

Pharmaceutical Pollution in the Environment: Issues for Australia, New Zealand and Pacific Island countries



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1 Summary

Wherever there are humans there is a risk of contamination of the environment from pharmaceuticals, principally from treated and untreated sewage. Over 200 different pharmaceutical agents, including antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, lipid-lowering drugs, estrogens, and drugs from other therapeutic groups, have been detected in aquatic and terrestrial environments around the world, including areas as remote as the Antarctic.

Published data demonstrates the presence of multiple pharmaceutical compounds in treated wastewater, river systems, marine sediments and sewage sludge (biosolids) in Australia and New Zealand. Pharmaceuticals were detected in wastewater destined for recycling, despite the water having been processed through advanced wastewater treatment systems. Furthermore, pharmaceutical residues have been detected in biosolids planned for use in land remediation. Environmental contamination with pharmaceutical residues also occurs as a result of the incorrect disposal of unwanted pharmaceuticals through the sewage system or in solid waste destined for landfill.

There appears to be no published measurements of pharmaceutical pollutants in the environment in and around Pacific Island countries. However, it is expected that seepage from septic tank and pit latrine systems, disposal of minimally treated sewage into lagoons and the ocean, and use of sewage sludge/biosolids on agricultural land could result in pharmaceutical pollution of surface, ground and marine waters. Inadequate disposal of unwanted or expired pharmaceuticals may also result in localized environmental pollution.

Pharmaceutical residues mainly enter the environment through excretion, either as the original pharmaceutical compound, or as a derivative of that compound. Wastewater treatment plants are currently not designed to remove pharmaceutical compounds and both solid and liquid outputs from wastewater treatment plants contain a mixture of pharmaceutical residues. The discharge of treated wastewater into rivers and oceans or onto land, and the spreading of sewage sludge/biosolids onto land as fertiliser therefore result in the pharmaceutical contamination of the environment. The use of recycled wastewater for irrigation can result in persistent contamination of soil and groundwater by pharmaceuticals.

Pharmaceuticals are highly active compounds that target specific biologic systems that can have adverse impacts on the physiology and behaviour of a variety of organisms even at low concentrations. These impacts can be exacerbated by chronic, long-term exposure to a complex mixture of pharmaceuticals in the environment. The presence of antibiotics in wastewater may promote antibiotic resistance in bacteria used in the wastewater treatment process as well as the bacteria present in aquatic environments impacted by wastewater effluent.

2 Recommendations

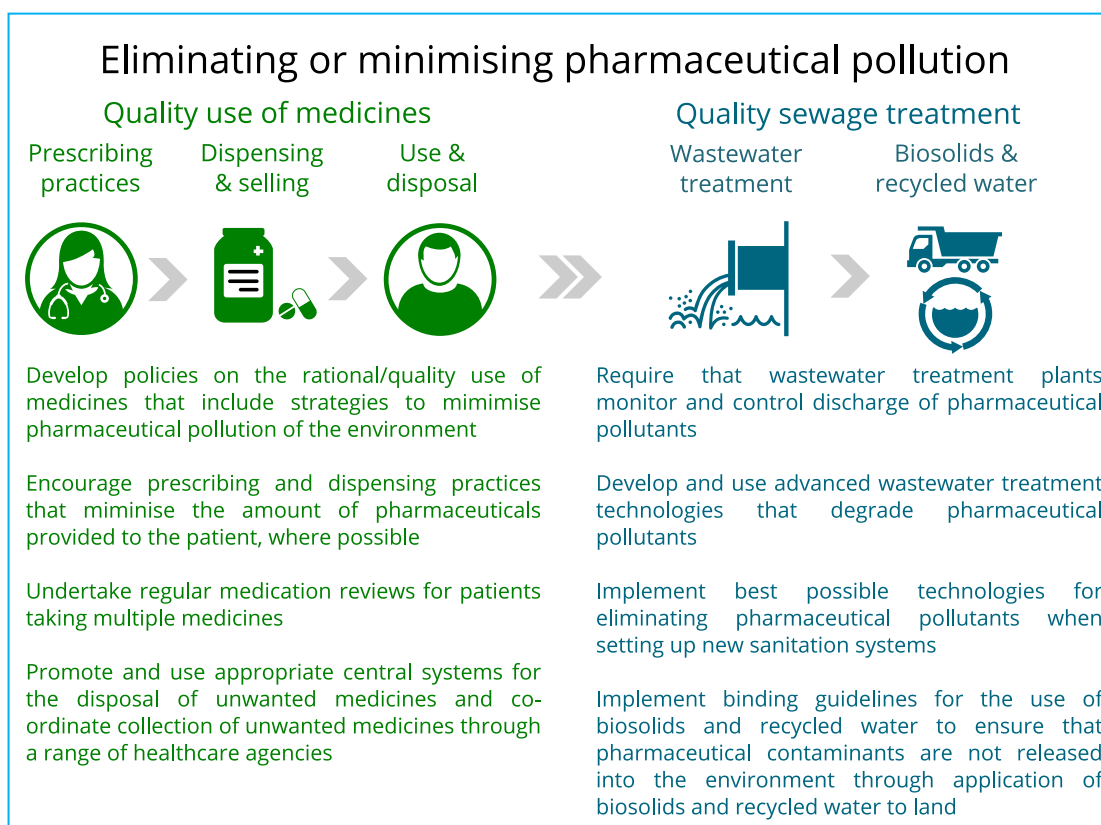
The elimination or minimisation of pharmaceutical pollution in the environment requires actions at both the level of the use of medicines and in the technologies for the disposal of sewage and wastewater treatment. The National Toxics Network recommends the implementation of policies for quality/rational use of medicines that include environmental considerations, and quality sewage treatment.

Quality use of medicines

The WHO's concept of rational use of medicines (also called quality use of medicines) should be expanded to include considerations of environmental impact. The implementation of this concept on a country level should include strategies for optimising systems for environmentally appropriate disposal of unwanted medicines, reducing the dispensing of excess medicines and providing regular medication reviews for patients.

Quality sewage treatment

A concept of quality sewage treatment should be developed that embraces advanced treatment technologies that remove and degrade pharmaceutical pollutants. Governments and industry need to recognise that even low concentrations of pharmaceutical residues released in treated water have the potential to cause serious environmental damage. Wastewater treatment plants should therefore be required to monitor and control the discharge of pharmaceutical pollutants. New sanitation systems should include technologies that remove and degrade pharmaceuticals as well as ensuring the removal of potential pathogens. Guidelines for the use of recycled water and biosolids should ensure that water and biosolids that are contaminated with pharmaceuticals are not applied to land.



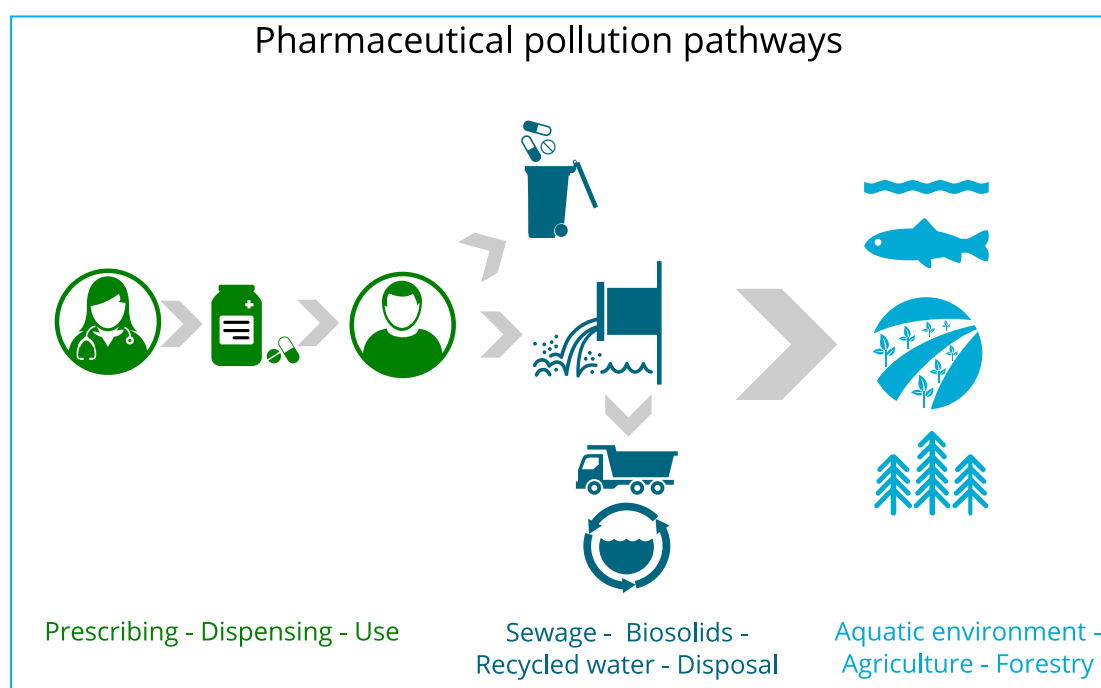


3 Pharmaceuticals pollutants are ubiquitous

Developments in medicine have resulted in an increasing use of pharmaceuticals, many of which are used to treat chronic conditions. During drug treatment, the active components of pharmaceutical products are largely excreted from the patient's body, either unchanged (as the same compounds that are present in the dosage form) or as derivatives or metabolites of these compounds. Excretion from patients thereby introduces pharmaceutical residues into the sewage disposal system and consequently into wastewater.

