Assessment of the Potential Health Hazards Posed by Hospital Wastewater

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ABBREVIATIONS

AMR	Antimicrobial resistance
ARG	Antibiotic resistance gene
BPA	Bisphenol A
CT	Computed tomography
GBCA	Gadolinium based contrast agent
HAV	Hepatitis A virus
HWW	Hospital wastewater
IARC	International Agency for Research on Cancer
ICA	Iodinated contrast agent
MRI	Magnetic resonance imaging
PET	Positron emission tomography
STEC	Shiga-Toxin producing *E. coli*
WHO	World Health Organization
WWTP	Wastewater treatment plant

EXECUTIVE SUMMARY

Hospital wastewater contains a large variety of contaminants that may pose a risk to public health. This report has been prepared for Te Whatu Ora/Health New Zealand to provide a high-level overview of the contaminants present in hospital wastewater and the potential health effects from exposure to these. The identified contaminants and health effects are based on international published literature.

The report focuses on the presence of contaminants in untreated hospital wastewater. Concentrations in untreated hospital wastewater were used to develop an understanding of potential concentrations present without treatment or dilution. Treatment processes will vary in the ability to remove contaminants found in hospital wastewater. Additionally, given hospital wastewater is discharged into the municipal system, overflows or spills could result in exposure to untreated wastewater from hospitals.

The contaminants reviewed in this report were identified through a scoping literature search and have been grouped into the following categories: Contrast agents, heavy metals, human bodily waste, other chemicals, pathogenic microorganisms and antimicrobial resistance, pharmaceuticals, and radioisotopes. Contaminants were included if they were present in hospital wastewater and had evidence of human health effects from exposure. For each of the categories of contaminants a review of the potential human health effects has been included.

Additionally, there is a section discussing Te Ao Māori perspectives on wastewater. This is a brief summary of the tikanga surrounding wastewater, and equity and te Tiriti o Waitangi considerations in the management of wastewater. It will not cover the full depth and breadth of Māori perspectives and should not serve as a substitute for partnership directly with Māori communities. While there was no literature identified specifically discussing hospital wastewater and tikanga Māori, the effects of wastewater discharge into waterways on hauora and concern regarding emerging contaminants present in wastewater for Māori is evident across the literature generally discussing wastewater.

For many of the contaminants detected in hospital wastewater, the concentrations and indeed presence of specific contaminants varied significantly between studies. The presence of contaminants and concentrations may vary depending on the type of hospital, treatments and service offered, pharmaceuticals available and prevalence of disease in the community it serves. While broadly similar, such as the overall presence of high loads of

pharmaceuticals, individual hospital wastewaters appear to each have unique characteristics and should be considered contextually to accurately assess potential health risks.

The potential health effects of exposure are largely well described in the literature for heavy metals and microbial pathogens present in hospital wastewater with known doses required for health effects. However, emerging contaminants may have limited epidemiological evidence on adverse health effects, particularly when considering chronic low dose exposure, with no health-based exposure guidelines available. There are several knowledge gaps when considering the health effects of chronic low-dose exposure to pharmaceuticals, contrast agents and some chemicals identified. Additionally, there is little understanding of the effects of interactions between contaminants and how this may alter the effects on human health.

A clear concern from the literature is the role of hospital wastewater in the discharge of resistant microbes and the development of antimicrobial resistance. Antimicrobial resistance makes infections harder to treat and increases morbidity and mortality. High concentrations of antibiotics create selective pressure and the ability for wastewater to act as a reservoir for horizontal gene transfer. The discharge of resistant microbes from hospital wastewater to receiving environments is a risk to public health.

This report provides a high-level assessment of contaminants present in hospital wastewater internationally and potential health risks. None of the literature identified was from Aotearoa New Zealand. Inclusion in this report does not mean that a contaminant poses a risk to public health in Aotearoa New Zealand. Similarly, exclusion does not mean a contaminant is not a significant public health risk. Further work will be required to develop an in-depth understanding of the health risks associated with hospital wastewater in Aotearoa New Zealand.

1. INTRODUCTION

1.1 BACKGROUND

Hospital wastewater (HWW) contains a variety of contaminants which may be hazardous to human health, including microbial pathogens and chemical contaminants (Ajala et al., 2022; Kumari et al., 2020; Majumder et al., 2021; WHO, 2014). Additionally, due to the prevalence of antibiotics in HWW it is often a hotspot for emergence of antibiotic-resistance genes and antibiotic-resistant bacteria (Kaur et al., 2020). The contents of HWW will vary depending on the type of hospital, the demographics of the population it serves, as well as the prevalence of infectious diseases (Kumari et al., 2020). Hospital policies for disposal of potential hazards, such as cytotoxic medications and antibiotics, will also influence the make-up of discharged wastewater (Kumari et al., 2020).

HWW is estimated to be 5 to 15 times more toxic than municipal wastewater, with the emerging contaminants present in high concentrations (Emmanuel et al., 2005; Kumari et al., 2020). Despite having different hazard profile compared to municipal wastewater systems, globally HWW is often treated in conventional municipal wastewater plants (Kumari et al., 2020). Standard municipal wastewater treatment plants may be insufficient for effective removal of the higher concentration, and composition of hazards in HWW (Kumari et al., 2020).

This HWW report has stemmed from a series of reports for Te Whatu Ora (Health New Zealand) and Manatū Hauora (Ministry of Health) on potential public health hazards from wastewater and stormwater in Aotearoa New Zealand. The aim of this report is to review the wide range of different contaminants which may be present in hospital wastewaters and summarise the potential health risks associated with exposure. Identified contaminants have been organised into the following groups:

- Contrast agents
- Heavy metals
- Human bodily waste
- Other chemicals (e.g., surfactants)
- Pathogenic micro-organisms and antimicrobial resistance
- Pharmaceuticals

- Radioisotopes

It is important to note that the aim of this report is to review the variety of contaminants which have been identified in HWW internationally. However, as this report does not include a full hazard assessment for each identified contaminant and inclusion in this report does not imply that a given contaminant will pose a human health hazard. Equally, non-inclusion does not imply that there are no human health risks. Finally, as there are no studies analysing hospital wastewater contaminants in New Zealand the report cannot imply that the contaminants identified in the literature will be present in the New Zealand context.

1.2 HOSPITAL WASTEWATER MANAGEMENT

The way in which HWW is managed varies around the globe (Kumari et al., 2020). In some counties it is treated before it is discharged to the municipal wastewater network or surface waters, whilst others discharge it directly to the municipal network where it is co-treated with municipal wastewater (Kumari et al., 2020). In many developing counties it is discharged directly to receiving environments without any treatment (Al Aukidy et al., 2018). International evidence shows that pre-treatment of hospital wastewater can reduce contamination before entering municipal wastewater systems for further treatment (Majumder et al., 2021).

In 1999, the World Health Organisation (WHO) released guidelines for safe management of wastes from health-care activities (updated in 2014). These guidelines recommend waste from certain departments (e.g., medical labs, dental, radiotherapy) be pre-treated before discharge to the sewer, and chemical waste (e.g., photochemicals, colourants, pharmaceuticals) be collected separately and not discharged to municipal wastewater (WHO, 2014).

Where it is pre-treated, the efficiency of removal of the different contaminants will depend on the treatment process used, with several different options employed globally (Majumder et al., 2021). Where it is discharged directly to the municipal network for co-treatment it is likely that many of the contaminants are poorly removed as conventional systems are often not designed for contaminants such as pharmaceuticals and persistent organic compounds (Eniola et al., 2022; Majumder et al., 2021). Additionally, HWW has a lower biodegradability index than municipal wastewater, reducing the efficacy of treatment in conventional wastewater treatment plants (Majumder et al., 2021). In Australia, hospital wastewater is known to generally be discharged directly to the municipal wastewater network and co-treated along with municipal wastewater (Kumari et al., 2020).

In New Zealand, hospital and healthcare waste is listed under the trade waste section in a Ministry for Environment report on the wastewater sector (MfE, 2020). The Auckland City Trade Waste Bylaw 2013 states that the discharge of hazardous or prohibited pharmaceuticals, and histological or pathological wastes to the public wastewater system are not permitted. Additionally, the New Zealand Standard 4204:2002 '*Management of Healthcare Waste'* details the standards for the disposal of health care waste. Readers are referred to this resource for detailed discussion of the acceptable waste management approaches for different categories of hospital waste.[1]

No publicly available information was found specifically detailing any hospital's wastewater consents in New Zealand. A resource consent for the new Dunedin hospital was reviewed with only a brief mention of the site already being situated near wastewater infrastructure.[2] Hospitals will have waste management policies for hazardous substances. It is assumed that non-prohibited hospital wastewater is discharged directly into municipal systems and co-treated. Municipal wastewater is included in councils' long term regional planning, with resource consents required which vary from 2-35 year duration (MfE, 2020). The Local Government Act 2002 requires councils to annually report on wastewater system performance. In general, there appears to be inconsistency between resource consents, particularly around monitoring, reporting, compliance limits and iwi considerations (MfE, 2020).

1.3 UNDERSTANDING THE RISK

This report is focused on the contaminants present in liquid untreated (raw) HWW. It does not factor in treatment methods and how this may change concentrations of contaminants. Untreated wastewater was chosen for review as all treatment methods have different efficacies which will vary across the range of contaminants present. Additionally, it does not consider the effects of treatments processes that result in contaminants being moved into the solid fraction, and the potential health consequences of this. Also, in considering exposure routes from untreated HWW, public health may be compromised by leaks, treatment plant failure or overflows. Ineffective wastewater treatment may result in poor removal of contaminants, and high concentrations being discharged into receiving environments. Figure 1.1, taken from the Ministry for Environment wastewater sector report (2020), details the type of wastewater overflows that may occur to cause exposure (MfE, 2020).

[1] NZS 4304:2002 :: Standards New Zealand
[2] NDH-Stage-3-Inpatient-Building-Resource-Consent-Application-11-August-2023.pdf (epa.govt.nz)

Figure 1: Type and description of wastewater overflows (MfE, 2020)

Wastewater overflow Type	Description
Dry weather overflow	Overflows from system failure, which normally would be either blockage or pump failure.
Combined sewer overflow	Overflows from combined stormwater and wastewater networks are combined sewer overflows. These combined systems are no longer constructed. However, some historic wastewater networks do overflow to the stormwater system in rainfall events or are design to convey combined stormwater and wastewater flows. Overflow points to either the coast or freshwater are included in these systems and designed to operate when it rains.
Uncontrolled wet weather overflow	Uncontrolled wet weather overflows are those that occur within a network in places that were not designed to overflow e.g. via manhole lids.
Controlled wet weather overflow	Controlled wet weather overflows in a network such that in rainfall events, where system capacity is exceeded, the overflow goes to a designated location – often a stream or river.

Wastewater systems in New Zealand may be impacted by aging or poorly designed infrastructure or be designed to out-dated environmental standards (Hughes et al., 2021). Inadequate wastewater infrastructure will be exacerbated by the implications of climate change on wastewater systems, including infrastructure damage from extreme weather events. Impacts from climate change, such as droughts or heavy rain, may include increased risk of system failure or leakage. (Hughes et al., 2021). Recent events in Tāmaki Makaurau, with a collapsed sewer line resulting in hundreds of litres of raw sewerage discharging into the Waitematā Harbour every second, highlights the importance of developing an understanding of the potential risks to public health from exposure. Events such as this may expose the public to untreated HWW if the site of the leak includes discharges from a hospital source.

1.4 APPROACH AND SCOPE

This report is part of a staged multipart analysis of the human health risks associated with wastewater, and how these could be managed in New Zealand. A high-level approach has been taken for this report aiming to provide an overview of the potential health hazards in HWW. Key contaminants of interest were identified during the proposal process for the project. No further categories were added by the lead author from this initial assessment.

Contaminants present in HWW that are known to present ecological risks but not health risks are not included in the report.

Relevant studies were identified by completing a scoping literature review on all categories of contaminants. Key words were identified to complete a literature search for each category, and where relevant, subcategory, of contaminants. Reference lists were also reviewed to further identify relevant studies. Broadly, literature selected for inclusion were primary studies or review articles detailing contaminants present in untreated hospital wastewater. Grey literature was not included in the assessment of presence of contaminants, however some sections include comparisons to standards for wastewater in Aotearoa and globally where relevant. Supplementary peer reviewed literature was accessed to describe the potential public health impacts of exposure to each group of contaminants. For the section on Te Ao Māori perspectives of wastewater a combination of peer reviewed literature, grey literature, and kōrero with ESR scientist Georgia Bell (Ngāti Maniapoto, Ngāti Pū, me Ngāi Te Rangi) were included to provide a broader perspective that may not be included in Eurocentric scientific journals.

Key aspects of this assessment include:

- A review of contaminants of concern to human health that may be present in hospital wastewater
- A broad overview of the potential human health risks of exposure to the identified contaminants

The report includes a brief summary of Te Ao Māori perspectives and considerations of wastewater. The lead author acknowledges their position as Pākehā, and the lens this will place on the report findings and interpretation. The section describing Māori perspectives on wastewater contamination is situated at the front. Readers are encouraged to consider this view of wastewater and the tikanga of wastewater contamination while reading the remainder of the report. Future work assessing hospital wastewater in New Zealand requires co-design and partnership with Māori to ensure they are meeting te Tiriti o Waitangi obligations.

As with previous reports in this series, the report focuses on the risks of contaminants present in untreated (‘raw’) wastewater. This means the findings of the report are relevant for potential hazards that would be present with illegal discharges, overflow, or treatment failure events. The report does not include the impact of treatment, movement of contaminants to the solid fraction, or dilution on the identified hazards. As a scoping assessment, it also does not complete detailed human health risk assessments for each contaminant. It is beyond the

scope of this report to comment on the potential concentrations of contaminants to complete a risk assessment for New Zealand HWW.

