Submission on Petition 2014/15 of Anthony Roberts and 40 others

9 May 2016

To the Health Select Committee

This submission is from Dr Kirstie Murdoch, Environmental & Human Health Aotearoa.

1. Summary

- Environmental & Human Health Aotearoa (EHHA) supports petition 2014/2015 of Anthony Roberts and 40 others, except that we consider incineration to be an inappropriate method of disposing of pharmaceutical waste
- Environmental pollution by active pharmaceutical ingredients (APIs) has been recognised globally as an issue of concern and action must be taken on multiple levels to reduce the entry of pharmaceuticals into the environment. Two of the levers that may be used to reduce levels of API pollutants are: (1) the reduction in dispensing of excess medication; and (2) providing suitable collection and disposal of unwanted medications. Both of these issues are addressed in the present petition.
- APIs require specific deactivation and should not be treated in the same manner as infectious medical waste.
- Given the considerable health problem of antibiotic resistance, particular care is required to minimize the entry into the environment of antibiotic APIs.
- Certain dosage forms, such as transdermal patches, retain substantial quantities of the active pharmaceutical after use. Such used dosage forms should also be part of a collection and disposal system.
- A national, consistent system needs to be set up for the collection and disposal of unused pharmaceuticals and used dosage forms that retain residual APIs. This system should encompass all healthcare providers, including community pharmacies, hospitals, rest homes and hospices.
- New Zealand Standard NZS4304:2002 (Management of Healthcare Waste) needs to be revised to include appropriate standards of treatment for APIs, including cytotoxic and antibiotic APIs.
- Chemical techniques for the deactivation of APIs need to be established as a component of standard methods for the treatment of pharmaceutical waste.

EHHA recommends that the following steps be taken

- Establishment of a nationally regulated, consistent system for the collection of unused pharmaceutical products as segregated waste from pharmacies, rest homes, hospices and hospitals.
- Establishment of a working party to investigate of appropriate state-of-the-art methods for the chemical deactivation of APIs in pharmaceutical waste. This working party should include all relevant stakeholders, such as regional councils, government departments, industry and civil society representatives.
- Updating of the current out-of-date NZ Standard for the managament of healthcare waste.
- Development of requirements for the sponsors/manufacturers of certain pharmaceutical dosage forms (e.g. transdermal patches) to provide collection and destruction systems as part of the market authorisation.
- Investigation of a role for the pharmaceutical industry in contributing to funding the development of the collection and disposal system

2. Background

2.1. Pharmaceutical pollution is an issue of global concern

Environmental & Human Health Aotearoa (EHHA) investigates the impact of pollution on both ecosystem and human health locally, regionally and globally. One of our areas of focus is environmental pollution by **active pharmaceutical ingredients (APIs)** in pharmaceutical products.

In May 2015 I published a report on the issue of pharmaceutical pollution in Australia, New Zealand and Pacific Island countries, which is appended to this submission and also available at: http://www.ehh-aotearoa.org/wp-content/uploads/2016/02/NTN-Pharmaceutical-Pollution-in-the-Environment-2015-05.pdf

The issue of environmentally persistent pharmaceutical pollutions is of increasing concern globally. A recent review undertaken for the German Federal Environment Agency identified that 631 different pharmaceutical substances have been detected in

the environment in 71 countries.[1] These substances include antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, lipid-lowering drugs and hormones. The origin of the majority of these pharmaceutical pollutants is urban wastewater, however other sources that can have a local impact include discharges from pharmaceutical manufacturing and hospitals.

It is unclear what are the long-term effects to human and ecosystem health of chronic exposure to mixtures of APIs, some of which may act synergistically to exert a greater biological effect in combination than predicted by exposure to individual APIs. There is also increasing concern that the pervasive presence in the environment of antibiotic APIs may also contribute to the development of antibiotic resistance in microorganisms that cause human disease.[2–4]

The international community is beginning to express its concern about the issue of pharmaceuticals in the environment in a number of ways. For instance, the recent 4th International Conference on Chemicals Management (ICCM4) adopted environmentally persistent pharmaceutical pollutants as an emerging policy issue in the context of the Strategic Approach to International Chemicals Management (SAICM).[5] SAICM is a global policy framework to foster the sound management of chemicals which is hosted by the United Nations Environment Programme. At ICCM4 I was the co-lead on the topic of pharmaceutical pollutants for the non-governmental organisation delegation to the meeting.

2.2. Active pharmaceutical ingredients are highly biologically active and resistant to degradation

APIs are designed to be highly biologically active in order to exert their therapeutic effect at low doses. APIs are also generally designed to resist degradation, to ensure that the API is not prematurely broken down by the body's metabolism. This high biological activity and persistence can mean that even low amounts of APIs can have serious adverse environmental impacts.

As discussed above, APIs that have been detected in the environment globally fall into a number of different categories in addition to the cytotoxic drugs that have been singled

out in the New Zealand Standard NZS4304:2002 (Management of Healthcare Waste), and also include endocrine disruptors, antibiotics, antidepressants and cardiovascular drugs.