Currently, wastewater treatment systems are not designed to remove pharmaceutical residues and many of these compounds are released in wastewater effluent and consequently into the aquatic environment. Furthermore, use of recycled wastewater or sewage sludge/biosolids on agricultural and forestry land may result in pharmaceutical pollution of the terrestrial environment.

A further pathway whereby pharmaceutical residues may be introduced into the environment is through the inappropriate disposal of unused or expired pharmaceuticals into the wastewater system or landfill. In addition to human pharmaceuticals, veterinary pharmaceuticals may also contaminate land and waterways through runoff from agricultural land or directly through treated animals. This report focuses on the environmental impact of human pharmaceuticals only, with a specific focus on Australia, New Zealand and Pacific Island countries.



Pharmaceuticals are a concern even at very low environmental concentrations

Pharmaceuticals occur globally in the environment. One project has collated measurement data from over 71 countries that identified 631 different pharmaceutical agents (or their metabolites and transformation products) in the environment, including antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, lipid-lowering drugs, estrogens, and drugs from other therapeutic groups.¹ In freshwater systems alone, over 200 pharmaceuticals have been identified around the world.² The largest group of pharmaceuticals detected are antibiotics, followed by painkillers, cardiovascular drugs or blood lipid regulators and antidepressants.² Pharmaceutical residues originating from

treated or untreated sewage effluent have also been detected in marine waters and sediments,^{3,4} including in sea ice, coastal seawater and clams affected by the sewage effluent of two Antarctic research stations.⁵

Pharmaceutical residues have been commonly measured at tens or hundreds of nanograms per litre (ng/l) in waters, and in the microgram per kilogram (µg/kg) range in sediments affected by wastewater treatment plants. While these concentrations may appear low, pharmaceutically active compounds are designed to be active at low concentrations. Therefore, the presence of pharmaceutical residues in the environment even at ng/l concentrations may adversely impact a variety of biological systems and have broader negative effects on ecosystems. The 61 most frequently encountered pharmaceutical compounds in river systems around the world have been detected at median concentrations ranging from 6.2 ng/l to 163 673 ng/l.²

Pharmaceuticals are designed to specifically act on biological systems and generally have a biological effect at very low levels. Such highly active pharmaceuticals include endocrine disruptors,^a such as synthetic estrogens, and other compounds that act very selectively on specific cellular protein targets, such as receptors and enzymes. Many of these drug targets are evolutionally conserved between species. This means that analogous proteins to those that human drugs target may also be present in other vertebrate and invertebrate animals and plants. A review of 1,318 human drug targets found that analogues of 86% of these targets are present in zebrafish (*Danio rerio*), 61% in the water flea (*Daphnia*), and 35% in a green alga (*Chlamydomonas reinhardtii*).⁶ This indicates the potential for pharmaceuticals present in the environment to have an impact over a diverse range of organisms.⁷

Environmentally relevant concentrations of pharmaceutical residues have been shown to adversely affect a variety of organisms

The effects of various pharmaceutical residues detected in the environment on plant, animal and microbial life is largely unknown. However, there is evidence that even low levels of certain pharmaceuticals residues have both acute and chronic effects on various organisms, as well as potential indirect effects on wider ecosystems.

A number of studies around the world have documented disruption of reproductive physiology of fish exposed to natural and synthetic steroid estrogens from treated or untreated sewage effluent (see references cited in ⁸). One experimental study found that chronic exposure of fathead minnow (*Pimephales promelas*) to low concentrations (5–6 ng/l) of the synthetic estrogen 17α-ethinylestradiol (EE2, used as a contraceptive) in a freshwater lake produced reproductive failure, resulting in the complete collapse of the fish population in that lake.⁹ The direct effect of EE2 on the fathead minnow population and other small fish species in the lake was found to have corresponding indirect effects on the whole lake ecosystem due to disruption of the food web.¹⁰ The loss of these small fish resulted in a reduction in food supply for larger predator fish such as trout, leading to a corresponding loss of condition in these predator species.¹⁰

Low levels of certain pharmaceutical residues have also been shown to alter apparently more subtle aspects of physiology and behaviour in fish, which may ultimately result in broader population or ecosystem effects. For example, the presence of the benzodiazepine drug oxazepam (which is used as a sedative and to treat anxiety) at a concentration of as low as 1.8 µg/l was found to alter the behaviour and feeding of the European perch (*Perca fluviatilis*), and the effects of this drug on fish behaviour are considered likely to alter fish

^a For a review of endocrine disrupting chemicals and their impact on human health see: The Endocrine Society and IPEN (2014) Introduction to Endocrine Disrupting Chemicals (EDCs): A guide for public interest organizations and policy-makers (available at <http://ipen.org/news/new-edcs-resource-guide>)

fitness and food web structures.¹¹ Similarly, environmentally relevant concentrations of the antidepressant fluoxetine have been found to affect the behaviour of the American native fathead minnow fish (*Pimephales promelas*)¹² and low concentrations (7.85 µg/ml) of carbamazepine (an anti-epilepsy drug and mood stabiliser) were found to alter brain physiology in atlantic salmon (*Salmo salar*).¹³

The effects of pharmaceutical residues are also not restricted to vertebrate species. A study into the effect on a marine polychaete worm of five pharmaceutical compounds commonly found in surface waters affected by wastewater (carbamazepine, ibuprofen, fluoxetine, 17α-ethynylestradiol and propranolol), has demonstrated that environmental concentrations of these compounds in sediments are sufficient to induce sub-lethal changes that may adversely affect the physiology of the organism.¹⁴ Low concentrations of fluoxetine have also been shown to have an effect on cuttlefish (*Sepia officinalis*) behaviour¹⁵ and to induce physiological changes in water fleas (*Daphnia magna*).¹⁶

Antibiotic pollutants exacerbate the problem of antibiotic resistance

Antibiotic compounds are designed to destroy microbes. Therefore the presence of antibiotic residues in the environment is likely to have a direct impact on the viability and diversity of microbial populations in aquatic and terrestrial ecosystems. Accordingly, antibiotics need to be considered as a distinctive class of pharmaceutical compounds with particular environmental and health implications.

In addition to the direct effect on microorganisms that are essential for many biological processes, there is also concern that environmental contamination with antibiotics could facilitate the development of antibiotic resistance in pathogenic (or potentially pathogenic) organisms. The presence of antibiotics in wastewater may promote antibiotic resistance in bacteria used in the wastewater treatment process as well as the bacteria present in aquatic environments impacted by wastewater effluent.^{17,18} Indeed, the presence of antibiotic residues in combination with the high bacterial density, high nutrient and high oxygen conditions in the biological treatment systems of wastewater treatment plants can provide ideal conditions for the transfer of antibiotic resistance genes, creating hotspots for the dissemination of antibiotic resistant bacteria into the environment.¹⁹

The development of antibiotic resistance has resulted in a reduction in the number of effective antibiotics available for the treatment of infectious diseases in humans. Antibiotic resistance is already occurring across a number of organisms known to cause serious disease in humans.²⁰ This has resulted in what the World Health Organization (WHO) describes as a major threat to human health globally.²⁰

‘Cocktail’ effects need to be considered

The wide range of compounds used as pharmaceuticals include groups of compounds that have similar effects, or target the same cellular systems. For example, the commonly used selective serotonin reuptake inhibitor antidepressants all act to prevent the reuptake of the neurotransmitter serotonin; a number of the pharmaceuticals prescribed for cardiac conditions have the same cellular target; and a number of the drugs used to inhibit stomach acid production act via the same cellular mechanism. Multiple examples of drugs in these categories have been detected in the environment (see Table 2 for examples from New Zealand).

Mixtures of pharmaceuticals may be more toxic than single pharmaceutical actives, particularly where a mixture of similarly acting pharmaceuticals is present. For example, the ecotoxicity of mixtures of the NSAIDs diclofenac, ibuprofen, naproxen, and acetylsalicylic acid (evaluated using acute *Daphnia* and algal tests) was found to be considerable, even at concentrations at which the single substances showed no or only very slight effects.²¹

Accordingly, it is important that any assessment of pharmaceutical residues in the environment takes into consideration a chronic exposure to mixtures of pharmaceuticals that can interact synergistically, additively or antagonistically.²²

Persistence and transformation products

Some pharmaceutical residues are resistant to degradation and are therefore more persistent in the environment. Other pharmaceutical compounds may ultimately degrade or transform in environmental systems to less environmentally toxic forms, but the constant re-introduction of these through discharge from wastewater treatment plants creates pseudo-persistence (i.e. continual and ongoing exposure) in the environment. Furthermore, degradation or transformation of a pharmaceutical compound does not always equate with detoxification. A number of pharmaceutical transformation products that are produced in the environment by physical, chemical or biological processes have been identified to be more toxic than the parent compound.²³ For example, two cephalosporin antibiotics, cefazolin and cephapirin, were found to undergo a light-induced transformation to form products that were more toxic and more resistant to photodegradation than the original compounds.²⁴

However, the assessment of the ecotoxicological effects of pharmaceutical residues often does not take into consideration the effects of such transformation products, and the measurement of pharmaceutical pollutants in the environment frequently does not include analysis for these transformation products. This may result in the ecological effects of pharmaceutical pollutants being greatly underestimated.

