The Royal Australasian
College of Physicians

12 January 2015

Emeritus Professor Lloyd Sansom AO
Chair
Review of Medicines and Medical Devices Regulation
Department of Health
GPO Box 9848
CANBERRA ACT 2601

Via Email: medicines.review@health.gov.au

Dear Emeritus Professor Sansom

Review of Medicines and Medical Devices Regulation

The Royal Australasian College of Physicians (RACP) welcomes the opportunity to provide feedback to the Review of Medicines and Medical Devices Regulation (the Review).

Medicines' prescribing is a core aspect of physician science, and many of the RACP's members are involved with hospital and community-based therapeutics committees. Thus, the regulation of medicines and medical devices is an issue of great importance to the RACP. Unfortunately, given the timeframe for response, the holiday period and the large scope of the review, the RACP is unable to provide a detailed submission. Instead, we have highlighted the general areas we consider vital to any effective regulatory framework.

Firstly, the RACP strongly supports the principles underpinning the Review. The RACP especially values the fundamental role of regulation in protecting public health and safety, that regulation should take a whole of lifecycle approach, and that the ultimate responsibility for regulation of medicines and medical devices in Australia should remain with the Commonwealth.

A robust regulatory framework for medicines and medical devices is critical to ensure public safety and the quality use of medicines (QUM). The Therapeutics Goods Administration (TGA) has demonstrated its ability to effectively regulate medicines and medical devices in Australia, and in doing so has gained strong international respect. We are aware and very supportive of the TGA's approach to continually reviewing and improving its processes to support continued patient safety and QUM, such as with the recent proposed update to medicine labelling requirements.

We strongly support the TGA's improvement processes considering and learning from developments being made overseas where these are relevant for Australia. For

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instance, we strongly recommend the TGA adopts the approach taken by the FDA and EMA in having specialised paediatric expertise to inform all aspects of decision-making for medicines intended for use, or likely to be used in, the paediatric population; from initial regulatory review through to all stages of post-marketing surveillance.

The RACP recognises that changes are occurring in the nature of medicines and medical devices. For example, there is a shift towards cancer medicines that try to block a gene in some parts of a tumour, as opposed to previous treatments which targeted all dividing cancer cells. These changes are highlighting the need for a regulatory system which promotes innovation. However, it is critical that any changes made are not at the expense of public safety.

There are concerns amongst some that the current system of regulation is overly burdensome, and characterised by a duplication of processes internationally. There is a perception that regulation increases costs and delays access to new medicines and medical devices. There may be elements of duplication within the system, but the RACP considers that some of this duplication may be necessary for the Australian environment, in that it acts as a 'double check' mechanism. Such a mechanism is especially important given that other systems may face different political or public pressures, and differing areas of expertise to Australia.

It is also important to highlight that delayed access to medicines and medical devices is not always a negative thing. Delayed access allows for more rigorous evaluation of medicines and medical devices in a real-world setting, as opposed to the homogenous setting of the clinical trial, which can result in improved quality and safety outcomes. There are examples where medicines approved through expedited pathways, for the purposes of faster access to innovative medicines, have been found to have serious public safety risks.

The initial step in any review of the regulatory system must be to consider the regulatory approach that is required for the future. While it is important to support innovation, it is fundamental that any revised regulatory framework places public safety first and foremost.

The RACP has developed the following high-level recommendations for the Review to consider:

1. <u>The TGA must be central in any revised regulatory system</u>
The RACP notes that the Review highlights the possibility of relying upon decisions made by 'trusted overseas regulators'. The RACP would expect that any change to allow a decision made by overseas regulator to be adopted in Australia would adhere to the core principles underpinning the Australian approach. These core principles should be clearly articulated to support this assessment.

It must be recognised that there would be situations where TGA assessment of a product is necessary. For example, if there were inconsistencies between approval decisions by different overseas regulators, the RACP would expect that the TGA would undertake a full assessment of the product. In addition, for generic medicines where an overseas decision had been made, the RACP would expect that the TGA assess samples of the generic reference product to ensure their bioequivalence to the Australian reference product.

In addition, there are situations where an Australian context is important in assessing new medicines or medical devices. A relevant example would be e-cigarette devices. The RACP would expect that any assessment of e-cigarette devices to be approved for use in Australia would include a consideration of the device's likely harms and benefits in the Australian population, taking into account Australia's low smoking rates and

recent cultural shifts in smoking acceptability. The Australian context may result in a harm-benefit analysis outcome that differs to that for other jurisdictions, and could therefore result in a different regulatory decision.

