



OFFICE OF THE PRIME MINISTER'S SCIENCE ADVISORY COMMITTEE

Professor Peter Gluckman, DCNZM FRSNZ FMedSci FRS
Chief Science Advisor

Consideration of reduction of access to, or elimination of, pseudoephedrine in 'cold and flu' preparations

Report to the Prime Minister

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Executive Summary

- Domestically diverted pseudoephedrine is a precursor for a significant proportion of the methamphetamine consumed in New Zealand, and is the predominant precursor in small-scale clandestine laboratories.
- Experience from other jurisdictions suggests that restrictions on the domestic availability of pseudoephedrine translate into reductions in the number of clandestine laboratories discovered. Given the high societal cost of such laboratories, this would be a public good.
- I have considered six options to restrict access to pseudoephedrine, and recommend consideration of either **Option 3** (introduction of an electronic point-of-sale monitoring system as used in Queensland) or **Option 5** (reclassification as a Class B2 controlled drug, leading to restricted ability to prescribe and availability only through hospital pharmacies) as having the potential to reduce domestic production of methamphetamine. **Option 5** is likely to have a greater effect, but is associated with greater inconvenience for the public.
- On balance, I recommend an evaluative implementation of **Option 5** by means of a three-year trial to determine public acceptance and effects on methamphetamine production.

Background

1. Pseudoephedrine is an orally active medicine that causes blood vessels in the nasal epithelium to contract, limiting inflammation and mucus secretion and thus relieving the symptoms of nasal congestion arising from viral infection ('colds and flu') or allergic reactions ('hay fever') in the upper respiratory tract.
2. A number of 'over-the-counter' (OTC) preparations containing pseudoephedrine alone or in combination with other medicines such as analgesics or antihistamines are available in New Zealand for the treatment of colds, influenza and allergies. Parenthetically, since decongestants undoubtedly improve wellbeing and functioning during colds and influenza, given the current context of the H1N1 pandemic there may be concern that any restriction on such agents might adversely affect the population. It is important to emphasise that these medications do not affect or treat the viral infection, and indeed their use allows individuals to resume employment or social contacts while they are still infectious.
3. Pseudoephedrine is the precursor of choice in New Zealand for the illicit manufacture of the Class A controlled drug methamphetamine. Pseudoephedrine for this purpose is obtained by diversion (theft or 'pill shopping') of OTC pseudoephedrine preparations, or by illegal bulk imports of pseudoephedrine-containing medicines (predominantly ' ContacNT' capsules manufactured legitimately in China).
4. Methamphetamine, like cocaine, acts on the brain by altering the levels of brain chemicals called neurotransmitters (particularly dopamine and norepinephrine), causing feelings of intense pleasure and euphoria. It also has effects on the rest of

the body, including rapid heart rate, high blood pressure, shortness of breath and high body temperature. Methamphetamine is highly addictive, causing compulsive drug seeking, and requiring the user to take increasingly higher doses to obtain the same effect. Use of methamphetamine over time may cause violent behaviour, anxiety, confusion, and insomnia. Heavy users may also display a number of psychotic features, including paranoia, auditory hallucinations, mood disturbances, and delusions. Unlike cocaine, methamphetamine is toxic to brain cells, and long-term users suffer irreversible brain damage.

5. New Zealand has the third highest reported use of methamphetamine in the world.¹ In part, this may reflect more limited access to other drugs of abuse such as cocaine and heroin. Societal harm from methamphetamine use extends to many areas, including criminal activity associated with drug-seeking behaviour, mortality and morbidity arising from methamphetamine use, and the costs of remediating the 200 or so clandestine laboratories ('clan labs') for methamphetamine manufacture discovered each year, mostly in urban areas. An estimate of total monetary value for these societal harms is not available. However, each clan lab discovered contains flammable and toxic materials requiring the attendance of police, fire service and ESR personnel. Subsequently, the commercial costs of decontamination usually fall on property owners. The total cost to the community of each lab discovered is therefore significant.
6. The value of the methamphetamine 'market' in New Zealand was estimated by the National Drug Intelligence Bureau in 2007 to be about 1 billion dollars (about 1000 kg of drug) per annum. At least 10% of this is derived from domestically diverted pseudoephedrine (although there are indications that this may be a significant underestimate), the remainder from illegal imports of pseudoephedrine and of methamphetamine itself. There is some evidence that importation of pseudoephedrine is increasing relative to that of methamphetamine.
7. However, the most commonly identified source of pseudoephedrine in small-scale clan labs in New Zealand is domestically diverted pseudoephedrine. Indeed, this is essentially the *only* precursor found in clan labs discovered south of the central North Island (advice from National Drug Intelligence Bureau).
8. Concerns about the use of pseudoephedrine as a precursor for manufacture of methamphetamine led in 2003 to the reclassification of pseudoephedrine as a Class C controlled drug (Schedule 3 of the Misuse of Drugs Act 1975). Pseudoephedrine preparations containing not more than 60mg per unit dose (or 240mg for a slow-release formulation) and supplied in packages containing not more than 1800mg may be sold by pharmacies without a prescription. All other dosage levels require a prescription.
9. In June 2009 the Prime Minister requested the Chief Science Advisor to consider the evidence relating to legal access to pseudoephedrine and advise whether a tightening of such access might be acceptable from a medical perspective without having any adverse effects on the population, in the presumption that reduced access might reduce the social harm relating to methamphetamine use.

