NUVASIVE®
Creative Spine Technology®

16 December 2010

The Coordinator
Re: Comment on Reforms in the Medical Devices Regulatory Framework
Office of Devices Authorisation
PO Box 100
WODEN ACT 2606

Dear Sir/Madam,

NuVasive Australia & NZ Pty Ltd, in conjunction with its parent company, NuVasive Inc., has provided the attached comments in relation to the proposed reforms in the medical devices regulatory framework.

Consultation with the relevant stakeholders is extremely important when Government proposes to make changes that could have an impact on commercial entities and healthcare organisations and providers, so I'd like to thank you for the opportunity given to the medical devices industry to provide comments.

I look forward to positive amendments to the proposed reforms based on the comments received by the TGA from the medical devices industry.

Yours sincerely,

Mery Kiley,
Managing Director,
NuVasive Australia & NZ Pty Ltd.

AUSTRALIA & NZ PTY. LTD. • ABN 65 111 751 243
GROUND FLOOR 620 HIGH STREET • KEW, VICTORIA, AUSTRALIA, 3101
tel: +61 3 9816 7200 | toll free: 1300 215 200 | fax: +61 3 9817 6191
www.nuvasive.com

NuVasive Australia & NZ, in conjunction with its parent company, NuVasive Inc., has identified the proposed reforms in the medical devices regulatory framework in bolded italics, with its comments provided after each.

Addition of a new classification rule to Schedule 2 of the medical device Regulations to reclassify all hip, knee, and shoulder joint replacement implants from Class IIb to Class III medical devices.

The reclassification from Class IIb to Class III has implications for the medical devices industry in relation to the proposed requirement that a TGA conformity assessment certificate be issued for all Class III medical devices. Please refer to NuVasive's comments below in relation to this proposed reform.

For medical devices that have already been included in the ARTG, a "grandfather" clause should be provided that automatically reclassifies these medical devices, rather having to resubmit to the TGA to assess the devices (within the two year transition period).

The removal of Subregulation 4.1(1) from the medical device Regulations, so as to no longer require Australian medical device manufacturers to hold TGA conformity assessment certification.

This proposed reform is supported by NuVasive.

At present, the current requirements for Australian manufacturers significantly increases their regulatory burdens compared to overseas manufacturers and is not in keeping with the Government's policy of creating a more productive economy by cutting the regulatory burden faced by business.

This proposed reform removes the disparity between Australian and overseas manufacturers, so this is seen as a positive for the medical devices industry.

The proposal to increase pre-market scrutiny for implantable medical devices by amending:

- ***Subregulation 4.1(2) of the medical device Regulations to require a TGA conformity assessment certificate to also be issued for all Class III and AIMD.***

NuVasive does not support this proposed reform.

Currently CE marked medical devices that are class III and AIMD have been assessed via a relatively straight-forward TGA approval process. This proposed reform would require a full assessment of these medical devices be undertaken by the TGA (and/or an Australian third party assessment body). This will result in additional fees and longer approval times for the medical devices industry.

Such a proposed reform cannot be supported without evidence to demonstrate that the current approval process has resulted in adverse performance and/or safety outcomes for

patients. As far as NuVasive is aware, no published data exists to suggest that patient safety has been compromised as a result of the current approval process.

As the TGA would be aware, the review of the 510(k) process in the USA has included suggestions that patient safety may be compromised by the current 510(k) process. However, there has been no published data that supports this conclusion, nor that the CE marking process in the EU has led to compromised patient safety. In fact, recent data has been published to demonstrate that the current 510(k) paradigm is an effective process for protecting public health.[1,2,3,4]

The current TGA approval process avoids, to an extent, duplication of regulatory authority assessments. This proposed reform introduces regulatory duplication and only increases costs and resources for industry, without any proven improvement in patient safety.

If TGA determines implementation of this reform is necessary in order to address patient safety concerns, NuVasive recommends that a "grandfather" clause be added for medical devices that have already been included in the ARTG.

- ***Regulation 5.3 of the medical device Regulations to require applications for all Class IIb implantable and long-term surgically invasive medical devices to also be selected for an application audit prior to inclusion in the ARTG.***

NuVasive does not support this proposed reform.