Further work is needed to assess the specific contaminant's concentration in HWW, pre and post treatment, and the magnitude of exposures to complete a comprehensive risk assessment. Hospital practices in disposal of contaminants may vary and will depend on the type and range of treatments and services offered at each hospital. There is potential for future reports to better characterise the public health risks and for case studies to quantify wastewater contaminants specifically in the New Zealand context.

2. TE AO MĀORI PERSPECTIVES AND TIKANGA FOR CONTAMINANTS IN WASTEWATER

2.1 BACKGROUND

This review recognises te Tiriti o Waitangi as the basis of the relationship between Māori and the Crown and the rights held by Māori in Aotearoa New Zealand. This section is a high-level overview of key themes relating to cultural perspectives of wastewater. It is not a definitive source of truth, and readers will still be required to undergo consultation with Māori stakeholders, including mana whenua, to inform and develop future projects in partnership. The author acknowledges this section is a broad overview and does not capture or represent all views held by Māori on wastewater. Perspectives and values held by iwi, hapū and whānau will not be uniform, and are influenced by specific relationships to the environment through whakapapa (genealogical links) (Afoa & Brockbank, 2019).

While there was no published literature identified specifically focusing on Māori views of hospital wastewater, there is published and grey literature commenting on wastewater in general. Additionally, the author notes that that much of the knowledge and values surrounding wastewater in Te Ao Māori may be held outside Eurocentric scientific literature. Using Mātauranga Māori alongside published scientific literature will deepen our understanding of the interconnectedness between the health of populations and the environment, and support positive outcomes for environmentally and socially sustainable wastewater management (Ahuriri-Driscoll et al., 2008; Broughton & McBreen, 2015).

There have been several Waitangi tribunal claims surrounding wastewater management. These highlight the importance of partnership on decision-making surrounding wastewater treatment and discharge options to ensure they incorporate Māori perspectives and priorities in a meaningful way (Ahuriri-Driscoll et al., 2008; Hepi et al., 2021; Pauling & Ataria, 2010). Utilisation of indigenous knowledge is best practice in the development of environmental health impact assessments due to indigenous relationships with the natural environment, indigenous rights under the United Nations Declaration on the Rights of Indigenous Peoples, and in the New Zealand context, te Tiriti o Waitangi (Broughton & McBreen, 2015). Further, Māori hold a role as kaitiaki (guardians) of the environment, a role that is active and requires the ability to exercise tino rangatiratanga, as guaranteed under te Tiriti o Waitangi (Ahuriri-Driscoll et al., 2008; Broughton & McBreen, 2015; Harmsworth & Awatere, 2013). The

relationship with, and health of the environment, is inseparably related to hauora (health and wellbeing) for Māori.

Alongside recognising the relationship between Māori and the environment is important to understand the interconnected cultural principles of tikanga, mauri, tapu, and noa when considering wastewater in the New Zealand context (Ahuriri-Driscoll et al., 2008). Each are summarised further below, but it is noted that briefly summarising outside of a cultural context will not adequately capture the essence of each principle.

Tikanga refers to a system of core values and standards that support or determine appropriate conduct (Afoa & Brockbank, 2019; Coxon & Eaton, 2023). It guides how Māori relate with all forms of life (Durie et al., 2017). Tikanga can be flexible and may be adapted to apply to a given situation. Mauri is best described as the life force or essence that life forms possess, which is interconnected with all other things (Ahuriri-Driscoll et al., 2008; Morgan, 2004). Given this, actions or pollutants that degrade the mauri of one life form, will impact the mauri of another it is connected to (Ahuriri-Driscoll et al., 2008). Mauri connects the physical and spiritual worlds and is derived from whakapapa (Harmsworth & Awatere, 2013). Māori exercise kaitiakitanga of the environment to protect the mauri of the people and the natural environment.

Tapu refers to a prohibition or restriction and describes something that sacred or untouchable (Ahuriri-Driscoll et al., 2008; Ataria et al., 2019). Conversely, noa describes people, settings or things as being free from restrictions (Ahuriri-Driscoll et al., 2008). Practically, tapu and noa can be seen as social codes that operate to protect the hauora of people. Tapu may be intrinsic or permanently attached to something, for example, a burial ground is always considered tapu (Ataria et al., 2019). Tapu can also be a temporal dimension, changing with time, situations or protocols. Tapu and noa are inter-relational concepts and must be considered in context, with guidance from mana whenua.

2.2 HOSPITAL WASTEWATER AND TIKANGA MĀORI

As previously highlighted, there was no literature identified that specifically focused on Māori perspectives and tikanga Māori for HWW. However, concepts included in general discussion of wastewater, and tikanga surrounding human bodily waste are relevant to discuss. Through the ongoing process of colonisation, Māori have experienced systematic loss of control over and decision-making power including in wastewater management (Durie et al., 2017; Hepi et al., 2021). Devaluing of Mātauranga Māori and tikanga Māori with power held by the crown has resulted in wastewater systems that are unacceptable to Māori (Durie et al., 2017). Tino rangatiratanga is a core element of te Tiriti o Waitangi (Durie et al., 2017).

Inability to exercise tino rangatiratanga over wastewater management, and the protection of wai, can be seen as a breach of te Tiriti o Waitangi (Durie et al., 2017).

Activities related to human waste are tapu. Separation of human waste and the food chain is an essential element of both traditional and contemporary tikanga Māori (Pauling & Ataria, 2010). Tikanga does not permit the discharge of waste into any form of wai (water) as it is the source of mahinga kai (food gathering) (Pauling & Ataria, 2010). In a paper discussing the influence of settler-colonialism and freshwater, a Māori scholar on tikanga, Sidney (Hirini) Moko Mead (Ngāti Awa), comments on the role of tapu surrounding waste (Parsons et al., 2021).

> "*The institution of tapu operates for the well being of people…Break the rules and immediately people are unsettled in the minds, are fearful of their well being because some very basic beliefs are being transgressed. Blood is tapu. Any part of a deceased person is tapu. Placenta and any part of the afterbirth is tapu. Menstruation blood is tapu. A body part of a living person is tapu. Excreta is tapu…There is no problem with the return of excreta or body parts to Papatūānuku…What is abhorrent is the idea of associating biosolids with the food chain*."

The tikanga surrounding human waste highlights the nature of the concepts of tapu and noa being grounded in keeping people safe (Georgia Bell, personal communication, (Parsons et al., 2021)). Another element of tapu and hospital wastewater is the consideration of waste originating from unwell or deceased people, including mortuary waste (MfE, 2020; Rangiwai, 2018). Human body waste in HWW may include tissue, blood, and excreta, all of which are considered tapu. Conventional wastewater treatment will also not remove the tapu associated with waste relating to illness or death (Georgia Bell, personal communication). Additionally, adaptation of tikanga may be required for understanding contemporary wastewater settings, particularly with emerging contaminants present in HWW.(Ataria et al., 2019). Respondents to a Ngāi Tahu survey identified hazardous wastes (e.g. chemicals, radioisotopes) as a specific area of concern, further highlighting the importance of developing an integrated science and Mātauranga understanding of wastewater contamination (Pauling & Ataria, 2010).

Wai is an essential ingredient of physical and spiritual life in Te Ao Māori. It is a cultural taonga (treasure) left by the ancestors for the life sustaining use of their descendants, and thus the descendants have the responsibility to protect it (Durie et al., 2017). Hāparu describes dirtying of the essence of life forms and applies to waterways that have become contaminated (Durie et al., 2017). No matter how well treated the wastewater, discharge into waterways is highly offensive in Te Ao Māori and will render it hāpuru (Durie et al., 2017).

This means that even if biological of physical water standards are met following treatment of wastewater, it may not be acceptable from a cultural perspective (Durie et al., 2017). Waterways that with waste discharged into them can diminish or destroy the mauri of the water, which can only be restored through Papatūānuku (Afoa & Brockbank, 2019; Pauling & Ataria, 2010). Treatment options involving the whenua (land), such as wetlands, are generally preferred by Māori. When wastewater is connected and interacts with the whenua, it can pass from tapu to noa (Afoa & Brockbank, 2019).

In 2021, local hapū representatives in Tairāwhiti successfully advocated for separate management of mortuary waste, highlighting the potential for shared decision making that meets all stakeholders needs (MfE, 2020). However, on the whole there are significant challenges for Māori to have meaningful partnership in the management of wastewater (MfE, 2020; Pauling & Ataria, 2010). There are numerous examples of resource consent processes where western science has been prioritised over Mātauranga Māori, and opportunities for tino rangatiratanga, meaningful partnership and shared decision making remain limited (Ataria et al., 2019; Durie et al., 2017). Research completed by Ngāi Tahu on values and issues regarding waste recommended that iwi and hapū are proactively involved in resource consents, explicitly listing hospital wastewater in this recommendation (Pauling & Ataria, 2010). Involvement is also required to meet Māori rights under te Tiriti o Waitangi obligations, allowing Māori to exercise tino rangatiratanga is central to honouring te Tiriti (Durie et al., 2017).

Clearly, wastewater discharge, and overflows, have an immediate impact on cultural relationships with the environment. Health impacts of HWW discharge and resulting contamination may be exacerbated due to the significance of such relationships to Māori (Hughes et al., 2021; King et al., 2013). Hauora is intricately and inseparably related to the health of the environment. It goes beyond physical health impacts from any exposures (Harmsworth & Awatere, 2013; Hughes et al., 2021). Contamination may impact physical health, spiritual health, mental health and disrupt iwi, hapū and whānau relationships to a sites of significance if it is no longer safe or acceptable to use (Hughes et al., 2021; King et al., 2013). This view of health and wellbeing is critical to understand when considering the public health and equity implications of HWW for Māori. Health impacts will go beyond the physical effects of exposure to the contaminants reported as even when ‘adequately’ treated, hospital wastewater discharge into waterways remains offensive. To equitably understand and address the risks discussed in this report, and meet te Tiriti o Waitangi obligations, they must be assessed and then managed from a Māori worldview (Durie et al., 2017; Moewaka Barnes & McCreanor, 2019; Pauling & Ataria, 2010).

3. CONTRAST AGENTS

Contrast agents are used for medical imaging, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), as a fundamental diagnostic and interventional tool to improve differentiation of blood vessels, organs and soft tissues (Zanardo et al., 2023). Contrast agents are primarily iodinated (ICAs) or gadolinium based (GBCAs) and both are classified as emerging micropollutants. Globally, the use of contrast agents has increased rapidly as availability of CT and MRI imaging has increased. ICAs are used for CT imaging and are mostly derived from triiodobenzoic acid. GBCAs are chelates of the trivalent ion of gadolinium and are used for MRI. Both ICAs and GBCAs are most often given intravenously (IV) and are excreted unmetabolized (Ajala et al., 2022; Sengar & Vijayanandan, 2021). Following administration, within 24h approximately 90% of the contrast media is excreted unmetabolized in urine in patients with normal renal function (Ajala et al., 2022; Lurosso et al., 2001).

Gadolinium is classed as a heavy metal. As with other heavy metals, it is a public health concern because it can bioaccumulate and is not biodegradable. Gadolinium used in GBCAs is chelated with larger molecules, resulting in a stable compound that can safely be used clinically as a contrast agent avoiding gadolinium toxicity. Wastewater treatment plants are unable to significantly reduce the amount of gadolinium in wastewater related to GBCAs due to this stability (Laczovics et al., 2023). Additionally, the high stability allows GBCAs to pass through drinking water treatment plants with high concentrations of gadolinium compounds reported in large cities drinking water supplies (Kulaksız & Bau, 2011; Souza et al., 2021). A Berlin study found the levels of gadolinium in the water supply were 32 times the natural background level (Kulaksız & Bau, 2011).

ICAs are also poorly removed through conventional wastewater treatment plants. ICAs are resistant to biological degradation and bind poorly to sludge (Ternes & Hirsch, 2000). This can result in high concentrations in treated wastewater and receiving environments. Similarly to GBCAs, ICAS are frequently detected in surface water and groundwater (Dekker et al., 2022; Sengar & Vijayanandan, 2021). Drinking water treatment methods have also been found to be largely ineffective at removing ICAs from water sources (Simazaki et al., 2015). Of further concern, ICAs can react with chlorine and chloramine in treated water to form iodinated disinfection byproducts (Sengar & Vijayanandan, 2021), which studies show are cytotoxic and genotoxic to mammalian cells (Duirk et al., 2011)

3.1 CONTRAST AGENTS IN HOSPITAL WASTEWATER

ICAs are one of the most frequently used compounds in hospitals. Owing to the frequent use at high dosages, and lack of human metabolism, the concentrations of ICAs in HWW are high (Pérez & Barceló, 2007; Sengar & Vijayanandan, 2021). Analysis of the wastewater for pharmaceuticals in a medium sized hospital in Spain identified that iomeprol (ICA) was present in the highest concentration across all compounds tested (Mendoza et al., 2015). Iomeprol was present at a maximum concentration of 2093 µg/L (Mendoza et al., 2015). GBCAs are less frequently used than ICAs but still have high concentrations in in HWW. The literature comments on the presence of gadolinium as a contaminant, rather than identifying specific medications or chelates of gadolinium. Therefore, unlike ICAs, gadolinium as a compound is included in the report instead of specific pharmaceutical substance names.

Table 3.1 summarises the maximum concentrations of ICAs and GBCAs across different studies including the countries they were detected in. Concentrations of contrast agents are likely to differ between weekdays and weekends, as outpatient and non-emergency imaging tends not to occur on weekends (Drewes et al., 2001). Therefore, where testing is performed over several days, the maximum weekday values are used. The ICAs approved for use in New Zealand as per the New Zealand Formulary include diatrizoic acid, ioxehol, iomeprol and iopromide. As shown in Table 3.1, these have all been detected at high concentrations in HWW internationally.

