Dear Ms McRae

Thank you for the opportunity to comment on the Therapeutic Goods Administration’s (TGA) preliminary draft Consultation: Draft clinical evidence guidelines – Medical devices.

Bupa Australia and New Zealand

As part of the international Bupa Group, Bupa’s Australian and New Zealand businesses share a common purpose of longer, healthier, happier lives. We are focussed on providing sustainable healthcare services, support and advice to people throughout their lives, and on leading the industry in the promotion of preventive health and wellness.

We provide a wide variety of services for over 6 million customers across Australia and New Zealand. In Australia, we are a leading provider of both health insurance and aged care services, as well as delivering other healthcare services. These include GP services (through Bupa Medical GP), health coaching (through Bupa Medical TeleHealth), corporate health services (through Bupa Wellness), eye care (through Bupa Optical), dental (through Bupa Dental Corporation) and audiology services (through Bupa Hearing). In addition, Bupa Medical Visa Services provides visa medical examinations to approximately 250,000 people annually across Australia and other visa and migration services to the Department of Immigration and Border Protection.

Since 2002, the Bupa Group has invested around $6 billion in Australia and New Zealand’s health and care sectors. This investment helped acquire and grow Bupa’s health insurance business in Australia, care services operations in both Australia and New Zealand, dental clinics in both countries and health services including preventative health and chronic disease management.

Bupa is dedicated to making a lasting difference to Australia’s health and care system, including through the Bupa Health Foundation. As one of Australia’s leading corporate foundations dedicated to health, it is committed to improving the health of the Australian community and ensuring the sustainability of affordable healthcare through collaborative partnerships. Over the past 10 years the Foundation has invested over $26 million in more than 100 projects, focused on translating Australian research into real health and care improvements.
The Bupa Group focuses on providing sustainable healthcare solutions that represent real value. Bupa's businesses are part of the international Bupa Group, which cares for around 32 million people in over 190 countries.

**Introduction**

We understand the guidelines are intended to assist sponsors and manufacturers of medical devices seeking to supply their products in Australia to compile relevant and complete clinical evaluation reports for the devices to meet regulatory requirements. Bupa HI Pty Limited provides feedback to this consultation process from the perspective of a health care funder through our health insurance businesses.

Bupa believes the TGA’s mandate to assess the safety and efficacy of medical devices, among other things, is a cornerstone for the protection of Australians from potentially harmful or ineffective health technology.

We believe it is commonly understood by the Australian public that approval and listing by the TGA of a therapeutic device gives assurance to consumers and health professionals that the device is safe and effective for the purposes for which it is listed. This has led to increasing recognition of the need for clinical evidence to demonstrate safety and efficacy. This becomes all the more relevant for increasingly complex medical devices, or where the potential risk created by the use of the device is greater.

We consider the final guidelines should provide clear and transparent guidance for applicants and those seeking to collect the appropriate clinical evidence to support an application. This should reduce the occurrence of rejections and returns with requests for additional information, and potentially increase the speed of passage through the assessment process.

Finally, the outcome of this review should define the requirements for clinical evidence that could consistently, appropriately and effectively protect the Australian public to the degree that they would expect from an approval and listing process administered by the TGA.

It is in this context that Bupa provides the following feedback on the draft guidelines.

**Primacy of clinical evidence**

There is a vast range of medical devices, from simple tourniquets, splints and tweezers, to complex machines such as artificial hearts and kidneys, for example. The expectations and availability of clinical evidence relating to simple devices is significantly less than it is for the most complex devices. Nevertheless, as a guiding principle, we believe it is essential that the safety and efficacy of devices should be evaluated in a clinical setting, and always when related to the most complex devices. We believe the assessment process, and the subsequent assurances that can be given to the Australian public because of these assessments, might be strengthened if further guidance was provided about this matter.