As above, without evidence to support this proposed reform, the additional fees and longer approval times for the medical devices industry cannot be justified and the current approval process should remain in place. Such a proposed reform cannot be supported without evidence to demonstrate that the current approval process has resulted in adverse performance and/or safety outcomes for patients. As far as NuVasive is aware, no published data exists to suggest that patient safety has been compromised as a result of the current approval process.

Increasing third party assessment of devices:

- ***That the TGA commence discussions with the EC over a program of confidence building with the designated Notified Bodies under the MRA, to include sharing of product assessments and joint audits of medical device manufacturers.***

It is unclear what the confidence building activities will entail. Will this require that, during the confidence building phase, all quality system and product assessment Notified Body audit reports will have to be submitted to TGA? Further clarification is required.

The proposal (by the TGA to give greater weight to CE certificates issued by a Notified Body that has undergone confidence building) should be undertaken with caution to ensure that it does not adversely affect companies with CE certificates that have not undergone confidence building due to reasons unrelated to medical device performance or safety.

- ***That further consultation be undertaken to investigate the development of a system whereby Australian based assessment bodies can be designated to issue conformity assessment certificates to Australian manufacturers.***

NuVasive supports this proposed reform.

However, the TGA should ensure that this change will mean the system in Australia mimics the Competent Authority plus Notified Body arrangement in the EU. That is, a company must be able to receive a conformity assessment certificate from the TGA-certified Australian based assessment bodies without having to also submit an application to the TGA.

Amending the way in which a medical device is included in the ARTG and enhancing identification of devices approved for supply in Australia.

NuVasive does not support this proposed reform.

This will result in significant additional burdens on the medical devices industry and it is unclear how this process would further improve TGA approval confirmation (based on, in particular, the logistical challenges associated with such labelling of non-sterile medical devices). The proposed change suggests that Sponsors will need to itemise the medical devices and/or various models that are supplied under the same ARTG entry. In addition, as new models become available, Sponsors will be required to submit an application to vary the existing ARTG record to add a new model of that type of medical device.

This proposed reform suggests additional assessment each time a new product is added, with additional fees and longer approval times for each. This reform will increase the overall cost for medical device manufacturers to introduce new models in the Australian market. Due to this increase, along with the cost of additional resources and time required to support this reform, there will be a delay in new model availability for the Australian market.

The requirement for the addition of the ARTG number to be added to the label for each medical device also has significant cost implications for the medical devices industry. While such a change may appear to be relatively straight-forward to the TGA, the practical implications are significant. Even if the ARTG number is added to the current Australian Sponsor label, given differing ARTG numbers for different medical devices supplied by a single Australian Sponsor, this will result in the need for multiple Australian Sponsor labels. For example, for products that are contained in a kit or procedure pack, which have different ARTG numbers, several Australian Sponsor labels will be required. As it will be difficult, if not near impossible, to clearly identify which component belongs to which ARTG number, this system will not prove to be helpful to end users in the manner in which TGA has intended. As a result of the additional resources required to manage the proposed Australian Sponsor labelling activities, the willingness of manufacturers to place new and innovative products on the market in Australia will likely decrease when launch of these technologies may be more easily made in other markets.

Publication of device product information on the TGA Website.

NuVasive believes that only information about medical device approvals should be made publicly available, and that this should only be for the higher risk classification devices such as Class III and AIMD. Any commercial-in-confidence information submitted to the TGA should not be made publicly available; for example, only published clinical trial data should be made publicly available, not unpublished clinical trial data.

The responsibility for authorship of the information should remain with the TGA; however, the Australian Sponsor must be consulted to review the proposed information before it is made publicly available. Responsibility for ensuring the information is up to date should also remain with the TGA.

As implied above, information relating to rejected or pending applications should not be made publicly available.

In relation to Instruction For Uses (IFUs) being made publicly available, the need to provide this information will result in additional burdens on the medical devices industry, which are regarded as unnecessary, given that such information is already supplied to end users and is, on the whole, not required by patients. As mentioned previously, the cost of additional resources and additional time for the medical devices industry associated with this proposed reform is overly burdensome.

REFERENCES

1. California Healthcare Institute. Upcoming Changes to the 510(k) Process: New Approval Pathways and the Impact on Medical Device Development and Innovation. 2010.
2. Leahey, M. B. Medical Device Manufacturers Association (MDMA) 2010 Letter to the U.S. FDA Regarding Proposed 510(k) Reforms.
3. Trunzo, J. Advanced Medical Technology Association (AdvaMed) 2010 Letter to the U.S. FDA Regarding Proposed 510(k) Reforms.
4. Makower, J. et al. FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies. 2010.