Effects on human health

The direct effects of environmental pharmaceuticals on human health are unknown. The potential human health risks of pharmaceuticals in the environment are often downplayed on the basis that the environmental concentration of these residues is low and therefore below the 'dose' that would have a therapeutic effect. However, the data on dosage effects for a drug may not include information on the whole population. For example, if a drug is designed to be taken only by adults, the effect of low concentrations of that drug on children or pregnant women may simply be unknown. Furthermore, there is unlikely to be information available on the effects of chronic exposure to a cocktail of pharmaceuticals in the environment, many of which may be designed to act on the same body systems.

It is therefore important to consider the complex context of the environmental exposure to pharmaceuticals rather than relying on toxicology information required for the registration of a pharmaceutical product for a particular use and in a particular group of the population.



4 Wastewater treatment

Wastewater treatment is not designed to remove pharmaceuticals

In urban environments, wastewater is transported through the sewage system to be treated at a wastewater treatment plant (WWTP). The treatment systems at WWTPs can be separated into primary, secondary and tertiary treatment. Primary treatment involves screening, settling and removal of solids, secondary treatment includes biological treatment using bacteria and tertiary treatment includes further filtering, chemical and/or ultraviolet light treatment processes.^{25,26} The products of the WWTP process are liquid effluent and solid sludge. The effluent is mostly discharged into surface water systems, but may also be recycled, for example as irrigation water for agriculture or process water for industry.²⁷ The sludge may be disposed of in landfill or by incineration. Increasingly, the sludge, often termed 'biosolids', is also used as a fertilizer or soil additive on agricultural land or in land remediation.

The focus of wastewater treatment is on the elimination of potential pathogens and the removal of solids. Wastewater treatment plants are therefore generally not designed to remove or degrade pharmaceutical residues, and numerous studies have shown the presence of pharmaceutical residues in both treated water and sludge from wastewater treatment plants.²⁸ Certain pharmaceutical residues have been demonstrated to be particularly resistant to removal using primary sedimentation and secondary microbial treatment processes. For example, secondary wastewater treatment does not eliminate carbamazepine (which is used to treat epilepsy and bipolar disorder), and this drug has even been detected at higher concentrations in treated water than untreated water.^{29,30} The increase in concentration during water treatment is hypothesised to be due to the conversion of metabolites of carbamazepine to the parent drug during microbial treatment.²⁹ The synthetic steroid estrogen EE2 is also resistant to removal by enhanced primary wastewater treatment, and has been shown to accumulate in sewage sludge.³¹

Many studies investigating the removal of pharmaceutical residues during wastewater treatment look at whether the form of the compound present in the pharmaceutical product (the 'parent compound') can be detected. Such analyses may therefore not detect the derivatives or metabolites of these compounds that may also have negative environmental effects. The absence of the parent compound does not necessarily indicate a complete degradation of the compound, but may reflect a mere chemical transformation into a different compound that may not be detectable with the used analytical method.²⁸ Accordingly, it is essential that methods for removing pharmaceutical residues take into account transformation products of the parent pharmaceutical compound that are formed by metabolism in the patient, the action of microbial enzymes during wastewater treatment or by chemical- or light-induced transformation processes.

The water discharged from WWTPs is the primary medium for the introduction of pharmaceutical residues into aquatic ecosystems. Accordingly, there needs to be a focus on the use of advanced treatment systems to remove pharmaceutical residues from treated wastewater before it is released into the environment.



Sewage sludge accumulates pharmaceuticals

WWTPs have two outputs: treated wastewater and sewage sludge. Certain pharmaceutical residues have been found to concentrate in the solid, sludge phase during wastewater treatment.³² There is an increasing trend to use treated sewage sludge (also termed ‘biosolids’) as a soil additive on agricultural land and this application of sewage sludge to land may provide another route by which pharmaceutical residues can contaminate the environment. Biosolids are generally not tested for the pharmaceutical residues prior to use. For instance, pharmaceutical residues have been detected in biosolids that had otherwise met the criteria for application onto land in Michigan, USA.³³ Pharmaceuticals have also been detected in stockpiled biosolids in New Zealand that are destined to be applied to land.³⁴

The pharmaceutical contaminants in biosolids may be taken up by any plants grown on land to which biosolids have been applied. For example, five types of vegetable plant (pepper, collard, lettuce, radish and tomato) have been shown to take up the pharmaceuticals contaminants diphenhydramine (an antihistamine) and carbamazepine from biosolids that were used to treat the soil.³⁵ Accordingly, the use of biosolids as a ‘fertiliser’ on agricultural land involves the risk of contaminating food crops with pharmaceutical residues.



Pharmaceuticals persist in soils irrigated with recycled water and can be taken up by crop plants

Wastewater from WWTPs not only impacts on surface waters that receive the wastewater, but can also directly impact the land through the use of recycled wastewater for land irrigation. Certain pharmaceuticals, such as antibiotics, may have a direct impact on the microbial population that is essential to soil function. Furthermore, there is evidence that pharmaceutical residues may be taken up into plants, including crop plants, grown on soils contaminated with pharmaceuticals.^{36,37}

Pharmaceutical residues can also persist in soils. For example, the pharmaceutical compounds carbamazepine, lamotrigine (an anticonvulsant), sildenafil (the active ingredient in the product Viagra), sulfapyridine (an antibiotic) and metoprolol (a beta-blocker) were found to be resistant to degradation in soil, and accumulated in soils irrigated with treated wastewater containing these compounds.³⁸ The reuse of treated domestic wastewater for irrigation has been found to contribute to pharmaceutical contamination of groundwater on Mallorca, Spain.³⁹ Accordingly, the use of recycled wastewater for irrigation can result in persistent contamination of soil and groundwater by pharmaceuticals.



5 Pharmaceutical pollutants in Australia, New Zealand and Pacific Island countries



To date there have only been limited analyses of pharmaceutical pollutants in the environment in Australia and New Zealand and no reported analyses in any Pacific Island country.

Tables 1 and 2 summarise the pharmaceutical residues that have been reported in WWTP effluent, river waters, sewage sludge and marine sediments in Australia and New Zealand. The data come from journal articles, a PhD thesis and two publicly available reports made for local councils in New Zealand.^{3,4,34,40–44} This information is not a comprehensive survey of the pharmaceuticals that are present as environmental pollutants in Australia and New Zealand, as the studies mostly focus on specific aspects of water treatment and on specific pharmaceutical compounds. However, one recent analysis of organic contaminants in rivers around Australia in different land use areas has found that six pharmaceuticals (salicylic acid, paracetamol, carbamazepine, primidone, phenytoin and gemfibrozil) were detected in more than 10% of samples.⁴⁰ Paracetamol was detected in 45% of these samples, with a maximum concentration of 7150 ng/l, and carbamazepine was detected in 27% of samples, with a maximum concentration of 682 ng/l.⁴⁰

The data from Australia and New Zealand indicate that there are similar levels of contamination of WWTP effluent, surface waters and sewage sludge with pharmaceuticals as have been measured in other parts of the world.

Potential for pharmaceutical pollution in the Pacific

While there is currently no published data on the presence of pharmaceutical pollutants in and around Pacific Island countries, it is to be expected that the pharmaceuticals used in these countries will find their way into the environment, as is the case in other parts of the world.

There is no readily available information on the quantity of pharmaceuticals prescribed and used in Pacific Island countries. Most Pacific Island countries have lists of medicines, based on the WHO's Model Lists of Essential Medicines, that are procured by the public sector for supply through the public health care system.^{45–56} Listed medicines include a number of pharmaceuticals that have been identified as environmental pollutants in other parts of the world. Private doctors in Pacific Island countries also prescribe drugs other than those included in the lists of essential medicines used in public health care systems and therefore other potentially polluting pharmaceuticals may also be present in these environments.

The Western Pacific region has the highest rates of diabetes in the world.⁵⁷ In 2014, prevalence of diabetes was 37.4% in the Marshall Islands, 30.8% in the Federated States of Micronesia, 29.8% in Tokelau, 25.4% in the Cook Islands and 23.9% in Kiribati (compared with 5.1% in Australia).⁵⁷ Metformin, which is listed in all essential medicines lists, is generally considered the first line drug treatment for diabetes mellitus type II.^{48,54,58} This is generally a long term treatment and the drug is not metabolised in the body, so is therefore excreted unmodified.⁵⁹ Metformin and its bacterial transformation product guanylurea are stable and persistent (or pseudo-persistent) in environmental waters and both compounds have been detected in lake, river, sea and drinking water in Germany.⁵⁹ Accordingly, this drug also has the potential to be an environmental pollutant in Pacific Island countries.

