffing complement of approximately 500 personnel of which perhaps 100 work in the medical device programme and approximately 60 technical experts, including a small number of personnel in the TGA laboratories. Precise resourcing is difficult to estimate as some TGA staff (e.g. auditors, microbiologists) are deployed across both devices and medicines programmes. Recruitment and retention of suitably experienced staff is particularly problematic for TGA given its geographical isolation from any significant medical devices manufacturing industry.

There are more than 1 million different medical devices supplied in Australia. At December 31 2010 there were 35,800 devices on the ARTG. However grouping of entries for the same "kind" of device means that each entry on the ARTG will cover an average of more than 30 individual devices.

In calendar 2010 TGA:

- Approved 5,890 device ARTG registrations;
- Completed direct assessments of approximately 130 manufacturers;
- Received 132 Clinical Trial notifications – note these were notifications only – each processed administratively in an average of 2 working days;
- Tested 266 device samples (0.03% of devices supplied);
- Supervised 365 recalls (0.04%);
- Received 1,938 adverse event reports of which 712 were investigated resulting in 9 safety alerts, 69 voluntary product changes, 29 recalls, 1 warning and 1 referral to compliance.

These figures indicate two things:

1. Medical devices supplied in Australia are very safe. Similar findings are seen overseas. For example recent figures presented to the US Senate Special Committee on Aging enquiry on FDA and the Reform of the Medical Device Approval Process[1] indicated US recall rates of well below 0.5% of devices subject to FDA review.
2. TGA resources, capabilities and activity levels are very modest compared to their European peers.
    a. Expert assessor numbers are a fraction of those available in Europe, yet the Australian Public would expect access to a similar range of medical devices;
    b. Very few devices or manufacturers were directly assessed,
    c. There was no direct supervision of clinical trials (The Therapeutic Goods Act provides for TGA audit of clinical trials but this has never been done for medical devices and only recently commenced for medicines.)
    d. the postmarket programme impacted only a tiny proportion of devices in the market.

Assessment Fees and Review Times

TGA is fully funded by industry fees. Cost comparisons between TGA and Notified Body Assessments are difficult because of the variability of commercially determined Notified Body Fees. Anecdotally, TGA per–assessment costs appear to be equivalent to or slightly higher than Notified Bodies.

However Australian assessment can take very much longer than in Europe or the US: the only statutory timeline for an TGA assessment is 255 *working* days i.e. a calendar year, compared to a typical Notified Body Assessment of 3 months (approx 60 *working* days) followed by an additional 6 weeks for independent review and confirmation of certification. The US FDA assesses Class II devices in a target 90 *calendar* days and high risk Class III devices in 180 *calendar* days.

Postmarket Regulation

The reality of medical device regulation is that premarket scrutiny is always imperfect. The DePuy ASR hip – which is of particular interest to the enquiry was granted premarket approval by regulators in Europe and Australia. Such cases reinforce the importance of effective postmarket regulation – to detect such failures as early as possible so that prompt action can be taken to correct the deficiency and remove the affected devices from the market place. This is never easy and TGA has historically applied more resources to premarket evaluation than to postmarket monitoring. Furthermore the small size of Australian market means that it is likely that significant trends will emerge overseas first – where statistical numbers are greater.

[1] http://aging.senate.gov/hearing_detail.cfm?id=332473&

Proposed regulatory reforms – direct assessment of all Class III devices

TGA's response to public concerns over the safety of, particularly, high risk devices has led TGA to propose to require direct TGA assessment of all Class III medical devices – including most cardiovascular devices such as stents, vascular prostheses, cardiac catheters, and (assuming up-classification proceeds as proposed), all orthopaedic hip, knee and shoulder joint implants. It is hard to envisage how the TGA will be able to deliver this increased level of regulatory review (almost all of these devices are currently imported) given the current resourcing and very small number of technical experts employed by the agency.

When questioned on this point during a series of public meetings conducted to explain the proposed regulatory reforms, TGA's response was that they were considering outsourcing to external contract reviewers. It would be, to say the least, challenging to ensure sufficient rigour, consistency and cost effectiveness from such an approach (if sufficient reviewers could be found). Such a proposal is also surprising given TGA's long standing reticence to initiate 3rd party conformity assessment by Notified Bodies, which are manifestly well resourced and competent, and working within an existing robust accreditation framework.