2.3. Preventing APIs from entering the environment

The main route of entry of APIs into the environment is through excretion from the patient, either as the original pharmaceutical compound, or as a derivative of that compound, and therefore into the wastewater system. Wastewater treatment plants are currently not designed to remove pharmaceutical compounds and outputs from wastewater treatment plants contain a mixture of pharmaceutical residues that can move out into the aquatic and terrestrial environment.

It must be a long-term goal to develop practical wastewater treatment technologies that deactivate APIs. However, in the meantime it is also essential to reduce to the maximum extent possible the entry of APIs into the environment at every stage of the pharmaceutical lifecycle: from manufacturing to use to disposal. Two of the levers that may be used to reduce levels of API pollutants are: (1) the reduction in dispensing of excess medication (which is ultimately not used by the patient); and (2) providing suitable collection and disposal of unwanted medications. Both of these issues are addressed in the present petition.

To join the global action against pharmaceutical pollution, New Zealand must implement a consistent and centralised system for the collection of unwanted or expired medicines and implement protocols that ensure the deactivation of APIs in this pharmaceutical waste.

3. Establishing a central pharmaceutical waste collection and disposal system in New Zealand

3.1. A central collection system is required that includes all healthcare providers

The safe collection of pharmaceutical waste and deactivation of the highly biologically active APIs in that waste requires specialised and consistent treatment. Accordingly, it is submitted that this can be best controlled through a centralised system.

This system needs to encompass not only community pharmacies, but also other healthcare providers such as rest homes, hospices and hospital facilities.

3.2. A collection system needs to encompass used dosage forms that retain APIs

It is not merely the disposal of unwanted or expired pharmaceutical products that can impact on the environment. Some pharmaceutical dosage systems, such as inhalers and transdermal drug delivery systems (e.g. patches), retain a significant proportion of API even after they have been used.

For example the mechanism of action of transdermal patch systems requires that there is an excess of pharmaceutical active in the patch, resulting in the presence of up to 95% of the original amount of the API being present in the patch at the end of the treatment period.[6] Therefore, the inappropriate disposal of these used dosage systems could result in environmental contamination by the remaining API. Used transdermal patches have also result in poisoning after children have come in contact with used patches discarded in the waste. This can have critical results in the case of patches containing the opioid fentanyl, and this was therefore the subject of a 2014 medication alert from the Health Quality and Safety Commission New Zealand.[7]

It is therefore submitted that a collection and disposal system for pharmaceutical waste must also encompass dosage forms that retain residual drug product after use such as inhalers and transdermal patches.

Specific facilities for the collection of such used dosage forms, such a dedicated sealable containers or bags could be provided by the drug manufacturer/sponsor with the dispensed dosage form. Therefore, it is submitted that this is an area where pharmaceutical companies could contribute to the cost and development of an appropriate return and disposal system.

3.3. Disposal methods must be suitable for pharmaceutical waste

3.3.1. The application of the New Zealand Standard for the management of healthcare waste

The disposal of pharmaceutical waste in New Zealand is governed by New Zealand Standard NZS4304:2002 - Management of Healthcare Waste (NZS4304:2002). NZS4304:2002 requires healthcare waste to be segregated into different categories for treatment and disposal (s4.5.1). Waste containing APIs would fall into one or both of the categories of: hazardous waste - cytotoxic (s3.3.1); or hazardous waste - other hazardous waste (which specifically lists medicines/pharmaceuticals, s3.3.2). In neither case is sterlization (e.g. by steam treatment/autoclaving) stated to be an acceptable method of waste treament/disposal under this standard (see Table 2 and s7.6).

Interwaste's 18 January 2016 submission in relation to this petitition acknowleges that 'some active ingredients may not be neutralised at sterlisation temperatures'. University of Otago chemist Associate Professor Barrie Peake also stated in a Radio New Zealand report on medicine disposal in July 2015 that he doubted that this steaming would inactivate APIs.[8] Indeed, certain pharmaceutical formulations, for example for injection or ophthalmic use, are sterilised by autoclaving as the final stage of the fomulation process.[9,10] Clearly, this process does not deactivate the API in any way.

While autoclaving/steam sterilisation is the ideal method for the destruction of biological pathogens in infectious medical waste (as required by NZS4304:2002), it simply does not reliably work for generally highly stable chemical entities that are APIs. Accordingly, it is unclear why pharmaceutical waste is currently treated in New Zealand using methods that are designed for a separate category of waste under NZS4304:2002.

Incineration of pharmaceutical waste is also not an option.

Regulation 12(1) of the *Resource Management (National Environmental Standards for Air Quality) Regulations* 2004 prohibits the operation of high-temperature hazardous waste incinerators in New Zealand. Exceptions to this prohibition provided for three high temperature waste incinerators in Auckland, Christchurch and New Plymouth (regulation 12(2)(b)). However, as discussed in the submissions by the Ministry of Health and Interwaste in relation to the present petition, the two incinerators in Auckland and Christchurch have now been decommissioned. We understand that the high temperature waste incinerator in New Plymouth is used for specific chemical waste incineration and is not available for healthcare waste.