In at least some Pacific Island countries there also appears to be a very high use of antibiotics. For example, a 2007 found that in public hospitals and private pharmacies in Samoa, 66.4% of prescriptions included an antibiotic (compared to an average in developing

countries of 40 to 60%).⁶⁰ Furthermore, in Palau, the costs of antibiotics in 2008-2009 were found to exceed 42% of hospital medicines budgets (compared with an expected 20-25%).⁶¹ Given that various antibiotics have been identified in environmental waters around the world (see Tables 1 and 2 for antibiotics identified in Australian and New Zealand waters), it is to be expected that members of this class of pharmaceuticals that are used in Pacific Island countries will also be present in Pacific Island environments.

Table 1: Pharmaceutical residues detected in the Australian environment

Pharmaceutical active	Therapeutic use	Source	Location	Average conc.	Max conc.	Ref
Amitriptyline	Antidepressant	Various river systems	Around Australia		62 ng/l	⁴⁰
Amoxicillin	Antibiotic	WWTP effluent	South-East Queensland		50 ng/l	⁴
		River waters	South-East Queensland		200 ng/l	⁴
Atenolol	Anti-hypertensive (beta blocker)	Various river systems	Around Australia		133 ng/l	⁴⁰
<i>o</i> -Hydroxy atorvastatin (metabolite of atorvastatin)	Lipid regulator - statin	Various river systems	Around Australia		20 ng/l	⁴⁰
<i>p</i> -Hydroxy atorvastatin (metabolite of atorvastatin)	Lipid regulator - statin	Various river systems	Around Australia		34 ng/l	⁴⁰
Carbamazepine	Anti-epileptic, treatment of bipolar disorder	Various river systems	Around Australia	30 ng/l	682 ng/l	⁴⁰
Cefaclor	Antibiotic	WWTP effluent	South-East Queensland		1800ng/l	⁴
		River waters	South-East Queensland		200 ng/l	⁴
Cephalexin	Antibiotic	WWTP effluent	South-East Queensland		250 ng/l	⁴
		River waters	South-East Queensland		100 ng/l	⁴
Ciprofloxacin	Antibiotic	WWTP effluent	Brisbane	640 ng/l	742 ng/l	⁴¹
		River waters	South-East Queensland		1300 ng/l	⁴
Clindamycin	Antibiotic	WWTP effluent	South-East Queensland	5 ng/l	70 ng/l	⁴
		River waters	South-East Queensland	1 ng/l	10 ng/l	⁴
Clozapine	Antipsychotic	Various river systems	Around Australia		90 ng/l	⁴⁰
Diazepam	Anti-anxiety	Various river systems	Around Australia		8 ng/l	⁴⁰
Doxycycline	Antibiotic	WWTP effluent	South-East Queensland	10 ng/l	150 ng/l	⁴
		River waters	South-East Queensland		400 ng/l	⁴
Fluoxetine	Antidepressant	Various river systems	Around Australia		22 ng/l	⁴⁰
Gemfibrozil	Lipid regulator	Various river	Around		213 ng/l	⁴⁰

Pharmaceutical active	Therapeutic use	Source	Location	Average conc.	Max conc.	Ref
		systems	Australia			
Ibuprofen	NSAID	Various river systems	Around Australia		44 ng/l	⁴⁰
		Tertiary treated wastewater	Western Sydney	16.9 ng/l	120 ng/l	⁴²
Ketoprofen	NSAID	Tertiary treated wastewater	Western Sydney	10.3 ng/l	20.7 ng/l	⁴²
Nalidixic acid	Antibiotic	WWTP effluent	South-East Queensland		450 ng/l	⁴
		River waters	South-East Queensland	50 ng/l	750 ng/l	⁴
Naproxen	NSAID	Various river systems	Around Australia		347 ng/l	⁴⁰
		Tertiary treated wastewater	Western Sydney	30.5 ng/l	178.9 ng/l	⁴²
Norfloxacin	Antibiotic	WWTP effluent	South-East Queensland	25 ng/l	250 ng/l	⁴
		Environmental waters	South-East Queensland	30 ng/l	1150 ng/l	⁴
Paracetamol	Analgesic	Various river systems	Around Australia	85 ng/l	7150 ng/l	⁴⁰
Penicillin V	Antibiotic	WWTP effluent	South-East Queensland		2000 ng/l	⁴
		River waters	South-East Queensland		10 ng/l	⁴
Phenytoin	Anti-epileptic	Various river systems	Around Australia		145 ng/l	⁴⁰
Primidone	Anti-epileptic	Various river systems	Around Australia		259 ng/l	⁴⁰
Roxithromycin	Antibiotic	WWTP effluent	South-East Queensland	20 ng/l	500 ng/l	⁴
		River waters	South-East Queensland	9 ng/l	350 ng/l	⁴
Salicylic acid - metabolite of acetylsalicylic acid (aspirin)	Analgesic	Various river systems	Around Australia	82 ng/l*	1530 ng/l*	⁴⁰
Sulphamethoxazole	Antibiotic	WWTP effluent	Brisbane	270 ng/l	320 ng/l	⁴¹
		WWTP effluent	South-East Queensland	50 ng/l	200 ng/l	⁴
		River waters	South-East Queensland	8 ng/l	2000 ng/l	⁴
		Various river systems	Around Australia		67 ng/l	⁴⁰
Sulfasalazine	Antibiotic	WWTP effluent	South-East Queensland	4 ng/l	150 ng/l	⁴
		River waters	South-East Queensland		30 ng/l	⁴
Tetracycline	Antibiotic	WWTP effluent	South-East Queensland		20 ng/l	⁴
		River waters	South-East Queensland		80 ng/l	⁴
Triamterene	Diuretic	Various river systems	Around Australia		14 ng/l	⁴⁰
Trimethoprim	Antibiotic	WWTP effluent	Brisbane	50 ng/l	70 ng/l	⁴¹

Pharmaceutical active	Therapeutic use	Source	Location	Average conc.	Max conc.	Ref
		WWTP effluent	South-East Queensland	10 ng/l	250 ng/l	⁴
		River waters	South-East Queensland	3 ng/l	150 ng/l	⁴
		Various river systems	Around Australia		657 ng/l	⁴⁰
Verapamil	Anti-hypertensive	Various river systems	Around Australia		36 ng/l	⁴⁰

*Salicylic acid produced by some plant species, notably willow (*Salix*) that frequently grows around Australian waterways. Accordingly, at least some of the salicylic acid detected may be of plant rather than pharmaceutical origin.

Table 2: Pharmaceutical residues detected in the New Zealand environment

Pharmaceutical active	Therapeutic use	Source	Location	Average conc.	Ref
Amytriptyline	Anti-depressant	WWTP effluent	Rotorua	29.5 ng/l	⁴⁴
Atorvastatin	Lipid regulator	Biosolids	Kaikōura	17 µg/kg	³⁴
Bezafibrate	Lipid regulator	Marine sediments	Auckland	0.16 µg/kg	³
		Biosolids	Kaikōura	8 µg/kg	³⁴
Carbamazepine	Anti-epileptic, treatment of bipolar disorder	WWTP effluent	Rotorua	709 ng/l	⁴⁴
		Final solids	Rotorua	49 µg/kg	⁴⁴
		Composted solids	Rotorua	29 µg/kg	⁴⁴
		Marine sediments	Auckland	0.67 µg/kg	³
		Biosolids	Kaikōura	105 µg/kg	³⁴
Cimetidine	Inhibitor of stomach acid production	Marine sediments	Auckland	0.94 µg/kg	³
		Biosolids	Kaikōura	10 µg/kg	³⁴
Ciprofloxacin	Antibiotic	Biosolids	Kaikōura	29 µg/kg	³⁴
Clarithromycin	Antibiotic	Marine sediments	Auckland	1.45 µg/kg	³
		Biosolids	Kaikōura	4 µg/kg	³⁴
Clenbuterol	Bronchodilator	Marine sediments	Auckland	0.75 µg/kg	³
Diclofenac	NSAID	Marine sediments	Auckland	1.95 µg/kg	³
		Biosolids	Kaikōura	8 µg/kg	³⁴
Diltiazem	Cardiovascular (calcium channel blocker)	WWTP effluent	Rotorua	133 ng/l	⁴⁴
17α-Ethinylestradiol (EE2)	Contraceptive	WWTP effluent	Rotorua	8.6 ng/l	⁴⁴
Famotidine	Inhibitor of stomach acid production	Marine sediments	Auckland	0.70 µg/kg	³
		Biosolids	Kaikōura	2 µg/kg	³⁴
Fenofibrate*	Lipid regulator	Marine sediments	Auckland	1.38 µg/kg	³
		Biosolids	Kaikōura	67 µg/kg	³⁴
Frusemide	Diuretic	Biosolids	Kaikōura	8 µg/kg	³⁴
Gemfibrozil	Lipid regulator	Biosolids	Kaikōura	1 µg/kg	³⁴
Hydrochlorothiazide	Diuretic	Marine sediments	Auckland	0.38 µg/kg	³
		Biosolids	Kaikōura	4 µg/kg	³⁴
Ibuprofen	NSAID	WWTP effluent	Rotorua	41 ng/l	⁴⁴
Mefenamic Acid	NSAID	Biosolids	Kaikōura	6 µg/kg	³⁴