Table 1: Summary of detections of contrast agents in hospital wastewater

Substance	Countries detected in	Max. conc. (µg/L)*	References
	ICAs		
Diatrizoic acid	France, Germany, Switzerland, Turkey	1,058.8*	Sordet et al (2018); Kraus (2014); Kovalova et al (2012); Gönder et al (2021)
Iobitridol	France	3,213*	Mullot et al. (2010)
Iohexol	France, Japan, Switzerland, Turkey	3,810*	Sordet et al (2018); Azuma et al (2019); Weissbrodt et al (2009); Gönder et al (2021)
Iomeprol	France, Germany, Japan, Spain, Switzerland, Turkey	2,400	Mullot et al (2010); Sordet et al (2018); Azuma et al (2019); Kraus (2014); Mendoza et al (2015); Kovalova et al (2012); Weissbrodt et al (2009); Gönder et al (2021)
Iopamidol	Germany, Japan, Switzerland, Turkey	2,599*	Kraus (2014); Azuma et al (2019); Kovalova et al (2012); Weissbrodt et al (2009);Gönder et al (2021)
Iopromide	Germany, Japan, Portugal, Sweden, Switzerland, Turkey	3,000	Kraus (2014); Azuma et al (2019); Santos et al (2013); Sörengård et al (2019); Kovalova et al (2012); Weissbrodt et al (2009); Gönder et al (2021)
Ioversol	France, Japan, Turkey	310	Sordet et al (2018); Azuma et al (2019); Gönder et al (2021)
Ioxitalamic acid	Switzerland	550	Kovalova et al (2012); Weissbrodt et al (2009)
	GBCAs/Gadolinium		
Gadolinium	France, Germany, Turkey	55	Wiest et al (2018); Goullé et al (2012); Kümmerer and Helmers (2000); Künnemeyer et al (2009); Hocaoglu et al (2021)

*Indicates that the maximum concentration identified was reported as an average value. Drugs indicated in bold are approved in New Zealand based on data obtained from the New Zealand Formulary (https://nzf.org.nz/).

3.2 HEALTH EFFECTS OF EXPOSURE TO CONTRAST AGENTS

The public health impacts of exposure to ICAs and GBCAs, including transformation products, are not well described in the literature. Overall, in a clinical setting the safety profiles of ICAs and GBCAs are relatively high (Dekker et al., 2022). When used as contrast agents they are dosed either according to a patient's body weight or to a maximum fixed dose. Side effects in this setting include short-medium term consequences such as hyper-sensitivity reactions or nephropathies for ICAs (Dekker et al., 2022; Sengar & Vijayanandan, 2021). Clinically, GBCAs have more medium-long term consequences, such as nephrogenic systemic fibrosis. There are also reports of the retention of gadolinium in the brain and other organs after repeated exposure to GCBAs for MRIs or in patients with poor renal function (Souza et al., 2021). The clinical significance of brain accumulation is currently unknown.

There are knowledge gaps in the fate, natural degradability and oral bio-accessibility of GCBAs which limit the ability to understand the risk to public health of wider contamination (Souza et al., 2021). While there is known gadolinium contamination of drinking water (Kulaksız & Bau, 2011), currently evidence is lacking on the long term public health implications from chronic low-dose exposure. Gastric acids can dissociate GBCAs which could allow gadolinium to enter the bloodstream through drinking water exposure (Kulaksız & Bau, 2011). The dissociated free gadolinium ions, which are highly toxic as they can interchange with the calcium and zinc ions in biomolecules, can accumulate in tissues, primarily the brain, bones and liver (Coimbra et al., 2024; Ebrahimi & Barbieri, 2019). However, further research is required to understand the human health effects of gadolinium retention following environmental low dose exposure (Coimbra et al., 2024; Ebrahimi & Barbieri, 2019; Souza et al., 2021).

ICAs are also not effectively removed in conventional wastewater treatments due to their stability (Ternes & Hirsch, 2000). This can result in high concentrations in treated wastewater and receiving environments. The iodine present in ICAs can result in development of iodinated disinfection byproducts in chlorinated water sources, which studies show are cytotoxic and genotoxic to mammalian cells (Duirk et al., 2011). Exposure pathways for IDBPs include inhalation, skin absorption and oral absorption (Villanueva et al., 2015). Epidemiological studies exploring the health impacts of exposure to IDBPs are challenging due to difficulties identifying the products, and accurate exposure assessments (Villanueva et al., 2015). As such, the long-term public health impacts of exposure to IDBPs are unclear. As a broader group, disinfection byproducts have been linked to bladder cancer and negative reproductive outcomes, such as foetal growth, however no causality has been established specifically, including for IBDPs (Diana et al., 2019; Villanueva et al., 2015).

4. HEAVY METALS

Heavy metals are metalloid or metallic elements with a high atomic weight. They have a density five-fold higher than water, greater than 5g/cm^3 (Järup, 2003). Heavy metals are naturally occurring elements, however environmental contamination occurs through industrial and anthropogenic sources, which has increased the potential for human exposure (Balali-Mood et al., 2021). Globally, there is widespread reporting of heavy metal contamination in soil and aquatic environments, impacting the food chain and drinking water supplies (Agoro et al., 2020). Wastewater treatment plants typically are not designed to removed heavy metals in the treatment process, and 80-90% of metals may end up partitioned off to accumulate in sludge (Agoro et al., 2020).

Some heavy metals play an essential physiological role in human health. Zinc, copper and selenium are components of enzymes while iron is essential for haemoglobin to carry oxygen. Inadequate intake of these metals may result in nutritional deficiency syndromes (Tchounwou et al., 2012). Other heavy metals have no role in biological process or human health and are considered non-essential including, mercury, lead, nickel, gold, cadmium and aluminium (Tchounwou et al., 2012).

Heavy metal exposure can have harmful effects on human health. Heavy metals can bioaccumulate in the body following absorption, and are not biodegradable, making environmental contamination a significant public health concern. While exposure through single events may be minimal, given the ability of heavy metals to bioaccumulate, efforts should be made to reduce concentrations (Agoro et al., 2020).

4.1 HEAVY METALS IN HOSPITAL WASTEWATER

A range of heavy metals have been identified in HWWs, as detailed in the Appendix and summarised in

Table 2. Additionally, the maximum concentration for each heavy metal in the New Zealand Standards Waste Bylaw are listed in

Table 2. Gadolinium, a metalloid element, is discussed in the previous Contrast Agents section owing to its use as an MRI contrast agent. Platinum is discussed in this section, however cytotoxic drugs (many of which contain platinum) are discussed as a class in the pharmaceuticals section. The literature surrounding heavy metals in hospital wastewater consistently includes the presence of Mercury, Platinum, Zinc, Lead, Copper, Chromium, Cadmium and Arsenic (Agoro et al., 2020; Boillot et al., 2008; Danchaivijitr et al., 2005b; Ghafuria et al., 2018; Goullé et al., 2012; Isidori et al., 2016; Kümmerer et al., 1999; Lenz et al., 2005; Pérez-Alvarez et al., 2018). As shown in table 4.1, Copper, Zinc and Platinum are found in the highest concentrations.

Similar to findings from municipal wastewater review by Coxon and Eaton, the concentrations of heavy metals in HWW vary between studies significantly (Coxon & Eaton, 2023). For many of the heavy metals in HWW, their presence could be attributed or partially attributed to certain medical treatments or procedures. For example, mercury and platinum are commonly identified heavy metals in HWW (Ajala et al., 2022; Kümmerer, 2001). Platinum is used in a number of antineoplastic medications such as cisplatin and carboplatin (Khan et al., 2020), and aluminium is used in anti-acid medications.

Mercury is present in previously common dental amalgams, disinfectants, and some medications, such as diuretics (Khan et al., 2020; Kümmerer, 2001). Though, efforts have been made in developed countries to reduce the use of mercury in such agents since 2017 so values may be lower in New Zealand HWW (Khanna et al., 2023). The WHO has listed mercury as a dangerous substance with an allowable limit of 5% in discharge of treated HWW. However, in the United Kingdon and Europe, over 50% of mercury, tin, silver, copper and zinc came from hospitals through dental amalgams (Kumari et al., 2020).

Table 2: Summary of studies assessing presence of heavy metals in hospital wastewater.

Substance	Countries detected in	Max. conc. (µg/L)	Max. conc. NZ Trade Waste bylaw[#] (µg/L)
Aluminium	Turkey	71	100,000
Arsenic	France, Indonesia, Portugal, Mexico, Nigeria, Turkey	100	5,000
Barium	Indonesia	140	10,000
Cadmium	Indonesia, Iran, Mexico, Nigeria, Thailand, Turkey	130	500
Chromium	Indonesia, Iran, Mexico, Nigeria, Portugal, Thailand, Turkey	95	5,000
Cobalt	Indonesia, Iran, Turkey	6.7	10,000
Copper	France, Indonesia, Iran, Mexico, Thailand, Turkey	854	10,000
Iron	Indonesia, Iran, Thailand	289	100,000
Lead	France, Iran, Mexico, Nigeria, Portugal, Thailand, Turkey	141	10,000
Manganese	Indonesia, Thailand, Turkey	93	20,000
Mercury	Iran, Mexico, Nigeria, Portugal, Turkey	17.2	50
Nickel	Indonesia, Iran, Mexico, Thailand, Turkey	170	10,000
Platinum	Austria, un-named EU countries, France, Germany, Iran, Slovenia	762	
Silver	France	2.7	2,000
Tin	Turkey	27.3	20,000
Zinc	France, Indonesia, Iran, Mexico, Thailand, Turkey	623	10,000

[#]Information from Standards New Zealand (2004)

Platinum from HWW is described as the second highest source of environmental platinum to overall platinum contamination following motor vehicles with catalytic convertors (Kümmerer et al., 1999; Lenz et al., 2005). However, platinum arising from antineoplastics have higher toxicological impacts as they are inorganic catalyst born compounds (Lenz et al., 2005). Not all excreted platinum from medications occurs in hospitals. The half-life of platinum containing pharmaceuticals means that considerable amount of excretion will occur into municipal wastewater.

Across the identified studies, total concentrations of heavy metals are variably meeting relevant jurisdictions standards for wastewater maximum concentrations of heavy metals. A study completed in Mexico found that HWW mercury concentration exceeded standards

(0.021 micrograms when the standards maximum is 0.01). All other studied heavy metals were below standard levels (Pérez-Alvarez et al., 2018). A Turkish study of a 350-bed hospital found that levels of cadmium, chromium and lead were higher than WHO limits (Akin, 2016). The varying concentrations and comparison to standards across heavy metals may be due to the treatments and diagnostic agents offered in the hospitals studied and products used, as well as variations in standards internationally.

4.2 HEALTH EFFECTS OF HEAVY METALS

The toxicity of heavy metals is influenced by a range of factors including age, genetics, environmental conditions, and chemical state (Tchounwou et al., 2012). Additionally, the health impacts of heavy metal toxicity depends on the metal exposed, as each has its own physiochemical properties (Balali-Mood et al., 2021). Heavy metals can affect several cell components and functions including, cell membranes, DNA and enzymes (Tchounwou et al., 2012). Health effects occur through damage to the cardiovascular system, central nervous system, lungs, liver, kidneys and blood cells. Long term exposures are notably associated with cancers, neurological conditions and endocrine and reproductive system disruption.

Currently, evidence suggest the main heavy metals with risks to human health include lead, cadmium, mercury and arsenic (Balali-Mood et al., 2021; Järup, 2003). Each of these are included in the WHO 10 chemicals of public health concern. Several heavy metals have been identified as known or probably carcinogenic, including arsenic and cadmium (Straif et al., 2009). Table 3 is a summary of the health effects associated with heavy metals identified in the review as being consistently present in HWW. The table provides a visual overview of the broad health effects caused by heavy metals across all body systems. Only health effects confirmed in epidemiological studies on humans are included in this summary table, though the author notes that for many of the heavy metals discussed, there may be animal studies showing impacts on other organs and tissues. The remainder of this section will discuss the health effects of the heavy metals consistently identified in hospital wastewater, and those of public health concern. Given that the primary contributor to platinum in HWW is through platinum containing antineoplastic pharmaceuticals, the health effects of platinum will be discussed in relation effects from platinum in this form.

Table 3: Summary of health effects of heavy metals consistently present in hospital wastewater by body system.

Heavy metal	**Human health effects (acute and chronic)**												
	Cancer	Skeletal	Cardiovascular	Liver	Lung	Kidney	Skin	Neurological	Reproductive	Endocrine	Blood and immune	Gastrointestinal	Development
Arsenic	x		x		x	x	x	x	x	x	x	x	x
Cadmium	x	x			x	x			x			x	
Chromium	x				x	x	x	x			x		
Copper				x								x	
Lead	x		x			x		x	x		x	x	x
Mercury			x		x	x		x			x		x
Nickel					x		x				x		
Platinum	x								x		x		
Zinc					x							x	

4.2.1 Arsenic

Inorganic arsenic is highly toxic. Exposure routes are through inhalation and ingestion. Groundwater contaminated with arsenic is the main source of public health risk of exposure globally. The WHO provisional guideline value for arsenic in drinking water is 10 µg/L. Approximately 140 million people are exposed to higher levels than this in contaminated water sources (Ravenscroft et al., 2009).

Acute arsenic poisoning includes vomiting and diarrhoea, followed by numbness in the extremities, muscle cramping, and death. Long term exposure to inorganic arsenic, for example in contaminated drinking water or food, initially presents with skin changes such as pigmentation, lesions and hyperkeratosis of the palms and soles of the feet (WHO, 2023a). These occur after approximately five years of exposure and may be a skin cancer precursor. Long term exposure may also cause lung and bladder cancers (Naujokas et al., 2013). Non-cancerous health effects include developmental impacts, diabetes, pulmonary and cardiovascular diseases (Naujokas et al., 2013). Additionally, it is associated with adverse outcomes in pregnancy, including infant mortality (Quansah et al., 2015). Arsenic exposure in utero is linked to increased mortality in young adults associated with cancers, lung disease, myocardial infarction and kidney failure (Farzan et al., 2013).

4.2.2 Cadmium

Cadmium is listed in the WHO top 10 chemicals of concern and is highly toxic. The main exposure routes include inhalation and ingestion of contaminated food (Tchounwou et al., 2012). Cadmium exerts toxicity on several organs and tissues, including the kidneys, skeleton and respiratory system (Genchi, Sinicropi, et al., 2020). Additionally, it is classified as a carcinogen. The provisional tolerable monthly intake as per the WHO is 25 µg/kg body weight.

