BioPharmica Limited

# Australian Technology to Monitor Brain Function in Clinical Trials

Press Release – 29 June 2006

**An Australian invention designed to decrease the likelihood of patients remembering parts of their surgery and improve their recovery from anaesthesia is poised to undergo clinical trials at Royal Melbourne Hospital.**

The Australian discovery is on the cusp of international recognition that could dramatically change the way in which global clinicians and researchers view the capacity of brain electrical activity to assist medical practice.

In a stunning effort to crack the code of brain electrical activity (EEG), inventor Dr Liley developed a new way of determining what is happening in the brain by creating a mathematical method (named the BAR Index) for how its electrical signals - shown in an electroencephalogram or EEG - are interpreted.

The BAR Index brain monitoring system will be trialled in 45 patients aged 18-60 years during elective surgery requiring general anaesthesia at Royal Melbourne Hospital.

The BAR Index has been used to quantatively characterise the functional state of the brain based on a detailed understanding of how millions of neurons coordinate their activity to produce the EEG.

**The aim of this clinical trial is** to determine if the BAR Index brain monitoring system exhibits superior performance to the current market leader, used in approximately 70% of hospitals in the USA, in clinical monitoring during anaesthesia containing an opioid. This competitor has a market capitalisation of approximately **USD 400M.**

The monitoring of opioid effects during anaesthesia is unreliable using existing monitoring approaches and thus new methods are required in order to ensure optimal standards of clinical care.

Listed biotechnology company BioPharmica Ltd (ASX code BPH) and partner Cortical Dynamics are targeting a depth of anaesthesia **market which, including consumables, predicted to be worth 1 Billion Dollars by 2008.**

The clinical trial will assist in the international validation of the BAR Index's potential to provide clinicians and researchers with an improved ability to detect and accurately quantify the effects of a number of drugs on brain function.

When patients have a general anaesthetic, an anaesthetist may administer a combination of drugs through the intravenous drip in the patients arm. These could include an anaesthetic drug to put the patient to sleep and a morphine-like drug as a pain-killer.

Once the patient is asleep, the anaesthetist keeps the patient in this state by using a drip of anaesthetic drug or by giving the patient an anaesthetic gas to breathe. Using these combinations of drugs, the patient should be completely anaesthetised and not feel any pain.

Anaesthetists can currently measure the effect of these anaesthetic drugs on brain waves (also known as the electroencephalogram or EEG) using a widely available, market leading competing device. The market leader is used on many patients having general anaesthesia at hospitals. This competing monitor records EEG through a sticky sensor attached to the forehead. The monitor then produces a single number between 0 and 100 that the anaesthetist can use to adjust the depth of your anaesthetic.

Studies have shown that the use of a monitor decreases the likelihood of patients remembering parts of their surgery and also improves their recovery from anaesthesia.

However, there is evidence to suggest that some montiors may not track the effects of a number of important anaesthetic agents. This may mean that the leading offering is less accurate when these agents are used. In particular, morphine-like drugs may interfere with the ability of the leading monitor to measure the depth of anaesthesia accurately, by indicating a patient is less asleep than they really are. This means that patients may be receiving more anaesthetic than necessary.

The **BAR Index** method of analysing the EEG may overcome this limitation and provide a more accurate Index of the depth of anaesthesia in the presence of morphine-like drugs. The EEG information is obtained the same way, with a sticky sensor on the patient's forehead, but the monitor uses a different, potentially more accurate, mathematical method to analyse it.

Opioid analgesics are increasingly being used as part of a drug combination in nearly all anaesthetic regimes, however current monitors of anaesthetic depth do not reflect the effect of opioids on anaesthetic depth well, possibly because opioids do not directly affect the cortical EEG.

Upon the completion of the clinical trial involving *opioid*s, BioPharmica and Cortical will be in a strong position to provide a select group of leading international companies with sufficient data to initiate licensing discussions, facilitate collaboration on development related to anaesthesia, as well as making a case for development of other areas involving drugs, brain state and function.

The clinical trial is being conducted by Associate Professor Kate Leslie, Head of Research, Department of Anaesthesia & Pain Management, Royal Melbourne Hospital and Honorary Principal Fellow, Department of Pharmacology, University of Melbourne.

Dr David Liley will also participate in the clinical trial. Dr Liley is registered as a medical practitioner, is inventor of the BAR Index and a Senior Lecturer, Faculty of Life and Social Sciences at Swinburne University of Technology.

The BAR Index has performed well in previous studies during midazolam and propofol-nitrous oxide anaesthesia providing the first indication that the BAR index is superior in a number of aspects to current approaches to measure brain function. It was able to measure separately both brain input - whether the patient is capable of receiving external input - and brain state -whether the patient is in a state of consciousness, hypnosis or amnesia.

The BAR Index has additional potential applications for the Alzheimer's and sedation markets. BioPharmica and partner Cortical Dynamics are working to develop the Bar Index as a monitoring tool in a number of neuro-diagnostic settings that include detecting the early onset of degenerative diseases like Alzheimer's or Parkinson's as well as being used in drug discovery and evaluation associated with these conditions.

To date Cortical Dynamics has designed and produced several prototype BAR monitor systems that incorporate the BAR Index and record brain activity. The systems have been evaluated as complying with international medical equipment safety standards. These monitors will be used in planned international trials in anaesthesia monitoring and collaborative work in neurodiagnostics.

Dr Liley said, “This clinical trial should clearly communicate the potential of the BAR Index. The competing leading monitor has been shown to correlate reliably with the concentration of a wide range of agents and the depth of sedation or hypnosis. However, a number of important and commonly used anaesthetic agents, such as opioids and $N_2O$ appear to have little or no effect on the competing index, thus limiting the use of the current leading monitor when these agents are used. Other monitors in the early phases of development or marketing suffer similar limitation”.

“A monitor incorporating the **BAR Index**, that could accurately predicts anaesthetic depth during administration of all commonly used agents would provide a world breakthrough in depth of anaesthesia monitoring and assist to decrease the likelihood of patients remembering parts of their surgery and improve their recovery’.

Please contact Dr Samantha Gallagher for further information on 61+ 8 9218 9422.

Yours faithfully,

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