IT could be argued that the additional resources will be funded from manufacturer assessment fees. However, given the relatively very high cost of TGA assessment for such a small market, a likely response from industry will be reduction in the range of products supplied in Australia and a reluctance to introduce new devices, to the detriment of the Australian Health care system and to patients in need of access to current medical technology.

Summary – Australia and Europe Compared

The contrasts are stark:

- TGA assessment costs the same or more than a European assessment, but can take more than twice as long to conduct and provides access to a market approximately 1/20th of that gained via a CE mark.
- TGA has only a small fraction of technical expertise that is available to European assessors
- It is not clear how TGA's proposed expansion to include direct assessment of all high risk devices may be resourced given TGA's already limited capacity.
- TGA is not subject to any external independent review of technical competence or quality or consistency of process, contrasted to the rigorous external supervision and accreditation processes applied to Notified Bodies.
- TGA undertakes no meaningful audit or supervision of clinical trials – which is devolved entirely to local ethics committees, whereas Clinical Trial Supervision is a key responsibility of Competent Authorities and is extensively resourced in the larger agencies particularly of the UK, Germany and France.
- TGA postmarket monitoring operates at a low level of activity and is of questionable effectiveness when focussed on a very small proportion of devices supplied in such a small marketplace.

An alternate model for Australia?

Australians demand access to the full range of advanced medical technology as afforded to patients in other advanced nations, and Australia needs a regulatory system that provides a high level of assurance of safety. But it must operate efficiently and at a cost level commensurate with market size and in the context of extensive global regulatory harmonisation and closely equivalent underlying technical standards in most markets.

It is abundantly clear that TGA, with only a very small fraction of the resources compared to overseas regulators, cannot possibly apply the same level of regulatory oversight as is achieved in Europe or other international markets for essentially the same range of products.

Australia has essentially agreed with use of the technical requirements and standards of Europe. It is recommended that it should similarly adopt implementation of regulatory oversight much more closely modelled on that of Europe.

This would involve TGA relinquishing direct assessment of medical devices, and adopting the role of Competent Authority, in exactly the same way as has been done, very effectively, by the larger medical device regulatory agencies in the UK, Germany and France.

TGA would be in a position to restrict accreditation to only those larger Notified Bodies which are adequately resourced and competent for the role, and so the concerns about the more recently established smaller Notified Bodies would not apply in Australia.

Benefits of Alternative Model

Within the new framework TGA could apply its resources to the services with greatest opportunity to deliver safe devices for use in Australia:

- supervision and accreditation of a limited number of Notified Bodies.
- Meaningful review, approval and audit of clinical trials of medical devices (and pharmaceuticals).
- Development of an enhanced postmarket system which is better resourced and much more closely linked to international sources of information including overseas registries and postmarket monitoring programs of other regulators.

Given the very close technical alignment of regulations, the Australian and European assessments would be able to be combined providing for large cost savings. This will encourage global manufacturers to offer the latest high performance devices to the Australian market.

This arrangement would both significantly expand the available regulatory resource and introduce a demonstrable independent scrutiny of the devices assessor, raising public confidence in the regulatory system.

Transition to the Alternative Model

A suitable transition strategy would be to commence with expanding the scope of recognition of those Notified Bodies already recognised under the Mutual Recognition Treaty with Europe, to allow them to make assessments of the full range of medical devices covered by their existing accreditations to the European Directives. This list could then be expanded by addition of a small number of additional Notified Bodies as market capacity would allow.

The impact of such a proposal on the current Mutual Recognition Agreement with Europe would need to be considered. Currently, Australian manufacturers are required to be directly assessed by TGA, yet many seek both TGA and CE approval by a Notified Body in parallel because of the more rapid CE assessment process providing quicker access to the larger European market compared to slower approvals for Australia by TGA. CE marking can also be used to leverage access to a number of other markets especially in Asia. Should Australia accredit third party assessors for the purpose of Australian regulatory approval, it is almost certain that those assessors which seek accreditation would be already accredited as European Notified Bodies as well as being accredited assessors for Canadian, Japanese and US third party approvals. In this case the arrangement would simply negate the requirement for the MRA, removing the need for an Australian manufacturer to approach TGA for European Assessment and providing an alternate pathway to Australian approval for European manufacturers.