NCETA
Australia's National Research Centre on AOD Workforce Development

THE NATIONAL CENTRE FOR EDUCATION AND TRAINING ON ADDICTION

Level 3B,
Mark Oliphant Building
Laffer Drive, Science Park
Bedford Park, SA 5042

Tel +61 8 8201 7535
Fax +61 8 8201 7550

nceta@flinders.edu.au
www.nceta.flinders.edu.au

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[redacted]
Deputy Secretary for Health Products Regulation
Therapeutic Goods Administration
PO Box 100 Woden ACT 2606

Dear [redacted]

Re: Consultation: Prescription strong (Schedule 8) opioid use and misuse in Australia – options for a regulatory response

Thank you for the opportunity to provide a submission to the above consultation process.

The submission is provided by the National Centre for Education and Training on Addiction (NCETA). NCETA is an internationally recognised research centre that works as a catalyst for change in the alcohol and drugs field. NCETA is one of three national centres of excellence focusing on alcohol and other drug issues in Australia. It is funded by the Australian Government Department of Health and Flinders University.

The Centre has a longstanding interest in problems related to the poor quality use of psychoactive pharmaceutical drugs in general, and pharmaceutical opioids in particular.

NCETA is currently developing a resource for prescribers to assist them to assess and respond to patients experiencing difficulties with their use of prescribed and over the counter opioids. This resource, funded by Indivior Pty Ltd., will be available in coming months.

NCETA was also responsible for the development of the National Pharmaceutical Drug Misuse framework for Action (2012-2015). This involved an extensive national consultation process consisting of written submissions, consultation workshops, a review of the literature and discussions with key experts.

Those consulted included:

- Health and welfare professionals including prescribers, pharmacists, psychologists, physiotherapists, nurses, counsellors, drug treatment agencies and needle and syringe providers
- Government-funded stakeholders including regulators of drugs and poisons, (the then) Medicare locals, law enforcement agencies and a range of other Australian government-funded agencies
- Peak pharmaceutical advisory bodies
- Consumers
- The prescription and non-prescription pharmaceutical industry.

This broad consultation process provided NCETA staff with a unique understanding of the factors involved in reducing the harm associated with pharmaceutical drug problems in Australia from a variety of perspectives.

The implementation of the Electronic Recording and Reporting of Controlled Drugs (ERRCD) was a key recommendation of the National Pharmaceutical Drug Misuse framework for Action. The ERRCD represents the most substantial regulatory approach that could be introduced to enhance the quality use of Schedule 8 opioid drugs in Australia. It is also a fundamentally important clinical tool.

In this regard, the allocation of funds by the Australian Government for the ERRCD rollout, as mentioned in the consultation paper, is welcomed. It is to be hoped that this leads to expeditious national implementation.

NCETA welcomes this exploration of the potential for regulatory approaches to improve the quality use of, and reduce the harm associated with, strong pharmaceutical opioids in Australia. As the Consultation paper notes, a range of issues beyond regulation affect patterns of opioid use. Nevertheless, regulation can have an important role to play in improving the situation.

Each of the options considered in the Consultation Paper is addressed below.

Option 1: Consider the pack sizes for Schedule 8 opioids

NCETA strongly supports the requirement for sponsors to register, and make available for supply, smaller pack sizes of Schedule 8 opioids (e.g., three day's supply) for the treatment of acute pain. The existing arrangements increase the risk of patients developing opioid dependence because of the routine prescribing and dispensing of 20-28 dose packs. Having alternative pack sizes should not interfere with the availability of relevant medicines for people with longer-term or malignant pain, but should reduce barriers to dispensing smaller amounts. Having the option to prescribe standardised smaller pack sizes is also likely to lead to prescribers considering more carefully the *duration* of opioid therapy required as well as the dosage.

Situations in which large pack sizes result in medicines not being fully consumed by the person to who they were prescribed, lead to more unused opioid medicines in the community. This increases the risk of:

- Accidental poisonings where children or opioid naïve individuals consume the drugs
- The selling, bartering or provision of these drugs to people to whom they were not prescribed
- The leakage of the drugs into the illicit market.

Option 2: Consider a review of the indications for strong opioids

As noted in the Consultation Paper, the approved indications from the Australian Register of Therapeutic Goods (ARTG) entries for different strong opioids are inconsistent between both products and Schedule 8 opioids. As such, NCETA supports a review of the current indications for strong opioids to more closely align them with current clinical guidelines for the appropriate use of these products. This is particularly relevant in relation to the use of strong opioids for persistent

non-cancer pain[1] (PNCP), for which there is little evidence of efficacy and considerable evidence of harm.