The International Agency for Research on Cancer (IARC) has classified cadmium and cadmium compounds as carcinogenic to humans (Group 1). There is sufficient epidemiological evidence showing that cadmium and cadmium compounds cause lung cancer (IARC, 2012). Evidence for cancers of the kidney and prostrate are limited but current evidence suggests an association (IARC, 2012). The carcinogenicity of cadmium from low levels of environmental exposure is unclear.

Cadmium primarily accumulates in the kidneys, with a biological half-life of 10-35 years (Balali-Mood et al., 2021; Genchi, Sinicropi, et al., 2020; WHO, 2019a). The accumulation can cause renal tubular dysfunction (WHO, 2019a). Depending on the exposure dose, this may result in reversible or permanent damage to renal function (WHO, 2019a). Chronic low-level exposure to cadmium is also associated with reduced bone mineral density and

osteoporosis due to disruption of calcium metabolism, independent of kidney dysfunction (Genchi, Sinicropi, et al., 2020). Inhalational exposure to cadmium oxide can result in an acute pneumonitis and pulmonary oedema, which may result in death (WHO, 2019a). Long term inhalational exposure is associated with chronic obstructive pulmonary disease (ATSDR, 2012a).

4.2.3 Chromium

Chromium naturally occurs in the earth's crust as is present in various states of oxidation from chromium (-II) to chromium (VI), primarily in the trivalent (III) and hexavalent (VI) forms. Health effects depend on the state of chromium a person is exposed to. Environmental contamination though anthropogenic activities are mainly with Chromium (VI), which is more toxic than Chromium (III) (ATSDR, 2012b; Tchounwou et al., 2012). Exposure routes are largely inhalation and ingestion; however skin absorption has been reported occupational exposure settings (Tchounwou et al., 2012).

The primary health effects of exposure to chromium (VI) are respiratory (nasal and lung irritation, reduced pulmonary function), developmental, reproductive (decreased sperm count), haematological (microcytic anaemia), immunological (hypersensitivity reaction), and gastrointestinal (ulceration of the upper gastrointestinal system) (ATSDR, 2012b). Occupational exposure to chromium (VI) has been associated with respiratory cancers, mainly nasal and bronchogenic (ATSDR, 2012b).

There is significantly less evidence available for the health effects of chromium (III), though it appears to be less toxic than chromium (VI) (ATSDR, 2012b). Health effects from chromium (III) have been reported in occupationally exposed populations. However, the analysis of the exposure effects is complicated as these populations are usually also exposed to chromium VI. It appears the primary health effects of chromium (III) and dermatological hypersensitivity reactions, and respiratory point-of-entry effects (nasal and ling irritation from inhalation) (ATSDR, 2012b).

4.2.4 Copper

Copper is an essential micronutrient for human biological function. However, excess consumption can cause toxicity and result in adverse interactions with other heavy metals, for example zinc (ATSDR, 2022a). The level at which copper becomes toxic is not clear. The gastrointestinal system is the main target of copper toxicity. When ingested, copper is absorbed rapidly by the stomach and small intestine causing pain, nausea and vomiting (ATSDR, 2022a). Females appear to be more sensitive to copper gastrointestinal health effects compared to males (ATSDR, 2022a). Doses between 0.07 to 0.17 mg/kg/day were associated with pain, nausea and vomiting, but not diarrhoea (ATSDR, 2022a). Copper

toxicity can also impact the liver. Human studies have identified increased levels of liver enzymes, liver impairment, hepatomegaly and jaundice following exposure to high doses of copper (ATSDR, 2022a; Gaetke et al., 2014; Uriu-Adams & Keen, 2005). Low-level exposure in controlled studies did not show any evidence of liver damage in adults, children or infants (ATSDR, 2022a).

4.2.5 Lead

Lead is a highly toxic pollutant with a range of health impacts. It is mostly absorbed through inhalation and digestion. Lead has no biological function in the body and any level detected is considered abnormal (Hauptman et al., 2017). In children, levels below 10 µg/dL are associated with adverse health impacts (Lanphear et al., 2019).

Children are at higher risk of lead poisoning and its effects due to having a less-developed blood-brain barrier and higher gastrointestinal absorption (Hauptman et al., 2017; Järup, 2003). Children absorb 4-5 times as much lead as adults and there is no identified threshold for the development of health effects (WHO, 2010). Lead exposure in children, including low level, may lead to reduced intellectual capacity, behavioural issues, and reduced educational attainment (Hauptman et al., 2017).

According to the International Agency for Research on Cancer (IARC) inorganic lead compounds are classified as probably carcinogenic to humans. There is some evidence of the development of cancer following long-term occupational exposure to lead (ATSDR, 2020). Chronic lead exposure causes a range of adverse health effects across numerous body systems (ATSDR, 2020; Hauptman et al., 2017; WHO, 2010). Health effects include.

- Haematological - anaemia
- Neurological – depression, fatigue, convulsions, ataxia, muscle weakness, tremors, impaired hearing, and headaches.
- Gastrointestinal – abdominal colic and kidney dysfunction
- Cardiovascular – hypertension, ischaemic heart disease and stroke
- Reproductive – abnormal sperm and reduced sperm count

4.2.6 Mercury

Mercury is listed in the top 10 chemicals of concern by WHO. It is found in three main forms, inorganic, organic and elemental. Each form of mercury has its own toxicity profile. Elemental mercury and inorganic mercury are not classifiable as carcinogenic (Group 3) by the IARC (ATSDR, 2022b). Organic, or methylmercury compounds, are classified as possibly carcinogenic (Group 2B) by the IARC (ATSDR, 2022b).

Elemental mercury health effects have been observed for vaporised exposure. Neurological effects in adults include visual defects, tremor, reduced cognitive performance, mood swings, irritability, nervousness and fine motor coordination (ATSDR, 2022b; Park & Zheng, 2012; Rice et al., 2014). Renal effects include reduced glomerular function and renal tubular injury (ATSDR, 2022b). High doses of vaporised elemental mercury at near fatal levels may cause severe respiratory effects including pneumonitis and respiratory failure due to significant pulmonary oedema (ATSDR, 2022b).

The evidence for health effects from inorganic mercury salts primarily comes from animal studies with some case reports from acute poisoning in humans. Inorganic mercury salts are nephrotoxic. Impaired renal function and permanent damage have been shown in humans following acute poisoning (ATSDR, 2022b). Neurological and neurodevelopmental effects have been seen in animal studies (ATSDR, 2022b).

Organic mercury, also known as methylmercury, exposure causes a wide range of health effects. Bioaccumulation of methylmercury in fish is a significant concern and exposure route, particularly in subsistence populations relying on fish consumption. There is well established epidemiological evidence of neurological and neurodevelopmental adverse health effects following exposure (ATSDR, 2022b; Rice et al., 2014). Neurological and psychological damage including muscle weakness, ataxia and speech disturbances result when chronic elevated exposure occurs (Järup, 2003; Kannan[1] et al., 2021; Rice et al., 2014). Prenatal exposure may result in cognitive dysfunction and neurosensory disturbances (ATSDR, 2022b). There is also evidence of renal, cardiovascular, immune and reproductive effects in human and animal studies (ATSDR, 2022b; Rice et al., 2014).

4.2.7 Nickel

Exposure to nickel primarily occurs through contaminated food and drinking water for the public. Evidence on health effects from nickel exposure is primarily from occupationally exposed populations through inhalation of nickel (Genchi, Carocci, et al., 2020). Higher incidence of asthmas has been reported in populations with an increased ambient concentration of nickel (ATSDR, 2023). Occupational exposure may be associated with an increased risk of pulmonary fibrosis and asthma (Genchi et al., 2020; ATSDR, 2023). Immunological responses are also seen with exposure to nickel. Contact dermatitis from an allergic reaction to nickel is prevalent amongst occupationally exposed populations (Genchi et al., 2020; ATSDR, 2023). There is increased prevalence of asthma among populations exposed to higher concentrations of nickel in air, whether in ambient air or through occupational exposure, and may be related to immunological reactions (ATSDR, 2023).

4.2.8 Platinum

The health effects of platinum in platinum containing pharmaceuticals, such as cisplatin, are primarily understood through occupational exposures for medical professionals, and pharmaceutical studies. Platinum based drugs have been detected in hospital workers urine and blood (Nygren & Lundgren, 1997). Health effects are of particular concern for sensitive sub-populations, such as pregnant people. Cisplatin, other antineoplastic drugs containing platinum have been classed as group 2A (probable carcinogens) carcinogens (IARC, 2020). Handling of these medications occupationally is also associated with hypersensitivity, worsening asthma, miscarriages, premature delivery and low birth weight (Dranitsaris et al., 2005; Ravindra et al., 2004). The human health risks associated with chronic low-dose environmental exposures are not clear.

4.2.9 Zinc

Zinc is an essential nutrient for health. It is required for a large number of enzymes and zinc deficiency may result in dermatitis, anorexia, hypogonadism, reduced cognitive function and impaired immune function (Chasapis et al., 2012).

Long term low dose zinc exposure may result in copper deficiency due to interactions between enzyme binding for copper and zinc (ATSDR, 2014). Gastrointestinal symptoms are common with higher doses of zinc, including nausea, vomiting, and diarrhoea (ATSDR, 2014). Acute inhalation of zinc may cause metal fume fever, an acute respiratory disorder which does not usually result in long term lung disease (ATSDR, 2014; Plum et al., 2010). Metal fume fever is largely characterised by chest pain, cough, and dyspnoea. Inhalation of zinc chloride compound causes damage to the mucous membranes and irritation of the respiratory tract due to its corrosive nature (ATSDR, 2014; Plum et al., 2010).

5. HUMAN BODILY WASTE

Hospital wastewater contains human bodily waste. As highlighted in other chapters, this includes urine, faeces, sputum, blood, and vomit. Additionally, HWW may contain human tissues. The New Zealand Standards 4204:2002, Management of Health Care Waste, states that liquid body parts, diluted embalming and body fluids may be disposed of to the sewer. Additionally, solid body parts that are minor, minute or non-recognisable may be disposed of in the sewer.

As highlighted in the Te Ao Māori perspectives on HWW section, there are significant tikanga issues surrounding human bodily waste in HWW being discharged into waterways. The disposal of human waste, notwithstanding it being waste from a hospital with potential other contaminants, is not permitted into waterways under tikanga Māori. There are broad health and equity concerns regarding the effects this will have on hauora for Māori, and these likely need further exploration.

A primary public health risk from human body waste is the contents of the waste. For example, through infection with pathogens present in the waste or the excretion of other contaminants such as contrast agents or radioisotopes. The presence and impact of contaminants that may be present in human bodily waste will be discussed in each relevant section. There was no literature identified by the author discussing human bodily waste specifically in hospital wastewater. Literature discussed waste such as urine, faeces and blood as being infectious or excreting contaminants, in relation to the assessment of pathogens or other contaminants in HWW.

6. OTHER CHEMICALS

6.1 OTHER CHEMICALS PRESENT IN HOSPITAL WASTEWATER

A wide variety of other chemicals have been identified in HWWs around the globe, as summarised in Table 4. These include bisphenol analogues, corrosion inhibitors, disinfectants/antiseptics, flame retardants, organophosphates, and surfactants. These groups of chemicals are heterogenous and may be compounds used in cleaning products, medical products or treatments, pharmaceuticals, plastics and more. Concentrations of these chemicals are highly variable.

Many of these chemicals are also found in municipal wastewater at comparable or even lower doses. For example, Bisphenol A is found in similar, or slightly lower concentrations in HWW compared to municipal (Coxon & Eaton, 2023). Bergé et al (2018) found high concentration of surfactants in both urban and hospital wastewater, however the types of surfactants present in high concentration differed between each.

Bergé et al (2018) identified nine different surfactants in varying concentrations in HWW. Surfactants are essential stabilising compounds in a range of products including detergents, disinfectants, and cosmetics (Bergé et al., 2018). Given the widespread use, they can be found in high concentrations in the environment, even though treatment systems remove surfactants effectively (González et al., 2007). Boillot et al (2008) found high concentrations of surfactants, particularly cationic detergents, in HWW. Additionally, volatile halogenated organic compounds, formaldehyde, acetaldehyde and total free chlorine were detected in high concentrations in this study.

Several pesticides, including organophosphates, have been identified in HWW, however the majority of these were identified at levels less than the limit of quantification (LOQ). Additionally, of the compounds with detectable quantifiable levels, the concentrations detected were variable. The highest concentration of organophosphates identified was 12.9 µg/L (TBEP) and lowest was 0.02 µg/L) (DEHPA) (U. Kraus, 2014; Sörengård et al., 2019a). For pesticides the variability was also in orders of magnitudes with values from 0.003 µg/L (DEET) to 0.5 µg/L (Climbazole) (Gönder et al., 2021a; Sörengård et al., 2019a).

Table 4: Summary of studies assessing the presence of various other chemicals in hospital wastewater.