Effectiveness of pseudoephedrine and alternatives in nasal congestion

10. Pseudoephedrine has been used as a nasal decongestant since the 1940s. This is well before the introduction of modern regulatory procedures for drug development, and its continued use is based on 'grandfather clauses' in various regulatory regimes deeming well-established medications to be 'generally recognized as safe and effective'. Thus, the objective evidence of efficacy is limited. Nevertheless, there is reasonably good evidence from clinical trials conducted in the 1960s and 1970s that pseudoephedrine is an effective nasal decongestant (summarised in a US FDA monograph²), and more recent studies have supported this conclusion.^{3,4}
11. Nasal congestion arising from viral infection of the upper respiratory tract is usually a self-limiting condition that lasts for a week or so before spontaneous recovery. There are generally effective alternatives to pseudoephedrine-containing medications in this situation: the most commonly used are tablets containing phenylephrine (most often with other ingredients) and/or nasal sprays containing oxymetazoline or xylometazoline.
12. The evidence supporting orally administered phenylephrine as a nasal decongestant at the doses available in New Zealand is less good than that for pseudoephedrine. The earlier FDA monograph² classified it as 'safe and effective', whereas some⁵ but not all⁶ more recent analyses have questioned the scope of its effectiveness in nasal congestion arising from the common cold, and the FDA has recently called for more studies.⁷ Certainly, there is little evidence for its effectiveness in nasal congestion arising from allergic rhinitis (that is, congestion arising from allergy as opposed to infection).⁸ At least some of this discrepancy may represent inter-individual variation among the small numbers of patients recruited for these trials. Anecdotal evidence suggests that phenylephrine will work for at least 80% of people but not for others. However, most of these formal trials of phenylephrine have been studies of the effects of single doses on laboratory measures of nasal congestion rather than 'real-world' trials of repeated doses on patients' subjective measures of improvement.
13. In spite of the uncertainties arising from the lack of quality scientific data, most manufacturers of OTC 'cold and flu' tablets containing pseudoephedrine introduced a parallel range of phenylephrine-containing products in the early 2000s, possibly anticipating restrictions on sales of pseudoephedrine, and these products now have 60 to 70% of the market share (information provided by NZ Self Medication Industry Association), suggesting that the majority of consumers find phenylephrine to be an acceptable alternative to pseudoephedrine. Phenylephrine cannot be used as a precursor for methamphetamine.
14. The effectiveness of the nasal sprays is clinically well established² and they represent a useful alternative to oral pseudoephedrine for nasal congestion arising from colds or influenza. With prolonged use, these agents may contribute to nasal blockage (rhinitis medicamentosa or 'rebound congestion'⁹), making them unsuitable for long-term treatment of allergy, but this is unlikely to be a problem over the few days needed to treat a cold or influenza.¹⁰ However, these sprays do require patients to purchase an additional product if their nasal congestion is accompanied by other symptoms (e.g. analgesics for pain relief).

15. Nasal congestion as a result of allergy is often a medium- to long-term condition for which treatment with symptom-relieving decongestants alone is usually inappropriate and not generally recommended.¹¹ Rather, this condition is best treated with allergy-relieving medications such as antihistamines (oral or intranasal) or intranasal corticosteroids.¹¹