NCETA also strongly supports a review of the indications regarding the use of codeine, given that:

- It is a pro-drug which is subject to highly variable rates of metabolism
- There is evidence that the low dose codeine-containing products, which moved to Schedule 4 on 1 February 2018, are no more effective in reducing pain than the single compound non-steroidal anti-inflammatory drugs or paracetamol.

The outcomes of the review should also be comprehensively communicated to prescribers and the broader community.

Option 3: Consider whether the highest dose products should remain on the market, or be restricted to specialist / authority prescribing

There is a clear dose-response relationship in harms associated with strong opioid use. These risks include:

- Fatal and non-fatal overdose (particularly with fentanyl because of its potency)
- Diversion
- Iatrogenic dependence
- Harms related to opioid exposure (opioid endocrinopathies, fractures, hyperalgesia, decreased immunity, sleep disturbance, depression).

Nevertheless, there are circumstances in palliative care when high doses are required to achieve effective analgesia. For this reason, these products should remain available but their use in non-palliative care patients should be subject to specialist endorsement.

It is important to be mindful that access to specialist pain medicine physicians is currently very limited in Australia. Waiting periods can extend to years. Therefore, if restrictions are to be placed on prescribing, arrangements will be required for legacy patients already receiving high doses of opioids who cannot access these specialists quickly.

In addition to dosage, consideration should also be given to the continued PBS subsidisation of non-abuse deterrent opioid formulations, particularly higher dosages. The rational for this ongoing subsidisation is unclear.

The review of the indications for strong opioids outlined at Option 2, if undertaken, is likely to determine that the use of the high dose products should largely be confined to palliative patients and opioid legacy patients[2].

There is also a wealth of opioid prescribing guidelines which indicate that, in those rare situations in which opioids can play a beneficial role in PNCP treatment, the dose should not exceed approximately 40mg oral morphine equivalent daily dose (oMEDD).

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[1] In this submission, the term *persistent non-cancer pain* includes cancer survivor pain.

[2] Legacy patients are those who have been inappropriately prescribed high doses of opioids over a long period and are now unable to stop or reduce their intake.

In relation to high-dose oxycodone, for example:

- 80mg sustained release is approximately 120 oMEDD
- 30mg immediate release is approximately 45 oMEDD.

Consequently, both of these formulations exceed the maximum daily recommended oMEDD of 40mg. Increasing awareness among prescribers of the oMEDD of the opioids they are contemplating prescribing is likely to be a more beneficial approach than removing the higher dose formulations.

Option 4: Strengthening Risk Management Plans for opioid products

The Consultation Paper indicates that the major outcome that would stem from enhancing risk management plans (RMPs) is the provision of education programs for prescribers. The Consultation Paper also notes that RMPs specifying educational activities have been beneficial in the introduction of new and novel products (such as new anti-coagulants). However, opioids are hardly new or novel drugs. Opioids are like many other drugs for which best practice guidelines evolved over time. Consequently, it is unclear whether RMPs specifying educational activities would be beneficial in the context of opioids.

In addition, as the Consultation Paper notes, Australian prescribers already have access to NPS MedicinesWise which provides education to prescribers. MedicineWise is seen as an independent and therefore a reputable source of information which has CPD accredited activities related to opioid use in PNCP.

Clearly, more education is required regarding the prescribing of strong opioids in Australia, particularly for PNCP. It is, however, unclear that RMPs are the best avenue to achieve this.

Option 5: Review of label warnings and revision to the Consumer Medicines Information (CMI)

As is noted in the Consultation Paper, to-date no prescribed pharmaceutical product has a boxed warning on the packaging. The Consultation Paper also notes that while a boxed warning could be included on the packaging identifying the risks of long-term use, this may deter the appropriate use of opioids where they are indicated. It is unclear why the inclusion of a boxed warning on the packaging would deter the appropriate use of opioids any more than the inclusion of a warning on the CMI. Nevertheless, if no other prescribed pharmaceutical product has a boxed warning on the packaging there seems no compelling reason to include one on strong opioids. Such boxed warnings also risk increasing the stigma already experienced by PNCP patients.

There is, however, likely to be benefit in updating the consumer warnings in the CMI to more clearly advise that opioids are not generally recommended for long-term use in PNCP (beyond trial periods) and that acute treatment should be limited to a few days, after which pain can be managed by non-opioid medication. The CMI could also include information about:

- The risks of overdose associated with high doses of opioids
- The importance of keeping opioids where they cannot be accessed by others (particularly children)
- The risks associated with mixing opioids with other CNS depressants, such as alcohol or benzodiazepines

- The risks associated with opioid use and driving or operating machinery.