Group	Substance	Average conc. (µg/L)	Max. conc. (µg/L)	Country	Reference
Bisphenol analogues	Bisphenol A	0.2 ± 0.02 – 1.0 ± 0.03		China	Huang et al. (2021)
		7.9 ± 4.6	14	Turkey	Gönder et al. (2021b)
	Bisphenol AF	0.002 ± 0.000.3 – 0.008 ± 0.002		China	Huang et al. (2021)
	Bisphenol E	0.003 ± 0.001		China	Huang et al. (2021)
	Bisphenol F	0.002 ± 0.001 – 0.03 ± 0.003		China	Huang et al. (2021)
	Bisphenol S	0.0008 ± 0.0005 – 0.006 ± 0.0006		China	Huang et al. (2021)
Corrosion inhibitors	Benzotriazole		~100	France	Bergé et al. (2018)
		24.8 ± 22.4	78	Turkey	Gönder et al. (2021b)
		23.6 ± 9.1		Switzerland	Kovalova et al. (2012)
		0.4 – 9.6		Turkey	Yilmaz et al. (2017)
	Dimethyl benzotriazole	0.34±0.45	1.3	Turkey	Gönder et al. (2021b)
	4/5-methylbenzotriazole (MeBT)	223 ± 132		Switzerland	Kovalova et al. (2012)
		0.01 – 0.9		Turkey	Yilmaz et al. (2017)
		0.8 ± 0.8	2.6	Turkey	Gönder et al. (2021b)
	Tolytriazole	1.2		Sweden	Sörengård et al. (2019b)
Disinfectants/antiseptics	Benzalkoniums		~550	France	Bergé et al. (2018)
	4-Chloro-3-methylphenol (p-Chlorocresol)	<0.05		Sweden	Sörengård et al. (2019b)
	Acridine	0.03	0.05	Japan	Azuma et al. (2019)

	Acridone	<LOQ	0.003	Portugal	L. H. M. L. M. Santos et al. (2013)
	Chloroxylenol	Not quantified		USA	Meza et al. (2020)
	Chlorophene	Not quantified		USA	Meza et al. (2020)
	Triclosan	Not quantified		USA	Meza et al. (2020)
Group	**Substance**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Country**	**Reference**
Flame retardants	Tris(2-butoxylethyl) phosphate	0.7		Sweden	Sörengård et al. (2019b)
Organophosphates	Di-(2-ethylhexyl) phosphoric acid (DEHPA)	0.02		Sweden	Sörengård et al. (2019b)
	TBEP	12.9		Germany	U. R. Kraus (2014)
	TCEP	0.07		Germany	U. R. Kraus (2014)
	TCPP	<LOQ		Germany	U. R. Kraus (2014)
	TDCPP	<LOQ		Germany	U. R. Kraus (2014)
	TiBP	<LOQ		Germany	U. R. Kraus (2014)
	TnBP	0.07		Germany	U. R. Kraus (2014)
	TPP	<LOQ		Germany	U. R. Kraus (2014)
Parabens	Ethylparaben	0.2		Sweden	Sörengård et al. (2019b)
	Methylparaben	0.6		Sweden	Sörengård et al. (2019b)
	Propylparaben	0.3		Sweden	Sörengård et al. (2019b)
Pesticides	Climbazole	0.2±0.2	0.5	Turkey	Gönder et al. (2021b)
		0.02		Turkey	Yilmaz et al. (2017)
	DEET	0.003		Sweden	Sörengård et al. (2019b)
	Dichlorobenzamide	<0.05		Sweden	Sörengård et al. (2019b)

	Diuron	0±0.1	0.2	Turkey	Gönder et al. (2021b)
	Isoproturone	<LOQ	<LOQ	Turkey	Gönder et al. (2021b)
	Metconazole	<LOQ	<LOQ	Turkey	Gönder et al. (2021b)
	Quinnoxyfen	<LOQ	<LOQ	Turkey	Gönder et al. (2021b)
	Terbutryn	<LOQ	<LOQ	Turkey	Gönder et al. (2021b)
Group	**Substance**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Country**	**Reference**
Pigments	Ricinoleic acid	0.8		Sweden	Sörengård et al. (2019b)
Surfactants	Comperlan 100		~0.5	France	Bergé et al. (2018)
	Cetyl betain		~0.9	France	Bergé et al. (2018)
	Triton X 100		~5.5	France	Bergé et al. (2018)
	Stepanquat GA 90		~0.1	France	Bergé et al. (2018)
	Incromine SD		~0.3	France	Bergé et al. (2018)
	Laurilsulfate	0.9		Sweden	Sörengård et al. (2019b)
	Sodium 2-ethylhexyl sulfate		~50	France	Bergé et al. (2018)
	Sodium dodecyl sulfate (SDS)		~20	France	Bergé et al. (2018)
	Linear alkylbenzene sulfonate (LAS)		~2000	France	Bergé et al. (2018)
	Texapon N 701 S		~1000	France	Bergé et al. (2018)
UV filters	Sulisobenzone	<0.005		Sweden	Sörengård et al. (2019b)
Volatile organic compounds	Trichloromethane	2.4		France	(Boillot et al., 2008)
	Freon 113	2.6		France	(Boillot et al., 2008)
	Formaldehyde	70		France	(Boillot et al., 2008)
	Dibromodichloromethane	0.7		France	(Boillot et al., 2008)

Tribromethane	0.6	France	(Boillot et al., 2008)

*Range of averages for different hospitals assessed in these studies

6.2 HEALTH EFFECTS OF EXPOSURE

It is beyond the scope of this report to comment on the health effects of all the chemicals listed in table 4. The health impacts of chemicals will be discussed for a selection of chemicals identified, either by group of chemicals where possible, or specific compounds with established evidence of health impacts, for example Bisphenol A. It is important to note that exclusion from the section below does not mean that a chemical does not have potential impacts on public health.

Of the bisphenols identified in HWW, bisphenol A (BPA) had the highest concentration. BPA is widely used in the production of plastics and epoxy resins. In healthcare settings specifically, it is used in dental composite resins for dental restoration (Khanna et al., 2023). BPA is a hormone disrupter and interacts with estrogen receptors, but the available data shows the interactions are complex and involve other receptor targets (Rochester, 2013). Health effects associated with exposure to BPAs may include infertility, decreased male sexual function, reduced sperm quality, polycystic ovary syndrome, insulin resistance, and cardiovascular disease (Rochester, 2013).

Parabens are classified as endocrine disrupting chemicals (Nowak et al., 2018). They are used as preservatives in foods, cosmetics, and pharmaceutical products. The health effects of parabens are not well established in human studies. They have been associated with breast cancers, metabolic syndromes and male infertility (Fransway et al., 2019; Golden et al., 2005; Nowak et al., 2018).

The health effects of pesticides depend on the chemical properties of the specific pesticide. Additionally, the exposure route impacts the health effects seen for a given pesticide. Exposure routes include the gastrointestinal system, skin, eyes and respiratory system. There is limited epidemiological evidence for the health effects of chronic low dose exposure for many pesticides (Kim et al., 2017). However, there is evidence of neurological, cardiovascular, renal, developmental, and reproductive effects from chronic low dose exposure for some pesticides (Kim et al., 2017; WHO, 2019b). Additionally, some pesticides are classified as known, possible, or probable carcinogens by the IARC (WHO, 2019b).

7. PATHOGENIC MICRO-ORGANISMS

Pathogens are microorganisms that can cause disease. Microorganisms include bacteria, viruses, protozoa, fungi and parasites. HWW is noted to be a hotspot for pathogenic microbes (Yuan & Pian, 2023) and an ideal medium for the growth of pathogens (Kaur et al., 2020). Additionally, the highly infectious waste such as from hospital diagnostic laboratories, and excreta from patients with highly infectious diseases housed in isolation wards is a particular concern (WHO, 2014). Pathogens may be present in HWW from faeces, urine, vomit, blood, sputum and other bodily wastes. Additionally, laboratory waste may contribute to pathogens in HWW.

The range and concentration of pathogenic micro-organisms present in HWW will depend on the prevalence of the disease in the community and what infectious diseases are present in the hospital at any given time. For example, Hepatitis A Virus is not endemic in New Zealand, so while identified in HWW internationally, the overall risk in the New Zealand context is considerably lower. Additionally, HWW microbial pathogen content may be of increased concern during an outbreak of enteric diseases (Amouei et al., 2015).

Several studies note that HWW should receive more specialised treatment for pathogens prior to release into municipal systems (Guo et al., 2021;(Yuan & Pian, 2023)). Despite there being a significant potential public health risk when certain pathogens are not sufficiently treated prior to discharge into municipal networks and onwards to the receiving environments, there is little discussion in the literature of the presence and removal of pathogenic microbes from HWW (Yuan & Pian, 2023). Enterovirus concentrations are shown to be two to three times higher in HWW than municipal (Ajala et al., 2022)

This section of the report provides an overview of the detection of pathogenic micro-organisms globally. Not all microorganisms identified in the literature have been included in the report body, as some are not pathogenic to humans. The studies cited have used a variety of detection methods for micro-organisms including targeted PCR and metagenomics. Therefore, the detection of certain micro-organisms does not always correlate with them having infectious potential. Additionally, the summary below will not be an exhaustive list of the pathogenic microbes present in HWW. Despite the various pathogenic microorganisms present in HWW, not all present a risk to public health through their presence alone. Those that are blood-borne or with aerosolised transmission routes present a low public health risk, as do those requiring a high infectious dose due to the dilution in wastewater.

7.1 BACTERIA

7.1.1 Presence of bacteria in hospital wastewater

Hospital wastewater contains a wide variety of different bacterial species, including antibiotic-resistant species, which will be discussed in more depth later in the chapter. Bacterial species that are pathogenic to humans identified in HWW are summarised in

Table 5 in the report with common bacterial pathogens included. Details of all the bacteria detected in HWW that are known to be pathogenic to humans are included in the appendix. There were numerous other bacteria detected in HWW that were either part of the normal gut microbiome, sewerage bacteria, or environmental bacteria that do not or are not known cause disease in humans.

It is important to note that where identification is made to the species level, the identified species may not necessarily be a pathogenic strain. For example, non-pathogenic *E. coli* strains are commonly present in the human intestinal tract and therefore likely present in HWW, but at the species level would be indistinguishable from the pathogenic *E. coli* O157:H7 strain (commonly known as STEC) (Kaur et al., 2020).

Several metagenomic studies have been completed on HWW to broadly assess bacterial diversity. Proteobacteria are often identified as the most common species present in HWW however there are differences in diversity between hospitals studied. In untreated wastewater collected from a general hospital in Takatsuki City, Japan, 684 different bacterial genera were detected, with the most common phyla being Proteobacteria (51%), Bacteroidetes (34%), Firmicutes (11%) and Actinobacteria (1%) (Azuma & Hayashi, 2021). Metagenomic analysis of HWW sludge from a hospital WWTP in India found a high proportion of nosocomial pathogens with the majority being emerging or rare pathogens (Bhatt et al., 2021).

Proteobacteria is the main phylum for gram negative bacteria. Examples of bacteria genus in the proteobacteria phylum of relevance to public health include, *Escherichia, Shigella, Salmonella, Vibrio,* and *Haemophilus*, which have all been identified in HWW. Other genus detected in HWW with species commonly causing disease in humans include *Staphylococcus, Streptococcus, Pseudomonas,* and *Mycobacterium*. Of interest, there were no studies identified that reported detection of *Campylobacter* in HWW.

The profile of bacterial communities differs between hospital and domestic wastewater samples (Ahn & Choi, 2016; Selvarajan et al., 2021). A study in India comparing domestic and hospital wastewater bacterial communities found differences in the dominant genera

and classes of bacteria between them. HWW had a greater abundance of *Enterococcus, Pseudomonas* and *Vibrio,* while in domestic wastewater the *Clostridium*, *Klebsiella, Corynebacterium, Bordetella, Staphylococcus* and *Rhodococcus* genera were significantly higher (Selvarajan et al., 2021). Additionally, the overall diversity of bacterial species may be lower in HWW, possibly due to the higher concentrations of antibiotics and disinfectants present in the wastewater (Ahn & Choi, 2016; Selvarajan et al., 2021).

Table 5: Summary of common genus that include pathogenic species detected in HWW.

Genus	Countries	References
Escherichia	Brazil, Scotland, China, Nigeria, Egypt, Greece, Pakistan, Norway, Germany	Perry et al (2021), Li et al (2022), Guo et al (2021), Eze et al (2016), Mehanni et al (2023), Sakkas et al (2019), Shahzad et al (2021), Paulshus et al (2019), Suliman et al (2017), Sib et al (2020), Chagas et al (2011), Chukwu et al (2018)
Haemophilus	Pakistan	Suliman et al. (2017)
Klebsiella	Thailand, China, Scotland, Pakistan, Brazil, South Africa, Nigeria, Greece, Germany	Danchaivijitr et al (2005), Li et al (2022), Perry et al (2021), Suliman et al (2017), Chagas et al (2011), King et al (2020), Eze et al (2016), Sakkas et al (2019), Sib et al (2020)
Mycobacterium	Pakistan, China, Scotland	Perry et al (2021), Li et al (2022), Suliman et al (2017)
Pseudomonas	Thailand, Romania, China, Scotland, Nigeria, Germany, Greece, Pakistan, India	Danchaivijitr et al (2005), Li et al (2022), Szekeres et al (2017), Guo et al (2021), Perry et al (2021), Ma et al (2022), Eze et al (2016), Sib et al (2020), Sakkas et al (2019), Shahzad et al (2021), Suliman et al (2017), Chukwu et al (2018), (Selvarajan et al., 2021)
Salmonella	Nigeria, Thailand, Pakistan	Chukwu et al (2018), Danchaivijitr et al (2005), Suliman et al (2017), Eze et al (2016)
Shigella	Nigeria, China, Pakistan	Chukwu et al (2018), Li et al (2022), Suliman et al (2017)
Staphylococcus	China, Nigeria, Greece, Pakistan	Eze et al (2016), Sakkas et al (2019), Shahzad et al (2021), Suliman et al (2017), Chukwu et al (2018, Ma et al (2022)
Streptococcus	Netherlands, China, Pakistan	Buelow et al (2018), Guo et al (2021), Shahzad et al (2021)
Vibrio	Thailand, South Africa	Danchaivijitr et al. (2005a), (Mavhungu et al., 2023), (Selvarajan et al., 2021)
Yersinia	Czech Republic	(Roulová et al., 2022)

7.1.2 Health effects of bacteria

The pathogenic bacteria present in HWW with the most significant risk to public health are those with a faecal-oral transmission route, as they are excreted in human faeces to wastewater and may contaminate waterways. These bacteria, such as *E. coli, Yersinia* spp., *Salmonella* spp., and *Shigella* spp., are known to be transmitted through contaminated water. Other bacteria identified present a lower risk to public health as they are not known to be transmitted through contaminated water, have a high dose required to cause infection, or are typically opportunistic microorganisms. Given this, the health effects of *E. coli, Salmonella* spp., *Shigella* spp., and *Yersinia* spp. will be briefly discussed, noting that they are by no means a complete coverage of the bacteria presenting a health risk to humans in HWW.