Effects of restricting access to pseudoephedrine

16. Various jurisdictions have severely restricted access to pseudoephedrine, either by complete withdrawal from the market or by requiring a prescription for its supply. There is little evidence that this has caused great inconvenience for consumers. The Netherlands withdrew pseudoephedrine from the market about 10 years ago because of concerns about cardiac safety. However, the Netherlands is not considered to have a major methamphetamine problem and the consequences for illicit drug manufacture do not seem to have been studied.
17. The state of Oregon in the US has imposed successively more restrictive regulations on the sale of pseudoephedrine, culminating in a switch to prescription-only in 2006. This has not affected methamphetamine-related harm, as reflected in the number of deaths from use of the drug, which has increased steadily from 1998 to 2008. However, the number of clandestine laboratories discovered in the state has reduced markedly, from a peak of 473 in 2003 to 21 in 2008 (statistics from Oregon State Police and Oregon State Medical Examiner).
18. Evidence from other jurisdictions suggests that making access to pseudoephedrine more difficult results in a reduction in the number of clan labs discovered. In Queensland, Australia, a pharmacy-based programme to eliminate ‘pill shopping’ (‘Project STOP’; discussed further below) has reportedly resulted in a 39% decrease in the number of clan labs.¹²
19. The potential effect of restricting access to OTC pseudoephedrine on clan lab discovery might arguably be discernable from New Zealand data. Legitimate domestic sales of pseudoephedrine (on a weight basis) have declined by more than half since 2000. This has been accompanied by a decline in the number of labs discovered since 2005. Again, however, access to methamphetamine appears not to have changed greatly, presumably because of increased importation of precursor and/or methamphetamine itself (information from NDIB).

Primary conclusions

20. I conclude from this review that acceptable alternatives to pseudoephedrine as a nasal decongestant do exist, or in the case of allergy that a more rational treatment approach to the underlying condition is preferable, and that further restriction on public access to pseudoephedrine would not place an undue burden or impose a health risk on consumers. On the other hand, while not in itself reducing the volume of methamphetamine abuse, such a measure has the potential to significantly reduce the number of illicit production laboratories and that in itself has a social benefit. More speculatively, it may also allow the police and other authorities to better focus their attention on border controls.

Options to restrict the domestic availability of pseudoephedrine

21. I have considered six basic options for restricting access, as discussed in the following paragraphs.
22. Of these, the first three would allow the population continued broad access to pseudoephedrine.

Option 1. Further restrict pharmacy supply of pseudoephedrine by reducing the pack size of over-the-pharmacy-counter pseudoephedrine-containing products from the present 1800 mg (typically 30 x 60 mg unit doses) to 720 mg (12 x 60 mg unit doses), and limiting sales to one pack per transaction, in conjunction with industry-based measures to reduce supply chain stocks of pseudoephedrine-containing medicines.

Option 2. Reclassify pseudoephedrine as a Restricted Medicine that requires oversight of sale by a registered pharmacist as well as recording of details of the sale.

Option 3. Introduce an electronic real-time monitoring system of pharmacy sales of pseudoephedrine, similar to 'Project STOP' used in Queensland (and being introduced into other Australian states).

Commentary on these options: any combination of these measures may be used together. However, any measures that retain non-prescription pharmacy sales of pseudoephedrine will continue to leave pharmacies vulnerable to pill shopping and theft. Most pharmacies are already alert to sales of pseudoephedrine and further oversight (Option 2) is unlikely to significantly reduce illegitimate purchase. Real-time monitoring of pseudoephedrine sales (Option 3) would require a mandatory system to be effective and would necessitate that all pharmacies have broad-band internet connection, which may not be easily achievable in more remote areas. However, the Pharmaceutical Society of New Zealand indicates that the Ministry of Health intends to have 95% of pharmacies connected to secure broadband (for online payment for dispensing) by July 2010. Once introduced, such a system could be used for monitoring of other pharmacy medicines for which there is concern about diversion (for example, codeine-containing products).

23. There is a more limiting option that would still allow relatively high access to pseudoephedrine.

Option 4. Reclassify pseudoephedrine as a prescription-only medicine (by removing the exemption provided in the relevant schedule of the Misuse of Drugs Act for supply of amounts under 1800 mg per pack).

Commentary on this option: the small proportion of patients who desire alternative nasal decongestants would visit a general practitioner, incurring additional costs. The burden of refusing supply of pseudoephedrine would shift from pharmacists ('pill shopping') to general practitioners ('doctor shopping', already known for other drugs of abuse). Pseudoephedrine would remain in the pharmacy supply chain, and indeed some pharmacies that

currently choose not to supply pseudoephedrine might be obliged to do so to fulfil prescriptions. Nevertheless, this option appears to have been effective in reducing the number of clan labs in Oregon.

24. Beyond that, there are two options that would effectively remove pseudoephedrine from public access.

Option 5. Further limit availability of pseudoephedrine by classifying it as a Class B2 controlled drug under the Misuse of Drugs Act 1975. This would have the effect of requiring a higher level of prescription record-keeping and restricting supply to hospital pharmacies only. Restrictions on eligibility to prescribe pseudoephedrine could be imposed by the Minister of Health.

Commentary on this option: this option maintains access to pseudoephedrine as a medicine while severely restricting its availability under the powers available under section 23 of the Medicines Act 1981 and regulation 22 of the Misuse of Drugs Regulations 1977. Unauthorised possession of pseudoephedrine would be subjected to increased penalties, providing further options for control both domestically and at the border.