The draft guidelines appear to accommodate the presentation of literature reviews and “equivalence” as being appropriate clinical evidence for a device, even where there are modifications to the device that would necessarily differentiate it from prior iterations.
Experience has shown that small changes in the design of replacement components in hip and knee joint replacements, for example, can impact the clinical outcome for patients. These components now specifically require direct clinical evidence in their assessment process. However, we believe the draft guidelines may provide too much flexibility for other devices, such as hydrocephalus drainage devices and vascular prostheses (other than for AAA repair), to rely on literature reviews as part of their assessment. We consider the scope for this to occur should be limited, given the potential such devices have to significantly impact the wellbeing of a recipient.

As a default position, we believe clinical evidence should be the primary focus for the justification for the listing of new devices, unless there are clear and compelling reasons justifying a lower benchmark. Failing to reflect such an approach in the final guidelines may risk certain devices gaining listing approval that may fail to deliver appropriate outcomes for patients.

**Essential Principles (EP)**

**Principle Six: Benefits must outweigh undesirable effects (PE 6)**
When assessing the benefits of a device, we believe there should be explicit consideration of the outcomes of a “do nothing” option. Under the current draft guidance, it is possible to compare the outcomes of a new device with some other intervention or device that shows adverse outcomes are no worse. However, if a “do nothing” option was considered, in some instance, this decision could deliver substantially fewer adverse effects, as opposed to comparing two interventions with similar potential for adverse effects. We believe this approach should be an explicit essential principle, rather than an assessment of undesirable effects.

In its current draft, PE 6 may not adequately reflect the fact that patients are likely to perceive benefits and risks differently from a device manufacturer or supplier. Explicit attention to patient weighting of perceived benefits and risks should be considered. We believe such an approach could lead to better informed decision making, backed by appropriate decision support tools.

Bupa believes it is important to encourage a more patient-centric view of health technology assessment, and not rely wholly on a technical or medical provider approach to such assessments. This is consistent with the growing demands by consumers to be fully informed of the benefits and risks of medical interventions.

In relation to the discussion of potential harm, there is a risk in any operative procedure over and above the specific risk posed by a device. That is why the minimal benefit approach must be weighed against the overall risk of, for example, an operation or procedure where a small risk of death or misadventure must be taken into account, as well as other risks such as infection or scarring. Failure to take this into consideration can result in perceptions of minimal specific risk from a device, such as a screw or staple, whereas the overall risk, while statistically small, may be life threatening.
This principle notes “Under the regulatory framework medical devices must have clinical evidence which provides assurance of safety and performance.” We note that performance is already covered under EP3. We believe it is essential that specific reference is made in EP 6 to clinical outcomes.

The effectiveness of a device must relate to its intended clinical function. If it is a device to, for example, deliver fluids in a certain way, then all it has to show is that it can deliver fluids without ill effect and in accordance with the level of accuracy of delivery stated. However if the device has the purpose of substituting, or altering, an anatomical part or physiological function, then it is essential that clinical outcome data be presented in the assessment process. If its intended use is to replace, for example, a bony part to relieve pain, then the clinical data presented should relate to the clinical relief of pain subsequent to, and dependent on, the use of said device.

The assessment of safety and efficacy cannot be left to evaluation of the materials of which the device is made, and the conformity of production with recognised standards. There must be some level of clinical evaluation that the device achieves the clinical outcome expected of it and this should be a minimum requirement for as many classes of device as possible.

Principle Fourteen: Clinical evidence (EP 14)

In its current draft, only one of the 15 essential principles that are part of “Clinical Evidence Requirements” actually refers and relates to clinical evidence. Even that one principle allows that the evidence presented doesn’t have to show that the device produces positive health outcomes when used on people. Bupa contends that it is a reasonable expectation that clinical evidence should be the primary focus for the justification for the listing of new devices, and that therefore the clinical evidence guidance should focus on the proper need for clinical evidence and not on how that need can be circumvented.

This principle states “Every medical device requires clinical evidence”, however there are a number of devices for which no clinical evidence can be supplied, such as surgical screws of a new design, for example. In these instances, making exceptions to this by requiring the “manufacturer to obtain clinical data…and/or ‘literature review’” reduces the efficacy of this principle to ensure the TGA decisions are based on clinical evidence.

We contend that an assessment of a medical device by the TGA should not be undertaken based on a lack of clinical evidence that is justified by a claim that such evidence is “not possible” to be obtained. PE 14 should clearly state that demonstrating substantial equivalence should be a requirement that is earned, and not presumption that can be made by the lack of clinical evidence.