There are various *E. coli* species, many of which are part of the normal human gastrointestinal microbiome. However, Shiga-Toxin producing *E. coli* (STEC) is pathogenic to humans. STEC infections cause an acute diarrhoeal illness (WHO, 2019c). Complications of STEC include Haemolytic Uraemic Syndrome (HUS) which is a severe complication causing kidney injury and, in some cases, permanent cerebral impairment (Lynn et al., 2005; WHO, 2019c). HUS is mostly seen in children and elderly. While the 0157:H7 serotype is most detected, other serotypes of STEC are also detected in New Zealand.[3]

Salmonella spp. can cause gastroenteritis, paratyphoid and typhoid fever. People may also be chronic carriers of *Salmonella typhi* (Eng et al., 2015). Symptoms of typhoid fever typically include fever, headache, anorexia, dry cough, malaise, hepatosplenomegaly, and relative bradycardia (Eng et al., 2015). The fatality rate when untreated is 12-30%. Paratyphoid fever typically follow a milder and shorter disease course compared to typhoid fever, but the disease is similar (Eng et al., 2015; Sánchez-Vargas et al., 2011). Salmonellosis describes gastroenteritis caused by non-typhoid salmonella species (Chlebicz & Śliżewska, 2018).

Shigella is has four species which can cause gastroenteritis in humans following ingestion of a low infectious dose (Baker, 2018). *S. dysenteriae* is associated with severe acute diarrhoea with blood or mucous, fever and abdominal cramps (Baker, 2018; Kotloff et al., 2018). It has a high secondary attack rate amongst contacts and has caused widespread and fatal epidemics (Baker, 2018; Kotloff et al., 2018). *S. sonnei* usually causes a milder illness (Baker, 2018). Infection with *S. flexneri* is associated with development of reactive arthritis (Kotloff et al., 2018).

[3] Verocytotoxin - or Shiga toxin-producing Escherichia coli (VTEC/STEC) – Health New Zealand | Te Whatu Ora

In New Zealand, Yersiniosis is primarily caused by two *Yersinia* species, *Y. enterocolitica* and *Y. pseudotuberculosis.* Yersiniosis is characterised by vomiting, fever, and diarrhoea in children less than five (Chlebicz & Śliżewska, 2018; Galindo et al., 2011). In older children and adults, non-specific abdominal pain is the predominant symptom particularly for *Y. enterocolitica* infection (Chlebicz & Śliżewska, 2018). In immunocompromised individuals' sepsis may occur with bacteraemia. *Y. pseudotuberculosis* can also cause abscess-forming mesenteric lymphadenitis (Galindo et al., 2011).

7.2 VIRUSES

7.2.1 Viruses in hospital wastewater

The presence of viruses in HWW is important not only due to the health hazard they pose but also due to their potential ability to affect the bacterial community by facilitating transfer of genetic material between organisms and inserting into the bacterial chromosome as prophages (Petrovich et al., 2020). Several studies have shown high levels of enteric viruses in effluent wastewater following treatment (Gyawali & Hewitt, 2018; Kargar et al., 2013; Nordgren et al., 2009). For many viruses, the exposure dose to cause illness is low. For example, the exposure dose for norovirus is thought to be less than 10 viral particles (Matthews et al., 2012).

A range of viruses have been detected in hospital wastewater across eight different countries. Table 6 details the range of viruses identified in the literature search for viral detection in HWW. Several have a faecal-oral transmission route, increasing the relevance of their presence in HWW as a risk to public health (Boussettine et al., 2020). Respiratory viruses, such as COVID-19, are also present in HWW, however the potential for transmission is unclear (Qamsari & Mohammadi, 2023). Some viruses identified are blood-borne and are not transmitted via water, such as Hepatitis B and C.

Table 6: Summary of relevant viruses identified in hospital wastewater.

Virus	Countries	Reference
Human adenoviruses	Brazil, Tunisia	Prado et al. (2011) Ibrahim et al. (2018)
SARS-CoV-2	Iran, Nepal, Slovenia, United States	Acosta et al. (2021); Gonçalves et al. (2021); (Qamsari & Mohammadi, 2023); Tandukar et al. (2022)
Rotavirus A	Brazil, Iran	Prado et al. (2011) Kargar et al. (2013)
Norovirus GI	Brazil	Prado et al. (2011)
Norovirus GII	Brazil	Prado et al. (2011)
Hepatitis A	Brazil	Prado et al. (2011)
Hepatitis B	Pakistan	Suliman et al. (2017)
Hepatitis C	Pakistan	Suliman et al. (2017)
Hepatitis E	Italy	La Fauci et al. (2010)

7.2.2 Health effects of exposure to viruses

The following section will describe the health effects of exposure to viruses in HWW with public health significance, a known faecal-oral transmission route and risk of water contamination from faeces and vomit. These include Hepatitis A, Human Adenoviruses, Norovirus, and Rotavirus.

Hepatitis A (HAV) causes inflammation of the liver. Symptoms commonly include fever, anorexia, nausea, vomiting and abdominal pain (Brundage & Fitzpatrick, 2006; WHO, 2023b). The viral load in human excreta of HAV is significant in infected individuals (Kaur et al., 2020). Of additional concern is the survival period of HAV with resistance to even harsh environmental conditions (Brundage & Fitzpatrick, 2006; Kaur et al., 2020). HAV is not endemic in New Zealand. Outbreaks have occurred recently due to frozen berries, and imported cases occur which may result in HAV presence in HWW. The incubation period is 15-50 days, on average being 25-30 days (Brundage & Fitzpatrick, 2006; WHO, 2023b). Peak infectivity occurs two weeks prior to the onset of jaundice or altered liver enzymes and infected individuals may shed the virus in stool for up to six months (Brundage & Fitzpatrick, 2006). Usually HAV infection is self-limiting, but it can result in fulminant liver failure (Brundage & Fitzpatrick, 2006). Infants and children tend to have mild or asymptomatic diseases, whereas adults, particularly elderly, can be more severely impacted (WHO, 2023b).

Human adenoviruses cause a range of illnesses including gastroenteritis, conjunctivitis, and respiratory tract infections. Transmission can occur through droplets and faecal-oral spread (Lynch & Kajon, 2016). Infections largely occur in children under four, and immunosuppressed people are more susceptible (Lynch & Kajon, 2016). Severe

disseminated infections can occur in immunosuppressed people. Recently, cases of hepatitis amongst children globally were associated with adenoviruses, however causation has not been confirmed (Rabaan et al., 2022).

Norovirus is a leading cause of diarrhoeal disease and infectious gastroenteritis worldwide (Kaur et al., 2020). Norovirus has an incubation period of 12-48 hours with symptoms including nausea, vomiting, diarrhoea, fever and abdominal pain. The illness duration is typically between 12-60 hours with most cases fully recovering. Waterborne gastroenteritis outbreaks can be caused by drinking water contamination with norovirus, with the faecal-oral route the primary route of transmission (Kaur et al., 2020; Matthews et al., 2012). Contamination of water is a public health risk given the low infectious dose, prolonged shedding, environmental stability and the genetic diversity present (La Rosa et al., 2010; Matthews et al., 2012).

Rotavirus is an enteric virus that represents a significant health burden globally for acute gastroenteritis (Bernstein, 2009; Crawford et al., 2017). The virus is largely transmitted through the faecal-oral route and very small doses are needed to cause infection (Crawford et al., 2017). Rotaviruses cause diarrhoea, fever and vomiting. It is a leading cause of severe diarrhoeal illness in children and infants resulting in dehydration, and in some cases death (Crawford et al., 2017). However, in adults the infection may be mild or asymptomatic (Anderson & Weber, 2004; Crawford et al., 2017). The introduction of a rotavirus vaccine has significantly reduced the morbidity and mortality associated with rotavirus in New Zealand (McAuliffe et al., 2018).

7.3 FUNGI

7.3.1 Fungi in hospital wastewater

Fungi are found throughout the environment. They have an environmental biomass similar to bacteria and higher than that of viruses (Assress et al., 2019). Fungi are commonly found in wastewater. Some pathogenic fungi can cause serious threats to human health and can produce mycotoxins which also impact human health. Like many other pathogens, fungi are not completely removed by wastewater treatment systems. Table 7 details specific species of fungi identified in HWW. As shown, the species identified were predominantly *Candida* with one study in Nigeria also identifying *Aspergillus* and *Trichophyton* species. Additionally, Assress et al (2019) identified the genera and compared fungal communities in municipal and hospital wastewater treatment plants. Fungal communities differed between hospital and municipal wastewater. Dominant genera for this study in HWW were *Derxomyces*, *Tricholoma*, *Cortinarius*, and *Pseudotomentella* which differed substantially from those in

municipal systems, noting that these genera are not pathogenic (though may be toxic) to humans (Assress et al., 2019).

Table 7: Summary of fungal species identified in untreated hospital wastewater.

Species	Country	Reference
Aspergillus niger	Nigeria	Chukwu et al. (2018)
Candida albicans	Turkey	(Mataraci-Kara et al., 2020)
	Nigeria	Eze et al. (2016)
Candida glabrata	Turkey	(Mataraci-Kara et al., 2020)
Candida tropicalis	Turkey	(Mataraci-Kara et al., 2020)
Candida guilliermondii	Turkey	(Mataraci-Kara et al., 2020)
Candida auris	USA	(Babler et al., 2023)
Trichophyton rubrum	Nigeria	Chukwu et al. (2018)

7.3.2 Health effects of exposure to fungi

Fungi can cause a range of different health effects with infection and severity depending on the fungi involved, and the immune status of individuals. Invasive fungal infections are more likely to occur in immunocompromised people. Over 90% of all deaths relating to fungi in humans are caused by *Aspergillus, Cryptococcus, Pneumocystis* or *Candida* species (Assress et al., 2019). Of the identified studies, only *Candida* and *Aspergillus* species were found in untreated hospital wastewater. Both are primarily opportunistic pathogens for severe disease and may pose less risk overall to public health.

Aspergillus species is primarily transmitted through airborne spores (Warris & Verweij, 2005). There is evidence it may contaminate and multiply in water sources, including through biofilm formation, and be aerosolized causing infection (Warris & Verweij, 2005). Ingestion of *Aspergillus* species may also cause infection (Anaissie & Costa, 2001; Warris & Verweij, 2005). In immunocompromised individuals, *Aspergillus* causes a range of non-specific symptoms relating to the area of infection. Infection may be disseminated, or occur in the respiratory tract, brain, or skin (Warris & Verweij, 2005).

Candida species cause a range of infections and can colonise individuals (Babler et al., 2023). *Candida* species are also found in water, with the potential for aerosolisation of spores or superficial infection (Akpor et al., 2014). Some infections may be mild and occur in otherwise healthy individuals, such as thrush. However, *Candida* species can cause severe, life-threatening illness when it is disseminated and colonises organs. The mortality rate in such infections is 30-50% and they largely occur in the immunocompromised population and/or through hospital acquired infections (Kabir & Ahmad, 2013; Lockhart, 2014).

7.4 PARASITES

7.4.1 Parasites in hospital wastewater

A range of parasites have been identified in HWW across the literature. Primarily worms, and protozoa. Table 8 details the parasites identified in the literature as being present in HWW. The presence of the protozoa *Giardia* and *Cryptosporidium* are the most significant for the risk to public health in New Zealand. *Giardia* and *Cryptosporidium* are mostly associated with overseas travel and rural exposure in New Zealand, and a recent outbreak of *Cryptosporidium* was thought to be caused by faecal contamination of the drinking water supply in Queenstown.[4] Several other pathogenic protozoa have also been identified, including *Entamoeba histolytica* and *Balatidum coli*, however, they are either uncommon or less clinically relevant in New Zealand.

Table 8: Summary of parasites identified in hospital wastewater.

Genus	Species	Parasite type	Country	Reference
Andolimax (*Endolimax*)	*A. nana*	Protozoa	Iran	Yousefi and Ziaei (2013)
Ascaris	Not further classified	Roundworm	Iran	Yousefi and Ziaei (2013)
	A. lumbricoides		Thailand	(Danchaivijitr et al., 2005b)
Balatidium	*B. coli*	Protozoa	Thailand	(Danchaivijitr et al., 2005b)
Blastocystis	*B. hominis*	Protozoa	Iran	Yousefi and Ziaei (2013)
Cryptosporidium	*C. hominis*	Protozoa	China	Jiang et al. (2020)
	C. parvum		China	Jiang et al. (2020)
	C. meleagridis		China	Jiang et al. (2020)
Entamoeba	*E. histolytica*	Protozoa	Iran	Yousefi and Ziaei (2013)
Enterocytozoon	*E. bieneusi*	Protozoa	China	Jiang et al. (2020)
Fasciola	Not further classified	Liver fluke	Iran	Yousefi and Ziaei (2013)
Genus	**Species**	**Parasite type**	**Country**	**Reference**
Fasciolopsis	*F. buski*	Giant intestinal flukes	Thailand	(Danchaivijitr et al., 2005b)

[4] Boil water notice remains in place as investigations identify water contamination as likely source of crypto outbreak | Southern Health | He hauora, he kuru pounamu

Giardia	Not further classified	Protozoa	Iran	Yousefi and Ziaei (2013)
	G. duodenalis		China	Jiang et al. (2020)
	G. intestinalis		Thailand	(Danchaivijitr et al., 2005b)
Gnathostoma	*G. spinigerum*	Nematode	Thailand	(Danchaivijitr et al., 2005b)
	No other details	Hookworm	Thailand	(Danchaivijitr et al., 2005b)
			Iran	Yousefi and Ziaei (2013)
Opisthorchis	*O. viverini*	Liver fluke	Thailand	(Danchaivijitr et al., 2005b)
Strongyloides	*S. stercoralis*	Roundworm	Thailand	(Danchaivijitr et al., 2005b)
Taenia	Not further classified	Tapeworm	Thailand	(Danchaivijitr et al., 2005b)
Toxocara	Not further classified	Roundworm	Iran	Yousefi and Ziaei (2013)
Trichocephalus	*T. trichiuris*	Whipworm	Iran	Yousefi and Ziaei (2013)

7.4.2 Health effects of exposure to parasites

Giardia intestinalis is a protozoon that causes gastrointestinal illness by infecting the upper small intestine (Einarsson et al., 2016). It is spread through the faecal-oral route. The incubation period is from 6-15 days after exposure. Infections may be asymptomatic, however primary symptoms include abdominal pain, and watery acute diarrhoea. The parasite can spread through contaminated water and may be endemic in developing countries around the world (Einarsson et al., 2016). Giardiasis is largely a self-limiting illness that does not require treatment, however chronic infections can occur and cases may develop symptoms of irritable bowel syndrome, food intolerances and malnutrition in children following infection (Einarsson et al., 2016).