Option 6. Reclassify pseudoephedrine as a Class B2 controlled drug under the Misuse of Drugs Act while also delisting it as a medicine.

Commentary on this option: this option would provide the tightest control on pseudoephedrine in that there would remain no legal basis for possession of the substance in New Zealand. However, there are (rare) medical situations in which the vasoconstrictor activity of pseudoephedrine is useful (for example, the treatment of priapism associated with overdosage of medication for erectile dysfunction) and this level of control may create clinical difficulties.

Conclusions and recommendations

25. The quality of objective evidence comparing the relative effectiveness of pseudoephedrine-containing to pseudoephedrine-free nasal decongestants is poor. Anecdotal evidence suggests that the pseudoephedrine-containing products provide greater consumer convenience and possibly effectiveness. However, several jurisdictions, including the Netherlands, Mexico and the state of Oregon, have eliminated pseudoephedrine-containing decongestants from either their OTC products or their total pharmacopoeia, apparently without unacceptable patient inconvenience. Certainly for common viral-induced nasal decongestion, safe alternatives are available that do not contain precursors for methamphetamine.
26. The options available depend on how one weighs up consumer convenience against the public interest in maximally eliminating access to methamphetamine precursors.
27. Eliminating legitimate pseudoephedrine-containing medicines on its own will reduce the number of clan labs, at least transiently, but without other measures will not reduce methamphetamine usage as it may merely shift the activity to imported pseudoephedrine or imported methamphetamine. However, reducing the number of clan labs will in itself be of value to public health and safety.

28. Strategies to reduce illicit drug use fall into three categories: supply reduction, demand reduction and harm reduction.¹³ Steps to reduce the availability of domestic pseudoephedrine fall into the first category, and other related measures might include:
- greater controls on access to other potential precursors and chemicals associated with manufacture through, at a minimum, requiring identification and certificates of intended usage, and
 - greater effort at border controls.
29. A holistic approach to the high usage of illicit methamphetamine would suggest that other measures should also be considered alongside the restrictions in precursor supply. These might include:
- more focus on the minor crimes associated with fuelling the methamphetamine epidemic, such as burglary,
 - improved access to acute therapy on arrest for methamphetamine users, and
 - greater emphasis on appropriate drug education.
30. Of the six options I have discussed above, two stand out as meriting definite consideration. These are discussed further in the next paragraphs.
31. **Option 3** requires adoption of a measure analogous to Queensland's reportedly successful STOP programme in which purchasers of pseudoephedrine are positively identified by means of their driving licence and this information is made instantaneously available online to other pharmacies, and to the police if necessary, to deter repeated sales to the same individual.¹² I am informed that implementation in New Zealand might require an exemption to the Privacy Act. The advantage of this option is that it allows general access for legitimate use, and based on Australian evidence does reduce but not absolutely eliminate pill shopping. It also allows for controls on other abused agents such as codeine to be put in place. The limitations are that pharmacies will still potentially be exposed to theft, pseudoephedrine will still be widely available in the community creating a route for corrupt access, and it has costs in terms of requiring pharmacies to have broadband access as well as establishment and operational costs. It is clear from my consultation with the Pharmaceutical Society of New Zealand that they believe that the capital and running costs of such a project should not have to be borne by pharmacies. Even if a more restrictive option is chosen, the establishment of such an infrastructure might have potential benefits in controlling other agents, but the privacy issues would need consideration.
32. **Option 5** effectively removes pseudoephedrine from legal public access except in very particular circumstances, making control easier at the expense of creating some consumer disadvantage. Exceptions would have to be provided at the border for overseas travellers in possession of small quantities of pseudoephedrine legitimately purchased overseas, such that the offence of possession would have some practical caveats on it. Otherwise, it is an easier option to administer.
33. Either option is feasible and scientifically supportable. Given the international experience with restrictions on access, the severity of the methamphetamine

problem in New Zealand, and the scientific validity of such an approach, my view is that it would be rational to favour **Option 5**.

- 34. I recommend that a three-year trial of Option 5 should be undertaken during which the effect on domestic methamphetamine production and on consumer acceptance of the restrictions could be evaluated.***

APPENDIX 1: REFERENCES

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APPENDIX 2: AUTHORSHIP, PEER REVIEW AND SOURCES

This report has been prepared by **Professor Peter D. Gluckman**, DCNZM FRSNZ FMedSci FRS (Chief Science Advisor) with the assistance of **Dr Alan S. Beedle**, BSc PhD (Chief of Staff), Office of the Prime Minister's Science Advisory Committee.

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The report was peer reviewed with respect to its scientific content by **Professor Ross McCormick**, MSc, PhD, MBChB, FRNZCGP, FChAM, Faculty of Medical and Health Sciences, University of Auckland

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