The banning of high temperature hazardous waste incinerators in New Zealand was an essential response to the serious and environmental health impacts of such incinerators. Therefore, pharmaceutical waste, including cytotoxic waste, can not (and indeed should not) be disposed of by incineration in New Zealand.

NZS4304:2002 states that cytotoxic pharmaceutical waste should be disposed of by incineration or sewering (Table 2, NZS4304:2002). As discussed above, incineration is not an option in New Zealand. The cost of the transport of cytotoxic waste to Australia may act as a disincentive to treat the full range of pharmaceuticals that have a cytoxic action. In addition, it is generally inappropriate to send hazardous waste to another country for disposal. The Ministry of Health in paragraph 33 of its submission dated 9 February 2016 in relation to the present petition, notes that NZS 4304:2002 is nearly 15 years old and unlikely to represent current accepted good practice, particularly in relation to the sewering of cytotoxic waste. The World Health Organization also specifically advises that the antibiotics or cytotoxic drugs should not be discharged into municipal sewers or watercourses.[11]

Furthermore, the direction in Table 2 of NZS4304:2002 to dispose of pharmaceutical waste ('other hazardous waste') in sanitary landfill is also inappropriate, given that the highly biologically active APIs in this waste are not deactivated prior to burial in the landfill. A study by the United States Geological Survey has demonstrated that API pollutants travel and persist for many years in landfill leachate.[12] We are not reassured by the statement in Interwaste's

submission in relation to the present petition that 'all leachate from the landfill is contained and treated'. We query what could be the suitable treatment for this mixture of still-active APIs, given the specific requirements for the deactivation and neutralisation of these chemical compounds.

Clearly, there is an urgent need to develop and enforce new standards for the treatment of pharmaceutical waste in New Zealand to ensure that APIs in the waste are deactivated and thereby rendered unable to adversely impact on human and ecosystem health.

3.3.2. Developing technologies for the deactivation of APIs

Given the considerable negative environmental impacts from the use of high temperature incinerators, international organizations such as the World Health Organization and the United Nations Environment Programme have been investigating alternative methods for the deactivation of APIs in pharmaceutical waste. The most promising technologies involve the chemical deactivation of the APIs. For example, alkaline hydrolysis[11,13] and another chemical process (based on a Fenton reaction) has been found to degrade cytotoxic pharmaceuticals.[14]

4. Conclusion

The establishment of a nationally regulated, consistent system for the collection of unused pharmaceutical products as segregated waste from pharmacies, rest homes, hospices and hospitals is clearly a necessity.

A working party, which includes all relevant stake holders, including civil society, needs to be set up to investigate appropriate state-of-the-art methods for the chemical deactivation of APIs in pharmaceutical waste. The current out-of-date NZ Standard for the managament of healthcare waste needs to be revised with urgency. The sponsors/manufacturers of certain pharmaceutical dosage forms (e.g. transdermal patches) need to be required to provide collection and destruction systems as part of the market authorisation. We would also like to suggest that the pharmaceutical industry contributes to funding the development of the collection and disposal system.

5. References

1. Aus der Beek, T. *et al.* Pharmaceuticals in the environment—Global occurrences and perspectives. *Environ. Toxicol. Chem.* **35,** 823–835 (2016).
2. Fisher, P. & Collingnon, P. The water industry needs to join the fight against superbugs. *The Conversation* (2015). http://theconversation.com/the-water-industry-needs-to-join-the-fight-against-superbugs-37233
3. Marti, E., Variatza, E. & Balcazar, J. L. The role of aquatic ecosystems as reservoirs of antibiotic resistance. *Trends Microbiol.* **22,** 36–41 (2014).
4. Rizzo, L. *et al.* Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review. *Sci. Total Environ.* **447,** 345–360 (2013).
5. SAICM. Environmentally persistent pharmaceutical pollutants adopted as an emerging policy issue. http://www.saicm.org/index.php?option=com_content&view=article&id=566&Itemid=775
6. U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER). *Residual Drug in Transdermal and Related Drug Delivery Systems. Guidance for Industry*. (2011). http://www.fda.gov/downloads/Drugs/Guidances/UCM220796.pdf
7. Health Quality and Safety Commission New Zealand. Medication Alert Transdermal Patches. **Alert 15,** (2014).
8. Radio New Zealand. Medicine disposal 'a national disaster'. (2015). http://www.radionz.co.nz/news/national/279943/medicine-disposal-'a-national-disaster'
9. European Medicines Agency. *Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container*. (2016).
10. Council of Europe. European Pharmacopoeia, Section 5.1.1 (2014).
11. World Health Organization. *Safe management of wastes from health-care activities*. (2014).
12. Barnes, K. K. *et al.* Pharmaceuticals and other organic waste water contaminants within a leachate plume downgradient of a municipal landfill. *Groundw. Monit. Remediat.* **24,** 119–126 (2004).
13. United Nations Environment Programme. *Compedium of Technologies for Treatment/Destruction of Healthcare Waste*. (2012).
14. United Nations Environment Programme. Global Healthcare Waste Project - Best Available Technologies. http://www.gefmedwaste.org/best-available-technologies-overview