Cryptosporidium spp. is another cause of diarrhoeal disease typically causing watery or mucous diarrhoea and abdominal pain (Hunter & Nichols, 2002). Infection resolves spontaneously and symptoms can last from days to several weeks (Gerace et al., 2019; Hunter & Nichols, 2002). *Cryptosporidium* spp. is spread through a faecal oral route, and can contaminate drinking water sources, as highlighted above in relation to the Queenstown outbreak in 2023, and swimming pools (Hunter & Nichols, 2002). In immunocompromised individuals disease is more severe, particularly in those with HIV, children with severe combined immunodeficiency syndrome, and people with CD40 ligand deficiency (Hunter & Nichols, 2002). In these individuals, infections can be prolonged with severe diarrhoea, and in some cases may be fatal (Hunter & Nichols, 2002).

7.5 ANTIMICROBIAL RESISTANCE

Antimicrobial resistance (AMR) occurs with changes to bacteria, viruses, fungi and parasites over time. These changes mean that the microbes do not respond to medications, which makes infections harder to treat. AMR increases the risk of severe illness and death, as well as increasing the risk of disease spread to others as medications become ineffective and infections persist. Antimicrobial resistance is an increasing issue of public health concern globally. In 2019 it was estimated that AMR directly caused 1.27 million deaths globally (ARC, 2022).

In some cases of AMR, strains may acquire resistance to multiple different drugs leading to the rise of multi- or pan-resistant strains which are untreatable with current antimicrobial treatments. The “ESKAPE” bacteria consisting of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species are leading causes of severe hospital-acquired infections with limited, or no antimicrobial treatment options remaining due to AMR (Sakkas et al 2019). There are some last resort antibiotics for treating resistant infections, including polymyxin E, vancomycin, daptomycin, tigecycline and linezolid (Li et al 2022). However, in recent years ARGs and strains resistant to these drugs have also been found (Li et al 2022).

HWW can both contribute to the development of AMR and contain resistant microbes. The WHO guidance of safe management of hospital waste highlights the extensive use of antibiotics in hospitals, and potential disposal and excretion of these as contributing to AMR through selective pressure (WHO, 2014). Additionally, HWW may be a potential reservoir for AMR. The primary antibiotic resistance genes discharged into municipal wastewater systems can become a source for horizontal gene exchange among bacterial community in main wastewater and onto the receiving environment if not adequately treated (Alam et al., 2013; Iweriebor et al., 2015; Timraz et al., 2017).

The presence of resistant microbes, specifically bacteria, in HWW is well studied. Hospital wastewater is a major source of antibiotic resistance genes (ARGs) and antibiotic-resistant bacteria into the environment (Guo et al 2021, Perry et al 2021). A wide range of ARGs and resistant bacteria have been identified in HWW. The higher prevalence of ARGs and resistant bacteria in HWW derives from the higher likelihood of patients with antibiotic-resistant infections being treated in a hospital setting, and higher concentrations of antibiotics and antimicrobials in HWW compared to municipal wastewater (Petrovich et al 2020).

AMR is present is significantly higher concentrations in HWW than in municipal wastewater systems with concentrations at least 2 -10 times higher (WHO, 2014). A study in India tested

ten HWW systems and eleven residential systems for AMR (Chitnis et al., 2000). AMR accounted for 0.58 to 40% of the bacterial population for hospitals, compared to 0.00002 to 0.025% in residential areas. AMR identified in these samples were against the most commonly used antibiotics by the health system (Chitnis et al., 2000). Further, a recent study comparing ARG diversity in wastewater from four hospitals, eight WWTPs and four community sites across Scotland found that ARGs are more enriched and diverse in HWW compared to other locations (Lepper et al 2023). A study by Perry et al (2021) tested wastewater from a hospital in Edinburgh across different departments and from a local WWTP. ARG composition varied between the different collection points and ARG abundance higher in hospital WW than the influent from the WWTP (Perry et al., 2021).

Studies have also identified variations between ARGs between different types of hospitals. Guo et al (2021) compared ARGs in wastewater from three hospitals in China - a general hospital, oral medicine (Stomatology) hospital and traditional Chinese medicine hospital. The three different hospital types showed different ARGs profiles with resistance genes against 34 types of antibiotics identified (Guo et al., 2021). ARGs associated with bacitracin were the most abundant ARGs in wastewater from the general and traditional hospitals, whilst in wastewater from the oral medicine hospital the most abundant ARGs were associated with tetracyclines (Guo et al., 2021).

Of concern, a study in Israel found ARGs conferring resistance to 22 classes of antibiotics with the most prevalent being for aminoglycoside, cephalosporin, macrolide, penam, and tetracycline antibiotics (Petrovich et al 2020). Three of the resistance genes identified, *mefA, mel* and *GES-5*, confer resistance of antibiotics considered critically important by the WHO (macrolides for *mefA* and *mel* and carbapenems and cephalosporins for *GES-5*). Additionally, Mcr-1 was identified by Hutinel et al (2022) which confers resistance to the last-resort antibiotic polymyxin-E (Petrovich et al 2020).

Almost all the data pertaining to AMR in HWW is related to bacteria, however, there was one study showing *Candida* species found in HWW as being resistant to fluconazole and itraconazole (Mataraci-Kara et al., 2020). There are limited treatment options for fungal infections, and the development of increasing resistance to available treatments are also of increasing concern to public health (Kaur et al., 2020; Pristov & Ghannoum, 2019).

8. PHARMACEUTICALS

Pharmaceuticals are some of the main chemical substances found in HWW (Zhang et al., 2020). These primarily enter HWW in the urine and/or faeces of patients, either in original composition or as metabolites (Zhang et al., 2020). Additionally, they can enter HWW via disposal of unused medicines into the sink or toilet. It is noted that the World Health Organization report on safe management of wastes from health-care activities recommends "pharmaceuticals should not be discharged into wastewater but collected separately and treated as chemical health-care waste" (WHO, 2014).

A range of different pharmaceutical classes have been identified in HWWs, including analgesics and anti-inflammatories, anticonvulsants, antihistamines, antihypertensives, antivirals, β-blockers, lipid regulators and a variety of psychiatric drugs. This chapter will detail the pharmaceuticals identified in HWW and discuss the possible health impacts of contamination. Cytotoxic pharmaceuticals are excluded from this report as they were comprehensively covered in a previous report prepared for the Ministry of Health (Eaton & Coxon, 2023).

8.1 PHARMACEUTICALS IN HOSPITAL WASTEWATER

Studies comparing domestic and hospital wastewaters have shown that the concentration of almost all pharmaceuticals is greater in HWW (Al Aukidy et al., 2014; L. H. Santos et al., 2013; Verlicchi et al., 2012). Where a hospital pre-treats their wastewater, these chemicals may be removed by advanced treatment processes. However, where HWWs are discharged to the municipal network for co-treatment it is likely that many of these chemicals will not be removed, or only partially removed as conventional wastewater treatment processes are not designed to treat/remove pharmaceuticals, as discussed in Coxon and Eaton (2023).

A wide variety of pharmaceuticals have been detected in HWWs around the world, as detailed in the appendix and summarised in table 9 for antibiotics and table 10 for other pharmaceuticals. Of the 10 drugs with the highest reported maximum concentrations in the assessed studies, nine are antibiotics and include ofloxacin (13,987 µg/L), norfloxacin (2,202 µg/L), sulfamethoxazole (1429 µg/L), ciprofloxacin (680 µg/L), cefepime (540 µg/L), trimethoprim (494 µg/L), clarithromycin (218 µg/L), azithromycin (201 µg/L) and roxithromycin (125 µg/L).

While antibiotics were detected in the highest concentration, there is also significant variability in concentration of specific antibiotics between studies. For example, the highest reported concentration of norfloxacin was 2201.9 µg/L, and the lowest concentration was 0.02 µg/L (Cai et al., 2022; Paulus et al., 2019). For azithromycin the concentrations ranged from <0.005 - 200.9 µg/L (Cai et al., 2022; Sörengård et al., 2019a). These differences could be explained by a range of factors including the different infections prevalent in the community, prescribing practices of medical professionals and different bacterial sensitivities to antibiotics.

Additionally, while not the focus of this report, the ongoing presence of antibiotics in post treatment HWW identified in a range of studies highlight the overall inefficiency of removal on antibiotics in treatment systems (Phoon et al., 2020; Watkinson et al., 2007). The presence of antibiotics in high concentrations in HWW, and on through to the receiving environment, is of particular concern for the development of antimicrobial resistance. Antimicrobial resistance is discussed in the pathogenic microbes' chapter of the report.

Table 9: Antibiotics detected in hospital wastewater.

Antibiotic class	Pharmaceutical	Countries detected in	Max. conc. (µg/L) *
Aminocyclitols	Spectinomycin	Kenya	0.3*
Aminoglycosides	Clavulanic acid	Qatar	41.2
	Gentamicin	Romania	7.9
Amphenicols	Chloramphenicol	Sweden	0.2*
Beta-lactamase inhibitors	Tazobactam	Romania	10.3*
Carbapenems	Imipenem	Romania, Iran	29.1
	Meropenem	China	0.2
Cephalosporins	Cefalotin	China	0.1
	Cefazolin	China, Turkey	5
	Cefdinir	Japan	0.07
	Cefepime	China, Romania	540.4
	Cefixime	Iran	12.4
	Cefoxitin	China	9
	Cefradine	China	2.4
	Ceftazidime	China, Romania, Turkey	31.2
	Cephalexin	China, Turkey	0.9
Diaminopyrimidines	Trimethoprim	Cameroon, China, Colombia, Germany, Iran, Kenya, Netherlands, Portugal, Romania, Spain, Sweden, Switzerland, Thailand, Turkey, Spain	493.8*
Fluoroquinolones	Ciprofloxacin	Cameroon, China, Colombia, France, Iran, Japan, Netherlands, Nigeria, Portugal, Qatar, Slovakia, Spain, Switzerland, Thailand, Turkey, USA	680
	Levofloxacin	Japan	0.7
	Lomefloxacin	China	2.3*
	Norfloxacin	China, Colombia, Netherlands, Nigeria, Spain, Switzerland, Thailand, Turkey	2201.9*
	Ofloxacin	China, Iran, Netherlands, Nigeria, Portugal, Spain, Turkey	13,987*
Glycopeptides and lipoglycopeptides	Vancomycin	France, Romania	14.0*
Lincosamides	Clindamycin	Colombia, Spain, Sweden, Switzerland, Turkey, USA	24.1
	Lincomycin	China, Thailand	66.9*

Antibiotic class	Pharmaceutical	Countries detected in	Max. conc. (µg/L) *
Macrolides	Azithromycin	Cameroon, China, Colombia, Japan, Portugal, Slovakia, Sweden, Switzerland, Turkey, USA	200.9*
	Clarithromycin	Cameroon, China, Colombia, Germany, Japan, Netherlands, Portugal, Spain, Sweden, Switzerland, Turkey	218.1
	Erythromycin	Cameroon, Colombia, Netherlands, Portugal, Qatar, Romania, Slovakia, Spain, Sweden, Thailand, Turkey	7.5
	Roxithromycin	China, Germany, Sweden, Switzerland, Thailand, Turkey	125.1*
	Spiramycin	Kenya	1.6*
Nitroimidazoles	Metronidazole	Colombia, Iran, Netherlands, Portugal, Qatar, Sweden, Switzerland, Turkey	12.3
Penicillins	Amoxicillin	China, Iran, Qatar, Thailand	7.9
	Ampicillin	China, Kenya, Romania, Turkey	53.1*
	Dicloxacillin	Kenya	17.3
	Oxacillin	Kenya	0.2
	Penicillin	Qatar	0.1*
	Penicillin G	Mexico, Portugal	3.8*
	Penicillin V	Mexico, Portugal	0.6
	Piperacillin	Romania	7.8*
Quinolones	Nalidixic acid	Belgium	<LOQ
Rifamycins	Rifaximin	USA	Not quantified
Sulfonamides	Sulfachloropyridazine	Netherlands	0.02*
	Sulfaclozine	Netherlands	0.04*
	Sulfadiazine	Kenya, Netherlands, Spain, Switzerland, Tunisia, Turkey	39.3
	Sulfadimethoxine	Germany, Tunisia, Turkey	2.7*
	Sulfaguanidine	Tunisia	0.3
	Sulfamerazine	Netherlands	0.01
	Sulfamethazine	Kenya, Portugal, Spain, Tunisia, Turkey	15.7*
	Sulfamethizole	Tunisia	1.1
	Sulfamethoxazole	Belgium, Cameroon, China, Colombia, France, Iran, Kenya, Mexico, Netherlands, Portugal, Romania, Spain, Sweden, Switzerland, Thailand, Tunisia, Turkey	1429.3*
	Sulfamethoxypyridazine	China, Netherlands, Tunisia	18.2*

	Sulfamonomethoxine	Netherlands	0.01*
	Sulfanilamide	Kenya	7.7*
	Sulfapyridine	Netherlands, Switzerland, Turkey	4.3
Antibiotic class	**Pharmaceutical**	**Countries detected in**	**Max. conc. (µg/L) ***
Sulfonamides	Sulfathiazole	Tunisia, Portugal	0.3
	Sulfisoxazole	Netherlands, Tunisia	1.1*
Tetracyclines	Chlortetracycline	Turkey	0.02
	Doxycycline	Portugal, Turkey	0.7
	Oxytetracycline	Turkey	0.03
	Tetracycline	Belgium, Iran, Portugal, Qatar, Romania, Sweden, Thailand	2.4

*Indicates value is the highest average value reported where this is higher than reported maximum values.