A further useful addition could be the inclusion of oMEDD information in the Product Information (PI) and CMI. Since oMEDD is a measure that allows comparison of the potency of all opioids, including this in the PI and CMI (along with an indication of what is a high dose of opioids in oMEDD) could empower consumers to become more involved in the self-management of their treatment. For example, if patients become aware that 40mg oMEDD is the maximum dose at which they are likely to receive any benefit from opioid use, they are less likely to try to escalate their use beyond this.

It is recommended that changes to on-pack labelling include a requirement for barcoding, or QR coding, to assist in supply chain management of these products and to reduce the risk of diversion. The advantages of this approach were raised by law enforcement officials and regulators during the consultations NCETA held for the development of the National Pharmaceutical Drug Misuse Strategic Framework.

Currently it is very difficult for law enforcement to prosecute those selling, or found in possession of, strong opioids if they cannot prove that the possession of the opioids was unlawful. The lack of traceable on-pack labelling is a major impediment in this regard.

The National Pharmaceutical Drug Misuse Strategic Framework called for consideration to be given to the feasibility of implementing pharmaceutical pedigrees[3] (Priority Area, 8 Action 8.2). It is now an opportune time to consider this issue.

Option 6: Consider incentives for expedited TGA review of improved products for pain relief and opioid antidotes

As the Consultation Paper points out, this is an option that should remain “on the table” despite the fact that there are few contenders for regulatory approval in the immediate future. This approach could be formal or informal and is most likely to be relevant to smaller pack sizes and/or abuse-deterrent formulations for opioids, new formulations or antidotes.

In the meantime, the key focus should remain on enhancing prescribing practices related to existing medicines.

Option 7: Potential changes to use of Appendices in the Poisons Standard to provide additional regulatory controls for strong opioids

The feasibility of limiting prescribing of certain S8 opioids to certain medical practitioners (such as palliative care physicians for high-dose opioids in patients with cancer pain and specialist pain medicine physicians for high-dose opioids in patients with chronic non-cancer pain), warrants further examination. However, the caveats outlined under Option 3, also apply in relation to this proposal.

In particular, any changes to the Appendices should not be at the expense of reducing access to these medicines for patients who would benefit from them.

[3] A pharmaceutical pedigree is an audit trail using barcoding, QR coding or other approaches that follows a drug from the time it is manufactured through the distribution system to pharmacies and individual patients.

It is also recognised that there may be legal difficulties associated with having limitations on products' doses rather than on specific products (as is the case with drugs such as isotretinion).

It is also unclear whether changes to the Appendices would be more beneficial than regulatory approaches taken at the jurisdictional level (for example when prescribers seek authorisation to prescribe high doses of opioids in non-palliative situations).

Option 8: Increase health care professional awareness of alternatives to opioids (both Schedule 4 and Schedule 8) in the management of chronic pain

There is a wealth of evidence-based resources concerning the management of malignant as well as persistent non-cancer pain. Enhancing the visibility of these resources to prescribers is critically important. There is considerable scope to work with clinical colleges to educate prescribers on judicious use of opioids, de-prescribing and the use of non-opioid pain relievers.

In addition, there would be considerable benefit in the TGA developing a resource on opioid prescribing, similar to the *Codeine Information Hub* to make relevant guidelines more accessible to prescribers. There is also merit in broader University implementation of the NPS National Undergraduate and Post Graduate Prescribing Curriculum focusing on the use of opioid analgesics in PNCP and opioid dependence.

Issues related to pharmaceutical opioid use will remain an important body of work for NCETA. A relevant NCETA publication *Responding to patients with pharmaceutical opioid related problems: A guide for prescribers* will be available in the near future. This will be supported by an extensive literature review on pharmaceutical opioids which will be available on the NCETA website: http://nceta.flinders.edu.au/ This resource should also increase health care professional awareness of alternatives to opioids in the management of PNCP.

Other NCETA resources are available at the links below.

Pharmaceutical drug misuse problems in Australia: Complex issues, balanced responses
Older Australians, opioids and the treatment of pain
Beyond the paper trail: using technology to reduce escalating harms from opioid prescribing in Australia

I trust this submission is of assistance to the Consultation Process.

Yours sincerely,

[redacted]

Professor Ann Roche
Director
National Centre for Education and Training on Addiction (NCETA)
Flinders University

www.nceta.flinders.edu.au @NCETAFlinders nceta@facebook