DISCUSSION PAPER :
REFORMS IN THE MEDICAL DEVICES REGULATORY FRAMEWORK

Response from :
Integra Neurosciences Pty Ltd
Unit 3, 24-30 Winterton Rd
Clayton VIC 3166

Contact : Shirley Bolis at shirley.bolis@integra-LS.com.au

Comments are provided for the following proposals:

Proposal 2	**2B (i) (ii)**	**Increasing pre-market scrutiny for implantable medical devices TGA issued CAC for Class III and AIMD implantables Application audit for Class IIb implantables**
	2C (i)	**Recognition of third party assessment bodies Confidence building for EU Notified bodies designated under the MRA**
Proposal 3	**3**	**Amending the way in which a medical device is included in the ARTG and enhancing identification of approved devices**

2 B(i) TGA issued CAC for Class III and AIMD implantables
2 B(ii) Application audit for Class IIb implantables
The TGA have stated that TGA issued conformity assessment certification will be required for all Class III/AIMDs implantables, and an Application audit for all Class II b implantables so as to address Recommendation 8 of the Health Technology Assessment Review (HTA).

Lack of lead- in time and cost details
The delays to the release of the HTA review and the TGA response to the HTA review were adequately explained at the Information session in Melbourne. However, this does not justify why sponsors who have had no forewarning or any consultation whatsoever prior to the release of the Discussion paper on the TGA website November 2nd, 2010 must now be expected to be ready and compliant for all new products in mid 2011 (mid 2011 being the date that was given at the Melbourne Information session as to when implementation is likely to occur for Proposal 2). Although Proposal 2A has been in discussion and consultation for some time now with stakeholders, Proposals 2B and 2 C have not. .

Planning for regulatory submissions is not a simple matter of getting documentation together - which in itself will increase exponentially with this "increased pre-market scrutiny". Not enough time has been allocated for new products (2011) for which increased documentation requirements will mean planning over a longer period of time. Planning a regulatory budget is not a month to month exercise, but a long term exercise over a number of years. This is especially true for sponsors who are part of larger corporations, who may also be located overseas. The increase in regulatory costs cannot be suddenly acquired within the next few months for an implementation date for all new products of 2011. In addition, other factors such as budgetary constraints, especially for low turnover products, have to be taken into account and how this may affect supply in Australia. Although the TGA allows exemptions for Annual charges, it does not as a cost recovery agency , do so for application or assessment fees.

Manufacturers located overseas will need sufficient time to be informed and educated about how this change will conceivably affect them. A conformity assessment, now being proposed for all ClassIII/AIMD implantables may include an on-site audit. Squeezing this into a busy manufacturing plant's schedule with 6 months notice is difficult to justify for the small market we are in.

No possible regulatory costs have been detailed as yet as the TGA do not have any detail of how the concept of a TGA conformity assessment certificate could change with these proposals. It appears the TGA have not themselves been provided with sufficient time to flesh out any details or give any guidance to sponsors.

The increase to sponsors costs is not just going to be increased assessment fees but also increased staff costs. A conformity assessment is complex and collating all the information, especially from overseas sites is not a simple and quick exercise, nor is it always clearly defined due to the nature of the breadth of differences in medical devices and the type of assessment that is a conformity assessment. Even collating documentation for an Application Audit, as defined as these requirements are, takes time and a different skill set, and this will also increase staff costs.

Whether this increased pre-market scrutiny will actually provide a "*sound evidence basis for Commonwealth HTA processes*" (HTA Report- Recommendation 8) as far as those involved in the Commonwealth HTA processes has not been determined, nor communicated with sponsors. To increase this regulatory burden by the TGA, and then for the Commonwealth HTA processes to still work in isolation from the TGA, as they do now, seems a pointless exercise.