Pharmaceutical active	Therapeutic use	Source	Location	Average conc.	Ref
Metoprolol	Anti-hypertensive (beta blocker)	Marine sediments	Auckland	2.06 µg/kg	³
		Biosolids	Kaikōura	42 µg/kg	³⁴
Nadolol	Anti-hypertensive (beta blocker)	Marine sediments	Auckland	0.31 µg/kg	³
		Biosolids	Kaikōura	1 µg/kg	³⁴
Naproxen	NSAID	WWTP effluent	Rotorua	987 ng/l	⁴⁴
		Marine sediments	Auckland	5.53 µg/kg	³
		Biosolids	Kaikōura	47 µg/kg	³⁴
Nifuroxazide	Antibiotic	Biosolids	Kaikōura	36 µg/kg	³⁴
Paracetamol (Acetaminophen)	Analgesic	Marine sediments	Auckland	7.66 µg/kg	³
		Biosolids	Kaikōura	76 µg/kg	³⁴
Pentobarbital	Barbiturate	Biosolids	Kaikōura	10 µg/kg	³⁴
Pindolol	Anti-hypertensive (beta blocker)	Marine sediments	Auckland	0.41 µg/kg	³
Propanolol	Anti-hypertensive (beta blocker)	Biosolids	Kaikōura	114 µg/kg	³⁴
Ranitidine	Inhibitor of stomach acid production	Marine sediments	Auckland	1.16 µg/kg	³
		Biosolids	Kaikōura	23 µg/kg [§]	³⁴
Roxythromycin	Antibiotic	Marine sediments	Auckland	1.28 µg/kg	³
Salbutamol	Relief of bronchospasm in asthma	Marine sediments	Auckland	0.53 µg/kg	³
Sotalol	Anti-hypertensive (beta blocker)	Marine sediments	Auckland	0.92 µg/kg	³
		Biosolids	Kaikōura	7 µg/kg	³⁴
Sulfadiazine	Antibiotic	Biosolids	Kaikōura	9 µg/kg	³⁴
Sulfamethazine	Antibiotic	Marine sediments	Auckland	0.44 µg/kg	³
		Biosolids	Kaikōura	3 µg/kg	³⁴
Sulfamethoxazole	Antibiotic	Biosolids	Kaikōura	15 µg/kg	³⁴
Timolol	Anti-hypertensive (beta blocker)	Marine sediments	Auckland	0.80 µg/kg	³
Trimethoprim	Antibiotic	Marine sediments	Auckland	0.23 µg/kg	³
		Biosolids	Kaikōura	5 µg/kg	³⁴

*Note: Clofibric acid, a compound related to fenofibrate, has been demonstrated to be persistent in the aquatic environment.⁶² This suggests that fenofibrate may also be resistant to degradation and accumulate in the sediment.



6 Wastewater treatment, water recycling and use of sewage sludge in Australia

Recycled water may still contain pharmaceuticals

Many parts of Australia have limited water resources and there has been a focus on the reuse of wastewater. Such recycled wastewater is used in Australia for pasture irrigation, industrial uses (e.g. cooling and process water for an oil refinery) and domestic and commercial non-drinking uses.²⁷ In Perth, Western Australia, a system is also being set up to use recycled water to replenish groundwater aquifers that ultimately supply the city's drinking water.⁶³

Water destined for recycling undergoes advanced wastewater treatment processes, including microfiltration and reverse osmosis. Both microfiltration and reverse osmosis involve passing the wastewater through a membrane that is intended to prevent the passage of contaminant. The process therefore leaves behind 'brine' with concentrated pollutants. Reverse osmosis is considered to be one of the most advanced methods designed to remove micropollutants from wastewater. However, it has been shown that at least some micropollutants are not completely removed in the reverse osmosis process, notably the endocrine disrupter bisphenol A,⁶⁴ as well as certain antibiotics.⁴¹ Where the reverse osmosis treatment is able to retain pharmaceuticals during water treatment, these pharmaceutical residues remain in the captured 'brine' and adsorbed onto the reverse osmosis membrane, and therefore still require appropriate disposal.²⁷

The use of current advanced wastewater treatment process, such as reverse osmosis, is therefore not a complete solution to the problem of pharmaceutical pollution.

Disposal and use of sewage sludge in Australia

Australia produces around 330 000 tonnes of dry sewage sludge solids (biosolids) per year.⁶⁵ Around 59% of these biosolids are used in agriculture, 10% in landscaping, composting and land rehabilitation and 20% are stockpiled.⁶⁵

Table 3: Biosolids Production and End Use (tonnes/year) by State (source: Australian & New Zealand Biosolids Partnership, <http://www.biosolids.com.au>)

	Agriculture	Landscaping (compost)	Land Rehabilitation	Landfill	Ocean discharge	Stockpile	Unspecified	Other	TOTAL
NSW & ACT	49,132.0	15,7245.0	8,577.5	1,499.5	3,942.0	238.5	4,416.5	14,600.0	98130.5
QLD	62,556.0		2,263.0	2,961.5			2,391.5		70,172.0
SA	30,477.5								30,477.5
TAS	2,993.0	473.0		3,359.5					6,825.5
VIC	29,617.0	2,690.0	962.0			62,051.0		317.0	95,638.0
WA & NT	20,440.0	2,007.5		2,874.5		2,935.0			28,256.5
TOTAL	195,215.5	20,895.5	11,802.5	10,695.0	3,942.0	65,224.5	6,808.0	14,917.0	329500.0

Regulation of biosolids in Australia

The use and disposal of biosolids is regulated through state guidelines.^{66–72} The objective of all the guidelines is to encourage ‘beneficial use’ of biosolids. The guidelines provide upper limits on certain contaminants in the biosolids in order to classify as a particular grade, and also limits on certain contaminants in the receiving soils. The contaminants include certain metals, DDT and derivatives, certain organochlorine pesticides and polychlorinated biphenyls (PCBs).

There is no requirement under any of the guidelines to assess biosolids for contamination with pharmaceutical residues or compounds from personal care products prior to land application. This is the case despite at least one study demonstrating the presence of the antimicrobial agent triclosan, which is used in many personal care products, in biosolids from 19 WWTPs around Australia at levels that may cause adverse effects in the soil environment.⁷³ Triclosan, like many pharmaceutical residues, is known to accumulate in sediment and therefore in sewage sludge. A South Australian study has also demonstrated that triclosan persists in soil to which biosolids have been applied.⁷⁴

Furthermore, estrogenic activity has been detected in biosolids in Australia and this activity persists in soil after application of the biosolids.⁷⁵ A contributor to this estrogenic activity is likely to be the contraceptive agent EE2.⁷⁵

The draft *South Australian Biosolids Guidelines for the safe handling and reuse of biosolids* (2009) does refer to the possibility of contamination of biosolids by pharmaceuticals and personal care products and state that further research is required into this issue.⁶⁹

The *Western Australian guidelines for biosolids management* (2012) provides ‘contaminant acceptance concentration thresholds’ for four metals and two pesticides (in Table 1, page 25) and states:

Other chemicals apart from those listed in Table 1 may be present in biosolids, including dioxins, pharmaceuticals and personal care products. Research to date has not demonstrated that these contaminants need to be regulated with respect to biosolids application in accordance with best management practices.

*In line with the intention of these guidelines to be a living document, they will be updated as required if evidence emerges that these contaminants are of concern to the environment or health.*⁶⁶

While waiting for the results of further research, biosolids can currently be applied to land according to these guidelines without any testing for pharmaceutical pollutants.

The biosolids guidelines for New South Wales,⁶⁸ Queensland (which applies the New South Wales guidelines), Victoria,⁶⁷ Tasmania,⁷⁰ and the Northern Territory (which applies the national guidelines⁷²) do not refer to pharmaceutical residues at all. The Australian Capital Territory (ACT) does not appear to apply specific guidelines.⁷⁶



7 Wastewater treatment and disposal of sewage sludge in New Zealand

The majority of domestic wastewater in New Zealand is treated at one of 320 public WWTPs, with the wastewater of 15-20 percent of the population being disposed of in septic tanks.⁷⁷ Only about half of wastewater in New Zealand cities has treatment to tertiary level.⁷⁸ Nearly half (47%) of the 125 WWTPs for which information is available discharge the wastewater effluent into a river or stream, 18% discharge onto land and 22% into the sea.⁷⁷

Twenty-six municipal treatment plants (that serve 30% of the population) divert most of the sewage sludge to land reclamation however just over one third of the sewage sludge is disposed of in landfill.⁷⁷

There is currently very limited information available on the contamination of the aquatic and terrestrial environment in New Zealand from pharmaceutical residues introduced into the environment from WWTPs. However, it is clear from studies around the world that WWTPs are a source of environmental contamination by pharmaceuticals. Indeed, a recent study of marine sediments around Auckland demonstrates that these sediments are contaminated with a number of different pharmaceutical residues,³ the majority of which are likely have been introduced into sediments via WWTP effluent. Conditions that can be imposed under resource consents for the disposal of effluent from WWTPs could provide a mechanism for the monitoring and elimination of these pharmaceutical residues from WWTP outputs in New Zealand.