Whilst it is possible that appropriating the decisions of overseas regulators could reduce duplication, there is the potential for it to negatively impact on patient safety, especially when there is pressure to approve products quickly. It is important to recognise that no regulatory body can ever guarantee to be mistake-free. The repetition of processes, such as assessments by multiple jurisdictions, can act as a review or validation mechanism whereby previously overlooked anomalies or safety signals can be detected.

2. Transparency of information must be improved

Any regulatory system must recognise and be able to deal with the drive of commercial companies seeking increased profitability; the regulator's pivotal role in guarding public safety must not be compromised. To this end, it is critical that all information regarding new medicines and medical devices be available to regulators, and the transparency around this must be improved.

There are examples of industry knowingly misleading regulators as to the risks of medicines to improve their chance of approval. The case of dabigatran is a recent example, whereby Boehringer Ingelheim was found to have withheld information which would have improved the safe use of the drug but which may have undermined its market success. [1] It is important to note that dabigatran was originally approved by the US Food and Drug Administration (FDA) through an accelerated approvals pathway, on the grounds that it was a new product. This example highlights the potential for issues to result from rapid assessment of medicines for the sake of facilitating innovation, and the potential for patient safety to be affected by commercial interests at play.

Given this, it is critical that any future regulatory system is as robust as possible, and that it has access to all relevant information and evidence, in order to identify potential anomalies during the assessment process.

The RACP would expect that the TGA have the authority to instigate proceedings to hold companies accountable for any wrongdoings that do or could impact on public health and safety.

3. Post-market surveillance and reporting must be strengthened

As the Review has identified, the regulatory system must take a whole of lifecycle approach, that doesn't cease involvement once the medicine or medical device has been approved. This must include rigorous post-market surveillance, including systems to support timely and accurate adverse event reporting.

The TGA has a strong history of identifying safety concerns before other regulators, examples of this include:

- Dabigatran, where the TGA identified and began to act on a pattern of major bleeds associated with its use before other regulators such as the FDA.[2]
- Cerivastatin, where the TGA were ahead of other regulators in identifying increased risks of rhabdomyolysis with use of cerivastatin compared with other statins. The TGA issued warnings regarding this risk in February 2001[3], prior to the drug being taken off the global market in August 2001.[4]
- Lumiracoxib, where TGA withdrawal of the drug from market in August 2007 for safety concerns prompted New Zealand, Canadian and European regulators to withdraw the product, and resulted in the FDA not approving the product for use.[5]

It is essential that the TGA continues to be a leader in the identification of safety signals once the product is being used. The Review is an opportunity to examine current processes for the reporting of adverse events, and identify ways to simplify these processes to encourage greater rates of reporting amongst consumers and health professionals. This will be even more important if the Australian system begins to rely upon the decisions of overseas regulator.

The RACP would also expect that the TGA have the full authority to remove products from market when there are significant public health and safety concerns. Unfortunately this is currently not the case, as highlighted by the case of dextropropoxyphene. In 2011, the TGA announced it intended to withdraw products containing dextropropoxyphene from market, as *"the overall risk of serious adverse reactions outweighs any benefits that may be provided by these medicines".*[6] However, following successful action by the drug's manufacturer before the Administrative Appeals Tribunal, dextropropoxyphene remains on the Australian market.[7]

It is important to note that dextropropoxyphene was removed by many overseas regulators, including the FDA in 2010 and the European Medicines Agency in 2009.[8] The RACP believes that stronger recognition of overseas responses to post-market safety concerns should be an aspect that is strengthened in this Review to support improved public safety.

In summary, the RACP strongly believes that the Review will be able to identify areas for improvement in the current system of medicines and medical devices regulation. However, we would encourage caution and thorough consultation on any proposed changes to ensure that public safety and quality use of medicines is not inadvertently undermined as a result.

Should you have any questions regarding the RACP's response, please do not hesitate to contact Emily Ofner [redacted]

Yours sincerely

[redacted]

Dr Catherine Yelland
President-Elect
Chair, RACP College Policy & Advocacy Committee

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[5] Medicines and Healthcare products Regulation Agency (2007) *Lumiracoxib (Prexige): Suspension of Marketing Authorisations* November 19 http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON2033073

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