Further, under Schedule 3 Part 8 of the Therapeutic Goods (Medical Devices) Regulations 2002 (TGA Regulations), an applicant has the option to present clinical evidence “or” a literature review in the absence of clinical evidence. Hence, under current arrangements, there is no regulatory requirement to produce clinical evidence. We believe this could undermine the TGA’s safety and efficacy assessments.
To reiterate, as a default position, we believe clinical evidence should be the primary focus for the justification for the listing of new devices, unless there are clear and compelling reasons justifying a lower benchmark. An example of this may include a device that does not produce clinical results on its own but enhances or enables the use of another device such as a screw being needed to make joint or fracture fixation work, yet it does nothing on its own.

While there may be devices for which no such evidence can be created, this should be a decision by exception, and exemption sought from TGA, rather than an applicant having the option to seek assessment without presenting clinical evidence. At the very least, there should be a clear explicit minimum complexity level for which different medical devices require direct clinical evidence rather than relying simply on literature reviews.

The TGA Regulations allow manufacturers to “ensure that all the clinical data held in relation to the device is critically evaluated by a competent clinical expert in the relevant field, and that the clinical evidence demonstrating that the device complies with the applicable provisions of the EPs is documented in writing." There is risk that this provision may create the potential for bias. There is no question that sponsors should be able to obtain endorsements and opinions from trusted sources, but there should also not be a presumption that an expert selected by a sponsor would necessarily provide an objective and unbiased report based on all the clinical investigation data related to the device.

Several well documented cases presented to the US Food and Drug Administration, such as for the drug Vioxx, and by medical devices manufacturer, Guidant, suggest the submission of all evidence may not be routine and cannot be presumed or relied upon. It may be argued that expert opinion should be referred to as testimony and not be given the status of arm’s length, objective, expert review.

EP 14 also states that “the clinical evidence must primarily demonstrate that the device complies with the EPs 1, 3, and 6”. This can be interpreted to imply that clinical evidence of safety, equivalent of a phase 2 pharmacy trial, is the basis for assessing that a device is effective. It should not be enough that the device performs as it was intended. There should be an inherent obligation that the device affords demonstrable clinical improvement over alternatives, which should include a “do nothing” option. While there is an obligation to first do no harm, because the use of devices is influenced by marketing, there should be an essential element of being able to show how much good a device can achieve.

It is a widely held view that for a great number of Australians the listing by the Australian Register of Therapeutic Goods is considered to imply efficacy of medical devices. Therefore it is incumbent that the assessment process looks at, and makes decisions based on, the benefit of a particular device being assessed as being clinically the same, or better, than alternatives. This should not be based on manufacturing standards, but on proper, independent assessment of clinical data, specific to the particular device to which the application applies.
Chapter 3. Clinical Evidence
We believe Chapter 3 Clinical Evidence of the draft guidelines should explicitly differentiate between short term, low risk, low benefit, and longer term, high benefit or potential benefit. We would argue that the greater the potential benefit and the time a device is in the body, if that is the intent, the greater the need to demonstrate, in clinical terms, the stated benefit.

With respect to the definition of “indirect clinical evidence”, we believe it is essential that instruction be given as to when indirect evidence alone will suffice, and when, alternatively, direct evidence is required. There have been many cases where equivalence has not resulted in either safety or proper evaluation of risks, ceramic acetabular component of hips being a good example.

Conclusion
Bupa submits that the review of the draft guidelines is an excellent opportunity for the TGA to consolidate the requirement to ensure proper and appropriate clinical evidence is the cornerstone for the approval for listing and use of clinical devices.

In its current form, the current draft guidelines leave too many opportunities for indirect evidence and literature review to suffice as “evidence” that a new clinical device is safe and effective. In the past, this has not been proven adequate on occasions. It would be preferable to reduce the reliance on indirect evidence and literature review in the future, so that approval for a new device does not just rely on perceived similarities with existing devices or perceived lack of key difference.

Please do not hesitate to contact me on [redacted] if you wish to discuss further.