Regulation of wastewater treatment discharges into the New Zealand environment

The discharge of wastewater and sewage sludge into the environment in New Zealand is regulated by the provisions of the *Resource Management Act* (1991) through regional councils. Resource Consents approved by regional councils can include monitoring of and restrictions on the levels of certain contaminants. To date, there appear to have been no specific requirements to test for pharmaceutical residues in wastewater and sewage sludge. However, conditions placed on the following two resource consents for wastewater discharge are attempting to address the issue of pharmaceutical contamination.

1. Environment Southland imposed the following conditions on the consent for the Milford Sound Development Authority to discharge treated wastewater into Milford Sound (RMA Consent M186-005):

By November 2018, the consent holder shall provide a report to the Council's Compliance Manager on the potential effects on the receiving environment at Deepwater Basin, Milford Sound of anthropogenic chemicals such as endocrine disruptors, pharmaceuticals and person care products likely to be present in the effluent from the Milford Sound wastewater treatment plant. The report shall include an assessment of whether there is the feasibility, including financial feasibility, to measure such chemicals in the treated effluent and/or receiving waters, and if so, what concentrations are considered to have an adverse effect and whether the chemicals are having an adverse effect on the receiving environment. [quoted in⁷⁸]

2. Environment Waikato imposed the following conditions on the Hamilton City Councils' consent to discharge treated wastewater into the Waikato River:

The consent holder shall in 2012 and thereafter on a five yearly basis undertake an investigation into the likelihood of viral pathogens and organic chemicals (including

but not limited to endocrine disrupting chemicals and steroid hormones) entering the river water from the discharge. An analysis of the likely removal of viral pathogens and substances within each stage of the treatment system (including bypasses) shall be made and based on actual results. The results of this investigation shall be compared with any relevant literature on the subject on removal of viral pathogens and organic chemicals within treated wastewater and their environmental fate/public health risk. A copy of the investigation and comparison shall be supplied to the Waikato Regional Council by 1 December each year the investigation is required to be undertaken [quoted in⁷⁸]

Disposal and use of sewage sludge in New Zealand

New Zealand produces around 74 000 tonnes of dried biosolids per year.⁷⁹ Around 60% of these biosolids are disposed of in landfill, 15% are used in agriculture and forestry, 10% are used in land rehabilitation, 5% are composted and 10% are disposed of by discharge into the ocean.⁷⁹

The disposal and use of sewage sludge (biosolids) in New Zealand is regulated through the resource consent process of Regional Councils, under the *Resource Management Act* (1991).

The non-legally binding *Guidelines for the safe application of biosolids to land in New Zealand*⁸⁰ was prepared by Water New Zealand (previously the New Zealand Water and Wastes Association), which represents, among others, the local government agencies responsible for wastewater treatment and disposal. These guidelines provide limits on the levels of certain metals and organic compounds for biosolids to be classified as 'A' or 'B'. Pharmaceutical residues are not included in the list of compounds.

Around a third of biosolids in New Zealand is disposed of in landfill.⁷⁷ The large amount of sewage sludge disposed of in landfill in New Zealand is a concern, as the degree of contamination by pharmaceuticals and the leaching and persistence of any such contamination, is unknown.

There is now an increasing trend to look at what is termed the 'beneficial' uses of biosolids to save on the costs of landfill. Such alternative uses include the application of biosolids to forestry land and in the production of fertiliser.⁸¹ These uses of biosolids are highly problematic, as they do not take into account the contamination of the biosolids with pharmaceutical pollutants and other endocrine disrupting chemicals.

For instance, the New Plymouth City Council produces a sewage sludge-based fertilizer that is sold in New Zealand under the name Bioboost®. Bioboost® is marketed as 'an organic, slow-release, granular fertiliser suitable for general garden use'.⁸² This fertiliser is stated to be manufactured in accordance with the biosolids guidelines, however the product is known to exceed the limits for zinc and copper required for the 'A' classification under the guidelines.⁸³ Furthermore, the guidelines do not require assessment for contamination by pharmaceutical residues. It is therefore unknown to what extent the product is contaminated with pharmaceutical residues. Nor is there any information on the persistence and toxicity of any such pharmaceutical contaminants in the soils to which the product is applied.

The resource consents for the application of biosolids to forestry land in the Nelson area require the monitoring of soil levels of certain metals and organochlorine and organophosphate compounds, but otherwise do not require monitoring for other organic pollutants, such as pharmaceutical residues.⁸⁴ The degree of pharmaceutical contamination of these biosolids is therefore unknown. The application of sewage sludge/biosolids to forestry land and as a fertiliser may potentially be providing a route for pharmaceutical residues to be introduced to the environment.

Case study: Proposed application of biosolids to land in Kaikōura

Kaikōura, a small town on the east coast of the South Island, has accumulated a stockpile of 1500 tonnes of sewage sludge under a resource consent granted for 10 years until 2016. The Centre for Integrated Biowaste Research (CIBR) has worked with the Kaikōura District Council to engage with the community to explore ‘beneficial options’ for reusing the sewage sludge.⁸⁵ In September 2013, the CIBR prepared a Case Study Report.³⁴ The Kaikōura District Council has agreed to adopt the recommendations of this report.

The CIBR report (on page 6) states the following under the heading ‘Organic contaminants in Kaikōura biosolids’:

International and New Zealand data on organic wastewater contaminants (OWCs) in biosolids and their fate and effects is insufficient to develop a suitable risk assessment under New Zealand conditions. However, there is little evidence to limit land application of biosolids for the purpose of rehabilitating degraded soils. The added benefits of nutrient input to facilitate vegetation and reestablishment of viable functioning topsoil can outweigh the potential risks arising from the presence of OWCs in the Kaikōura biosolids.

The report then proceeds to state that 27 pharmaceutical residues were measured in the Kaikōura biosolids. The authors of the report acknowledge that the long-term effects of the contaminants are unknown. However, they nevertheless consider that the large number of earthworms in the biosolids indicates that the material has negligible toxicity. The biosolids also showed no short-term acute toxicity to earthworms and springtails.

In fact, the CIBR report lists pharmaceutical residues detected in the Kaikōura biosolids at a concentration of 114 µg/kg for the beta-blocker propranolol, 105 µg/kg for carbamazepine and 76 µg/kg for paracetamol. The Kaikōura biosolids were also shown to contain 65 µg/kg of antibiotics (6 different compounds). A complete list of the pharmaceuticals detected in the CIBR study is provided in Table 2.

The Kaikōura biosolids have been accumulated over a number of years and are still contaminated with pharmaceutical residues, demonstrating at least some degree of persistence of these residues. The true accumulative effect and persistence of these compounds is unknown. The acute toxicity testing using the earthworm and springtail assay is clearly going to be insufficient to assess the broader environmental effects of these contaminants, including chronic effects on a variety of organisms from soil microbes to plants and human health.

There is therefore a need to more fully assess the extent and possible effects of pharmaceutical contamination of biosolids before these biosolids are spread more widely on land.



8 Wastewater treatment and disposal of sewage sludge in Pacific Island countries

Given the dispersed populations over numerous islands, most people living in Pacific Island countries do not have access to reticulated sewage systems, with septic tanks being the most common system in many countries.^{86–97} Facilities for the treatment of sewage from both reticulated and septic tank sewage systems are limited in the Pacific region. Reports on water resource management published in 2007 by the Pacific Islands Applied Geoscience Commission (SOPAC) identified a number of Pacific Island countries that dispose of raw or minimally treated sewage into lagoons or other marine systems.^{86,88,91,93,97–99} There is evidence of leakage of sewage from septic tanks and other systems (such as pit latrines) into the surrounding environment, including groundwater and marine waters.^{88,94,95}

In addition to the discharge and seepage of sewage into the environment, in some Pacific Island countries sewage solids and the contents of septic tanks are directly applied to agricultural land. For example, sewage sludge from the only wastewater treatment plant in Yap State, Federated States of Micronesia, is used for agriculture after only minimal treatment.¹⁰⁰ Pharmaceutical pollutants may therefore be applied to agricultural land and seeping into the ground water via this route.