If the TGA propose to require all ClassIII/AIMD implantables be subject to a conformity assessment instead of an Application audit as is currently required, and for all ClassIIb implantables to be subject to an Application audit instead of a simple Inclusion, then :

- far more than 6 months notice of an implementation date for all new ClasssIII/AIMD implantables is required; at a minimum, a 2 year implementation date for any new products is suggested as this gives sponsors sufficient time for firstly the TGA to provide detail and for sponsors to then inform manufacturers of the increased regulatory requirements and also plan for increased regulatory budget costs
- more consultation, and discussion papers such as option papers, are needed from the TGA with actual detail, that allow sponsors to be able to understand firstly the increased documentation requirements and then secondly, the corresponding regulatory costs so that sponsors can adequately plan
- the TGA, in any regulatory impact exercise, need to include not only the increased regulatory assessment fees but also the increased staff costs due to the increased complexity of submission requirements
- Both the TGA and the Commonwealth HTA processes need to provide evidence that this proposed increase to pre-market scrutiny by the TGA will actually "*provide a sound evidence basis for Commonwealth HTA processes*", and not merely increase the regulatory burden on sponsors. If there is no clear reduction in the requirements after TGA approval, or if the time to reimbursement ends up being longer, then Proposals 2A and 2b will not meet Recommendation 8 of the HTA review.

2 C(i) Confidence building for EU Notified bodies designated under the MRA
The TGA stated during the Information session in Melbourne that the reforms in Proposal 2 are proposed as a package. There was also a statement that confidence building exercises with EU notified bodies designated under the MRA are not going to occur prior to implementation of Proposal 2B.

It is difficult to see how any of this increase of pre-market scrutiny is conducted in the "*....context of international harmonisation*" (HTA Recommendation 8, Line 1) if the possibilities for using certificates issued by EU notified bodies designated under the MRA are not taken into account. There is no point in the TGA proceeding with implementing conformity assessment of ClassIII/AIMD implantables and Class IIb implantables if the TGA does not *firstly* establish how this will be conducted in the '*context of international harmonisation*' and does not look at mechanisms of utilising these MRA certificates to simplify the process.

The TGA should strongly consider that *prior* to any increase in pre-market scrutiny (for both ClassIII/AIMD implantables and ClassII implantables), they conduct these confidence building exercises. The TGA should also consider that there are other regulatory jurisdictions who issue certificates that may be able to be used by the TGA in the "context of international harmonisation". For example, Class 4 and 4 Product Licences issued by Health Canada may also be able to be utilised by the TGA along with consideration of CMDCAS certificates for quality systems.

- Unless this occurs, the transition time for those ClassIII/AIMD implantable devices where approval is dependent on an MRA certificate may actually only be 2 years, and not 4 years, if the TGA's estimate of how long it will take (2 years) to conduct any EU-Australia MRA confidence building exercise is accurate.
- Similarly, for ClassIIb implantables, the mechanisms for use of MRA certificates needs to be established prior to implementing legislation that all new such devices must undergo a mandatory Application audit
- The possible use of CMDCAS QS certificates and Health Canada Product Licences where the device classification is equivalent for those devices not manufactured in Europe or Canada. There is a significant proportion of imported devices that are not manufactured in the EU (or Canada) and thus cannot utilise the EU-Australia MRA.
- Consideration that certification issued by MRA designated notified bodies be acceptable for Application audits whether the device has been manufactured in the EU or not.

Proposal 3 Enhance the ability to identify devices that have been approved by the TGA for supply in Australia

It is a level of complexity greater for an ARTG number to be added to the label of a device compared to the name and address of a sponsor. A name and address is the same for all devices being supplied by one sponsor, but to match up the device to the correct ARTG number requires greater IT and logistics resources. A 12 month transition time to prepare after implementation is not enough time for a sponsor to prepare.

Depletion of stock considerations

The TGA stated at the consultation session in Melbourne that if product could not comply with the requirement to label with the ARTG number within the 12 months, that a sponsor could submit an application for a Reg 10.2 exemption to the TGA . To do so, a sponsor needs to be able to estimate when stock that does not comply will be depleted. Estimating this for a therapeutic that has an expiration date is not as difficult as there will be a definite time after which that therapeutic cannot be used. This is the case for medicines, but not all devices. There are many devices that do not an expiration date, so estimating stock depletion is not as easy, or sometimes not even possible.

The TGA needs to consider whether sufficient time is proposed for transition especially since the TGA also proposes that all Models/Trade names are proposed to be itemised under an ARTG entry. Not all these products under the one ARTG entry will all have the same expiration date or the same turnover; so will an application need to be submitted for each Model in each ARTG entry affected?

- At the least, if the TGA continue with this proposal, a longer transition time is needed than 12 months. Simple GMP changes, or application of a new edition of a Standard can sometimes have a 2 year transition time.