There is increasing evidence that pharmaceutical pollutants are present in marine environments around the world, even in such remote areas as the Antarctic,⁵ and that these pollutants are impacting on marine and coastal environments.¹⁰¹ While there are no data available on the presence of pharmaceutical pollutants in the Pacific region, it is to be expected that pharmaceuticals used by Pacific populations will end up in marine environments through discharge of wastewater and leaching and runoff from the land. These pharmaceutical residues may accumulate in marine sediments and have adverse effects on sensitive Pacific marine ecosystems.

There is a clear need for improvements in wastewater/sanitation systems in many Pacific Island countries. Projects to improve wastewater treatment and sanitation systems provide an opportunity to consider the use of technologies that not only remove pathogenic organisms from the wastewater, but can also minimise the release of other pollutants such as pharmaceuticals into the Pacific environment. Furthermore, the use of sewage sludge as fertilizer also needs to be regulated to ensure contaminated material is not being applied to land.



9 Disposal of unwanted or expired pharmaceuticals

The use and subsequent excretion of pharmaceuticals is likely to be the major route by which pharmaceutical residues enter the environment around the world. However, the improper disposal of unused or expired pharmaceuticals into sewage and landfill may also be a significant contributor to pharmaceutical pollution of the environment. As discussed above, WWTP processes often do not result in the removal of pharmaceutical compounds. Therefore, disposal of unwanted pharmaceuticals via the sewage system can ultimately result in the discharge of pharmaceutical residues into waterways. Pharmaceuticals disposed of in the solid waste generally end up in landfill, from where they can leach into, and persist in, the ground water.¹⁰²

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 pharmaceutical active even after they have been used. Indeed, 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 pharmaceutical active being present in the patch at the end of the treatment period.¹⁰³ Therefore, the inappropriate disposal of these used dosage systems could result in environmental contamination by the remaining pharmaceutical residue.

The presence of excess or unused medications in the home can be the result of patient non-compliance, over-prescribing by doctors, or policies that encourage initial dispensing of larger numbers of doses than may ultimately be required. Pharmaceuticals that have passed their expiry date also need to be disposed of appropriately.

Collection systems for unwanted pharmaceuticals, which generally have pharmacies as collection points, have been set up in many countries. However, even where these systems are in place, the most common methods of disposal of unwanted pharmaceuticals are the sewage system (via the toilet or sink) or as hard rubbish (that often ends up in landfill).¹⁰⁴

Once the pharmaceuticals are collected, they need to be safely destroyed. Systems such as the Return Unwanted Medicines (RUM) Project in Australia dispose of the collected pharmaceuticals by high temperature incineration, as recommended by the WHO. While this may be preferable to disposal of the pharmaceuticals via the sewage system or in landfill, the use of incineration for waste disposal generally is of concern, due to the risk of toxic emissions into the air. There currently appear to be no environmentally appropriate alternative methods for the disposal of unwanted pharmaceuticals. A potentially more environmentally benign method is likely to involve a chemical deactivation process. There is some indication that certain alkaline hydrolysis waste disposal methods may destroy certain pharmaceuticals, such as chemotherapeutic drugs,¹⁰⁵ and this type of technology may be able to be applied to the disposal of unwanted pharmaceuticals more generally. However, this is, as yet, untested.

Inappropriate disposal of unwanted pharmaceuticals or used dosage systems can result in pharmaceutical pollution in the environment. Therefore, every country needs to implement state-run schemes to return unwanted pharmaceuticals that are accessible and well advertised and understood by the public and health professionals. Clear information and

assistance on the appropriate disposal of pharmaceutical dosage systems such as transdermal patches is also required. One option may be to require manufacturers of such dosage systems to include sealable disposal bags that are returned to the pharmacy or hospital for safe disposal.

Disposal of unwanted or expired pharmaceuticals in Australia could be improved

In Australia, the Commonwealth Government funded Return Unwanted Medicines (RUM) Project has been set up to provide a system of disposing of unwanted or expired medicines through community pharmacies.¹⁰⁶ After collection, the pharmaceuticals are sent to Environmental Protection Authority (EPA) - approved high temperature incineration facilities in Victoria and Western Australia for destruction. While commendable, the RUM Project currently has limited funding for public awareness campaigns and it is unclear the extent to which the Australian public knows of and uses this system.

There is clearly scope to improve public awareness in Australia of both the impact on the environment of incorrect disposal of pharmaceuticals and in the availability of the RUM Project disposal system. Legislation that prohibits the inappropriate disposal of pharmaceuticals may also be required.

Disposal of unwanted or expired pharmaceuticals in New Zealand is unsatisfactory

In New Zealand unwanted medicines are most commonly disposed of by flushing down the toilet or in landfill, with only between 13 and 24% of medications being returned to a pharmacy for disposal.¹⁰⁷ There is no country-wide system for the collection and disposal of unwanted pharmaceuticals and the funding for such disposal systems varies between the District Health Boards that oversee community pharmacies.^{78,108}

A 2001 survey of pharmaceutical disposal practices has shown that not all pharmaceuticals returned to community pharmacies are disposed of in an environmentally appropriate manner.¹⁰⁸ This survey found that many pharmacists did not know whether the third-party contractors engaged to dispose of unused pharmaceuticals actually use environmentally appropriate disposal techniques.¹⁰⁸ In pharmacies themselves, liquid pharmaceutical formulations are often disposed of down the sink, or toilet.¹⁰⁸ Accordingly, there is a need for a state-run, co-ordinated and system of disposing of unused pharmaceuticals in New Zealand, together with increased awareness of the environmental issues around disposal of pharmaceuticals for pharmacists as well as the general public. Appropriate legislation that prohibits the inappropriate disposal of pharmaceuticals may also be required.

Disposal of unwanted pharmaceuticals in the Pacific region – coordinated systems are needed

There appear to be no co-ordinated systems for the disposal of unwanted or expired pharmaceuticals in Pacific Island countries, and a general lack of suitable health waste disposal facilities makes the environmentally acceptable disposal of such pharmaceuticals a serious challenge.

In 2014, a survey of hospitals in 14 Pacific Island countries was undertaken as part of PacWaste (Pacific Hazardous Waste), a four year (2013-2017) project funded by the European Union and implemented by the Secretariat of the Pacific Regional Environmental Programme (SPREP) to improve regional hazardous waste management across the Pacific.¹⁰⁹ In all hospitals surveyed, there were no facilities for the effective disposal of pharmaceutical waste. Such waste was found to be disposed of through landfill, on-site burning, or through low temperature, wood-fired incineration processes.¹¹⁰⁻¹²³ For example, out of date pharmaceuticals at one hospital in Kiribati are disposed of in landfill after being ground up and mixed with sand¹¹³ and at a hospital in Tuvalu pharmaceutical waste was observed being dumped as landfill without being treated in any manner.¹²²

Medical supply donations can exacerbate pharmaceutical pollution problem. Inappropriate donations of pharmaceuticals to Pacific Island countries can result in large stockpiles of unusable and/or expired products with no suitable method of disposal. The SPREP survey for Samoa identified that there was a large stockpile of out of date pharmaceuticals at a hospital in Upolu.¹¹⁹ A large proportion of these out of date pharmaceuticals were donated pharmaceuticals that had already expired before arrival in Samoa.¹¹⁹

Disposal of pharmaceutical residues through landfill or inadequate incineration clearly poses a risk of the leaching of these residues into the environment. Therefore, it will be essential for the PacWaste project to ensure that appropriate disposal protocols are set up that specifically deal with the issue of pharmaceutical waste to avoid environmental pollution.



10 Rational/quality use of medicines: strategies that include the environment

One approach to minimising pharmaceutical pollution is to reduce excess prescribing, dispensing and use of pharmaceuticals, without compromising health outcomes.

In the late 1970s, the WHO introduced the concept of ‘essential medicines’, which are medicines that satisfy the priority health care needs of the population.¹²⁴ Part of this concept was to define the ‘rational use of medicines’ whereby:

patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community¹²⁴

NTN recommends that the last phrase be amended to ‘and at the lowest cost to them, their community and the environment’, without substantially altering the remit of the ‘rational use of medicine’. Indeed, implementation of strategies that are currently already considered under this concept would have the effect of reducing the environmental impact of pharmaceuticals. For example, the WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, a considerable proportion of which is likely to involve overprescribing.¹²⁵ The rational use of medicines therefore includes strategies to minimise overprescribing or dispensing, which also reduces the environmental impact of these pharmaceutical products.

Including environmental considerations in the rational use of medicines also provides a platform to develop and implement policies around the appropriate disposal of unwanted pharmaceutical products and used packaging containing pharmaceutical residues. Accordingly, it is suggested that the introduction of environmental considerations into the rational use of medicines strategies implemented at the country level would be a valuable aid in reducing pharmaceutical pollution.

The Australian Department of Health and Aging has adopted the principles of the rational use of medicines in the Quality Use of Medicines strategy, which is central to Australia’s National Medicines Policy.¹²⁶ The definition of Quality Use of Medicines includes: “selecting management options wisely by ... recognising that there may be better ways than medicine to manage many disorders” and “choosing suitable medicines if a medicine is considered necessary so that the best available option is selected by taking into account ... costs for the individual, the community and the health system as a whole”.¹²⁶ Again, this definition should be amended to include the aspect of ‘costs for the environment’.

Rational use of antibiotics will reduce environmental pollution by antibiotics

There has been a particular concern about the overprescribing of antibiotics and the consequential increase in bacterial antibiotic resistance. In Palau, standard treatment guidelines for antibiotics have been developed as a response to the overprescribing of often broad-spectrum antibiotics and inappropriate prescribing of antibiotics for viral infections.⁶¹ In Australia, NPS Medicinewise (which was established to undertake work on the quality use of medicines) has a programme to encourage appropriate prescribing and use of antibiotics to counteract the trend towards antibiotic resistance due to overuse and resulting overexposure of microorganisms to these medicines.¹²⁷ A reduction in overall antibiotic use

will also result in a reduction in antibiotics as environmental pollutants, and corresponding reduction in the risk of the further development of antibiotic resistance in microorganisms in the environment. Accordingly, policies that promote the rational use of antibiotics not only improve health outcomes and reduce cost for the health system, but are also beneficial to the environment.

Reducing the number of medications used

Further strategies that could be promoted under rational/quality use of medicines policies include requirements for the regular assessment of medications in patients prescribed multiple pharmaceutical products for chronic conditions. Such 'polypharmacy' can be common in elderly patients, and may at least partially result from inappropriate prescribing and/or use of a medicine by the patient for longer than required.¹²⁸ A requirement for pharmacists and/or doctors to undertake regular medication reviews for such patients may enable a reduction in the number of pharmaceuticals used.

Prescribing/dispensing smaller pack sizes will have positive effects for the environment

A further approach to minimising the amount of excess pharmaceuticals provided to patients is to establish prescribing and dispensing practices that result in the patient only receiving the number of doses required.

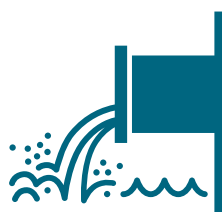
For example, to reduce the costs associated with the dispensing of pharmaceuticals at community pharmacies, there is a policy in New Zealand of dispensing government-subsidised pharmaceuticals as a three month supply all at once, rather than first supplying a smaller amount with repeats.¹²⁹ This policy means that the pharmacist is required to dispense a full three month supply, unless the prescription provides a limit on the total number of doses.¹²⁸ Unfortunately the introduction of this policy has contributed to an increase in the amounts of unused medicine that needs disposal, as patients may stop taking the medications before the end of the three month period, for example due to adverse drug reactions, a change in treatment, or the resolution of the condition.¹⁰⁷ 'All at once' dispensing may be appropriate where the patient has a stable, chronic condition and a regular dosing regimen. However, the use of this dispensing practice where the patient's condition is acute or unstable will lead to wastage of pharmaceuticals and the potential environmental impacts of incorrect disposal. Accordingly, pharmaceutical dispensing practices need to be designed to reduce wastage, with the corresponding cost and environmental benefits.

Policies that require the prescription and dispensing of smaller pack sizes or fewer doses where appropriate would assist in reducing the amount of pharmaceuticals that become environmental pollutants.

Collection systems for the disposal of unwanted or expired medicines are essential

Australia currently has a system for the collection and disposal of unwanted or expired medicines. However, it is unclear the extent to which this system is being used by the public and healthcare institutions. There is currently no general system of collecting and disposing of unwanted or expired medicines in New Zealand, and the methods for disposing of such pharmaceuticals in many Pacific Island countries are highly inadequate.

Policies around the rational/quality use of medicines should also include strategies for the development and effective use of systems for the environmentally appropriate disposal of unwanted or expired medicines and used packaging that includes residual pharmaceutical product (such as transdermal patches and inhalers). These collection and disposal systems should be well publicised, readily accessible and supported by healthcare workers in the community. For example, healthcare workers that attend to patients in the home could undertake regular audits of the medicines stored in the home and remove unwanted or expired medication for appropriate disposal.



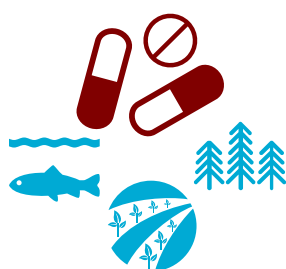
11 Advanced wastewater treatment technologies

The elimination of pharmaceutical pollutants from wastewater ideally involves the complete degradation of the pharmaceutical compounds. Reverse osmosis treatments, which are already used in some wastewater treatment plants may be capable of retaining some (although not all) pharmaceuticals from the wastewater stream.

However, reverse osmosis is an essentially physical process that does not result in the degradation of the pharmaceutical compounds. Rather, any pollutants captured during the reverse osmosis process are concentrated in the so-called reverse osmosis concentrate or brine, which then requires further treatment to remove or break down these contaminants. Clearly, reverse osmosis alone is not the solution to the problem of pharmaceutical pollution.

A number of chemical and biological degradation processes have been investigated for pharmaceutical pollutants in wastewater. Certain advanced oxidation processes, such as Fenton-like reactions, show a promising ability to degrade pharmaceutical residues in wastewater.^{130–132} For example, solar-driven advanced oxidation processes have been shown to remove carbamazepine¹³¹ and the antibiotics ofloxacin and trimethoprim¹³² from wastewater. However, there is still much research required into these processes, as in some cases advanced oxidation can result in the production of toxic transformation products of the compounds being oxidized.¹³³ Bioreactors containing white rot fungi such as *Trametes versicolor* have also been shown to be effective at removing certain pharmaceutical residues from wastewater.^{134,135} Furthermore, the combination of ozone treatment and biological activated carbon filtration has been shown to reduce the levels of certain pharmaceutical pollutants in wastewater at three Australian water recycling facilities. However it was unclear the extent to which this process resulted in the degradation of the pharmaceuticals in question.¹³⁶ For small wastewater treatment plants it may also be possible to implement the relatively simple, but effective technology of slow sand filters (as biofilm reactors) for the removal and degradation of certain pharmaceutical pollutants.¹³⁷

There are a number of technologies that could potentially be developed for routine use in WWTPs to remove and degrade pharmaceutical pollutants. It must be recognised that such advanced water treatment technologies are not to be reserved merely for specialised water recycling plants as the elimination of micropollutants such as pharmaceuticals from the wastewater flow is essential to prevent environmental pollution. The removal and degradation of these pollutants should be considered as essential to the functioning of any WWTPs as the removal of potential pathogens and the reduction in nutrient levels in effluent that enters the aquatic environment. There should be a focus on developing cost effective advanced water treatment technologies that remove and degrade pharmaceutical pollutants, which may be implemented in a variety of water treatment systems, including new sanitation systems being implemented in Pacific Island nations.



12 Conclusions: pharmaceutical pollution of the environment is a significant issue

Pharmaceutical pollution in the environment is a serious issue for human health and the environment globally. Complex mixtures of pharmaceutical residues are ubiquitous in aquatic systems impacted by treated or untreated sewage, and are continuously being introduced into these environments. Pharmaceutical pollutants have even been detected in areas of such low human population as the Antarctic.

The extent of the impact of this pollution on human health and the environment is unknown, however physiological and behavioural effects have already been detected in a number of species. This has the potential to result in adverse effects at the species and population level in sensitive freshwater and marine ecosystems. Many pharmaceuticals that are found in the environment act on the human endocrine system. There is growing evidence of the adverse impacts on human health of endocrine disruptors present at low levels in the environment. Furthermore, the ubiquitous presence of antibiotics in the environment is likely to be contributing to the global increase in antibiotic resistance and corresponding public health crisis.

Pharmaceutical pollution of the environment needs to be addressed through the quality use of medicines and quality wastewater treatment.

The quality use of medicines needs to encompass prescribing and dispensing practices which reduce the overuse and wastage of pharmaceuticals, as well as requiring robust systems for the environmentally appropriate disposal of unwanted or expired pharmaceuticals. In Australia, there needs to be more public awareness of the RUM Project for the disposal of unwanted medicines. In New Zealand and Pacific Island countries, consistent and appropriate collection and disposal systems need to be employed. Projects aimed at improving waste disposal in Pacific Island Countries, such as PacWaste, need to specifically address the disposal of pharmaceutical waste.

Quality wastewater treatment requires that priority attention to be given to advanced treatment technologies that remove and degrade pharmaceutical pollutants. There is also an urgent need for harmonised standards and binding guidelines in Australia and New Zealand to regulate pharmaceutical contaminants in treated wastewater and biosolids. In Pacific Island countries sanitation systems need to be introduced that address the issue of reducing environment contamination by pharmaceutical residues at the same time as addressing the already well-established need for eliminating the pathways of pathogens and excess nutrients into the groundwater and wider environment. The use of sewage sludge or biosolids as fertiliser in Pacific Island countries must also be regulated to ensure that contaminated material is not spread on to the land.

Through the appropriate use of pharmaceuticals and appropriate sewage and wastewater treatment the environmental impact of pharmaceuticals may be minimised without affecting the health benefits gained through the use of these medicines.

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