Table 10 summarises the non-antibiotics pharmaceuticals found in HWW, with the maximum concentration found across identified studies. Pharmaceuticals are organised by therapeutic class. Where pharmaceuticals have more than one therapeutic action, for example Gabapentin, they are listed under the class they are most used for in New Zealand medical settings. Not all the pharmaceuticals listed will be used in the New Zealand context. It was beyond the scope of the review to complete an assessment of whether pharmaceuticals were licensed for use in New Zealand.

With regards to non-antibiotic drugs, acetaminophen (paracetamol) was detected at the highest concentration in the assessed studies, with a maximum concentration of 1,510 µg/L. The next highest reported non-antibiotic drugs were an order of magnitude lower and include the anti-diabetic drug metformin (154 µg/L), analgesic tramadol (76 µg/L), non-steroidal anti-inflammatory drug (NSAID) loxoprofen (65.3 µg/L), and salicylic acid (62 µg/L). Other therapeutic classes with concentrations of pharmaceuticals found in this order of magnitude include, histamine H_2 receptor antagonists, lipid regulators, and analgesics.

As can be seen in table 10, there is a comprehensive range of therapeutic classes of pharmaceuticals identified in HWW. Concentrations seen in wastewater will also depend on the order of magnitude of dosages for a given pharmaceutical. For example, the dose of Ibuprofen for adults is 400 mg, while the dose of amlodipine (antihypertensive) may only be 5 mg. Equally, this means that higher concentrations in wastewater does not necessarily imply higher health risks.

In the identified studies, there were wide ranges of concentrations seen for individual pharmaceuticals, as discussed earlier in relation to the variable concentrations seen for antibiotics. This highlights that HWW is not uniform in its potential health risks, pharmaceuticals found in lower concentrations in the literature may be present in higher concentrations in other hospitals wastewater and vice versa. The concentrations and ranges of therapeutic classes identified will depend on the type of hospital and the pharmaceuticals licensed for use in the country or state the hospital is located in. For example, psychiatric hospitals would have higher concentrations of psychiatric medications. Paediatric hospitals would also have a different range and concentration value of pharmaceuticals given the different prevalence of conditions and in general lower doses used in children compared to adults.

Table 10: Non-antibiotic pharmaceuticals identified in hospital wastewater.

Therapeutic class	Pharmaceutical	Countries detected in	Max. conc. (µg/L) *
ACE inhibitors	Enalapril	Mexico, Spain, Turkey	0.3
Adrenergic agonists	Etilefrine	USA	Not quantified
Alpha blockers	Tamsulosin	Portugal	0.003
Anaesthetics	Bupivacaine	USA	Not quantified
	Ketamine	USA	Not quantified
	Levomenthol	USA	Not quantified
	Lidocaine	Sweden, Switzerland, Turkey, USA	9.1*
	Propofol	USA	Not quantified
	Ropivacaine	USA	Not quantified
	Thiopental	Switzerland, USA	0.8*
Analgesics and anti-inflammatories	Aceclofenac	Sweden	< 0.05*
	Acetaminophen	Cameroon, Colombia, France, Japan, Mexico, Portugal, Spain, Sweden, Switzerland, Turkey	1,510
	Anileridin	USA	Not quantified
	Celecoxib	USA	Not quantified
	Codeine	Germany, Portugal, Slovakia, Sweden	2.8
	Diclofenac	Colombia, France, Germany, Mexico, Portugal, Spain, Sri Lanka, Sweden, Switzerland, Tunisia, Turkey	8.0
	Dihydrocodeine	Germany	0.1*
	Ethenzamide	Japan	0.1
	Gabapentin	Spain, Switzerland, USA	23.0
	Glucosamine	USA	Not quantified
	Ibuprofen	Cameroon, France, Germany, Japan, Mexico, Portugal, Spain, Sri Lanka, Sweden, Turkey	38.1
	Indomethacin	Japan, Portugal, Spain, Sri Lanka, Switzerland, Tunisia	0.3
	Ketoprofen	France, Portugal, Spain, Tunisia, Turkey	20
	Loxoprofen	Japan	65.3
	Meclofenamic acid	Sweden	< 0.05*
	Mefenamic acid	Sri Lanka, Sweden, Switzerland, Turkey	12.1
	Methadone	USA	Not quantified

Therapeutic class	Pharmaceutical	Countries detected in	Max. conc. (µg/L) *
	Morphine	Germany, Switzerland	3.7*
	Naproxen	Colombia, Germany, Mexico, Portugal, Spain, Sweden, Turkey	30
	Oxycodone	Germany, Portugal, Slovakia, Sweden	0.3*
	Phenazone	Portugal, Spain, Sweden, Switzerland, Tunisia, Turkey	0.4
	Phenylbutazone	Tunisia	0.2
	Piroxicam	Portugal	0.05
	Propyphenazone	Portugal, Spain, Turkey	0.04
	Salicylic acid	France, Portugal, Tunisia	62
	Sulindac	Sweden	<0.003
	Tramadol	Cameroon, Slovakia, Spain, Sri Lanka, Sweden, Switzerland, Turkey	76*
Antiandrogens	Bicalcutamide	Sweden, Turkey	0.1*
Anticoagulants	Warfarin	Portugal, Sri Lanka, USA	0.008
Anticonvulsants	Lamotrigine	Sweden, USA	0.6*
	Levetiracetam	Switzerland	11.0*
	Oxcarbazepine	Mexico, Turkey	1.6*
	Phenytoin	Sri Lanka	6.1
	Primidone	Germany, Spain, Sweden, Switzerland	2.1*
	Valproic acid	Sweden, USA	0.5*
Antidiabetics	Glibenclamide	Mexico, Tunisia	1.9*
	Metformin	Cameroon, Mexico, Portugal, Turkey, USA	154*
Antifungals	Climbazole	Sweden	0.09*
	Econazole	France	0.02
	Fluconazole	Netherlands, Sweden, Switzerland, USA	13*
	Thiabendazole	Portugal, Sweden	1.7
	Voriconazole	USA	Not quantified
Antihistamines	Benadryl	USA	Not quantified
	Cetirizine	France, Sweden, Sri Lanka	1.5
	Chlorpheniramine	Sri Lanka	0.3
	Desloratadine	Portugal	0.01
	Diphenhydramine	Cameroon, Sri Lanka	0.4*
	Fexofenadine	Sweden, USA	0.4*

	Hydroxyzine	France	0.02*
	Levocetirizine	USA	Not quantified
	Loratadine	Mexico	0.3*
Therapeutic class	**Pharmaceutical**	**Countries detected in**	**Max. conc. (µg/L) ***
Antihypertensives	Amlodipine	Portugal, Sri Lanka	0.2
	Irbesartan	Colombia, Portugal, Spain, Sweden, USA	3.9
	Losartan	Colombia, France, Japan, Mexico, Portugal, Spain, Sri Lanka, Sweden, Turkey	7.7*
	Olmesartan	Japan	0.2
	Ramipril	Sweden	0.006*
	Valsartan	Colombia, Portugal, Slovakia, Spain, Sweden, Switzerland	19.8
Antiparasitics	Albendazole	Portugal	0.03
	Crotamiton	Japan	0.2
	Levamisole	Portugal	0.2
	Pyrimethamine	Sweden	0.0002*
Antiplatelet agents	Clopidogrel	Portugal	0.4
Antivirals	Aciclovir	Japan	0.1
	Famciclovir	Japan	0.06
	Nevirapine	USA	Not quantified
	Oseltamivir	Switzerland	0.03*
	Penciclovir	Japan	0.03
	Ritonavir	Switzerland	0.1*
	Valaciclovir	Japan	0.02
β–Blockers	Acebutolol	France	0.1*
	Atenolol	Cameroon, France, Mexico, Portugal, Slovakia, Spain, Sweden, Switzerland, Tunisia, Turkey	39
	Bisoprolol	France, Sweden, Turkey	0.2*
	Carazolol	Portugal	0.007
	Carvedilol	Sri Lanka	0.02
	Metoprolol	Mexico, Portugal, Spain, Sweden, Switzerland, Tunisia, Turkey	5*
	Propranolol	Cameroon, France, Portugal, Spain, Sri Lanka, Sweden, Switzerland, Tunisia, Turkey	3.8

	Sotalol	France, Portugal, Spain, Sweden, Switzerland, Turkey	0.8
	Timolol	Tunisia	0.02

Therapeutic class	Pharmaceutical	Countries detected in	Max. conc. (µg/L) *
Bronchodilators	Salbutamol	Portugal, Tunisia, Spain, Sweden	2.6
	Theophylline	France, Japan	6.4
Calcium channel blockers	Diltiazem	Portugal, Sri Lanka, Sweden	1.5
	Verapamil	Portugal, Switzerland	0.7
Dehydropeptidase inhibitors	Cilastatin	Switzerland, Turkey	13
Diuretics	Furosemide	Portugal, Spain, Sweden, Switzerland, Tunisia, Turkey	32.6
	Hydrochlorothiazide	Portugal, Spain, Sweden, Switzerland, Tunisia	2.1
Histamine H_2 receptor antagonist	Cimetidine	Cameroon, Portugal	34*
	Famotidine	Portugal, Tunisia	15.2
	Ranitidine[#]	Portugal, Sweden, Switzerland, Turkey	19.8
Hormones	17-α-Estradiol	Turkey	0.03
	17-α-Ethinylestradiol	Turkey	0.7
	17-β-Estradiol	Turkey	0.1
	Androstanedione	USA	Not quantified
	Cortisone	Turkey	4.4
	Estriol	Turkey	2.2
	Estrone	Turkey	0.2
	Hexestrol	USA	Not quantified
	Hydrocortisone	Turkey	0.3
	Prasterone	USA	Not quantified
	Testosterone cypionate	USA	Not quantified
	Testosterone propionate	USA	Not quantified
Immunosuppressive agents	Mycophenolate	USA	Not quantified
Lipid regulators	Atorvastatin	Portugal, Spain, Sri Lanka, Sweden, Turkey	4.1
	Bezafibrate	Germany, Portugal, Spain, Sweden, Switzerland, Turkey	5.5*

	Fenofibrate	Spain, Turkey	0.1
	Fenofibric acid	Sri Lanka	2.7
	Fluvastatin	Portugal	0.03
	Gemfibrozil	Portugal, Sri Lanka	1.1
	Pravastatin	Portugal	2.1
	Rosuvastatin	Turkey	0.64
	Simvastatin	Turkey	24
Melanin synthesis inhibitors	Mequinol	USA	Not quantified
Phytochemicals	Berberine	Japan	0.08
	Daidzein	Japan, Sweden	2.1
	Daidzin	Japan	0.2
	Genistein	Japan, Sweden	1.0
	Genistin	Japan	0.4
	Glycitein	Japan	1.4
	Glycitin	Japan	0.07
	Puerarin	Japan	2.6
Proton pump inhibitors	Omeprazole	Mexico	0.8*
	Pantoprazole	Spain	0.2

Therapeutic class	**Pharmaceutical**	**Countries detected in**	**Max. conc. (µg/L) ***
Psychiatric drugs	Alprazolam	Portugal, Spain, Sri Lanka	0.2
	Amitriptyline	Tunisia	0.09
	Azaperone	Portugal	0.004
	Benperidol	Turkey	0.05
	Carbamazepine	Cameroon, Colombia, France, Germany, Japan, Portugal, Slovakia, Spain, Sri Lanka, Sweden, Switzerland, Tunisia, Turkey	12
	Chlorpromazine	Brazil, Sri Lanka	0.5*
	Chlorprothizene	Turkey	0.05
	Citalopram	France, Portugal, Slovakia, Turkey	0.9
	Clozapine	Brazil, Turkey	1.0*

	Cyamemazine	France	0.3*
	Desvenlafaxine	Sweden	0.6*
	Diazepam	France, Germany, Portugal, Spain, Sri Lanka, Sweden, Switzerland	0.07*
	Doxepin	Germany	0.1*
	Escitalopram	USA	Not quantified
	Fluoxetine	France, Portugal, Sri Lanka, Sweden, Tunisia	0.8
	Haloperidol	Brazil, Sri Lanka, Turkey	2.7*
	Lorazepam	France, Portugal, Spain, Sri Lanka	1.3
	Melperone	Turkey	0.02
	Memantine	Sweden	0.02*
	Meprobamate	France	0.2*
	Mirtazapine	Sweden, Turkey	0.8
	Nordazepam	Germany	0.2*
	Norfluoxetine	France, Portugal, Sri Lanka	0.09
	Olanzapine	Brazil, Portugal, Turkey	0.8
	Oxazepam	France, Germany, Slovakia, Sri Lanka, Sweden, Switzerland, Turkey	7*
	Paroxetine	Portugal, Spain	0.9
	Pipamperone	Turkey	0.07
	Quetiapine	Sri Lanka	0.2
	Risperidone	Brazil, Turkey	0.77
	Sertraline	France, Portugal, Sri Lanka, Sweden	0.09
Therapeutic class	**Pharmaceutical**	**Countries detected in**	**Max. conc. (µg/L) ***
Psychiatric drugs	Sulpride	Japan	7.3
	Temazepam	Germany	0.02*
	Trazodone	Portugal	0.05
	Venlafaxine	Colombia, Portugal, Spain, Sweden, Switzerland, Turkey, Slovakia, USA	1.9
	Zuclopenthixol	Turkey	0.9
Sedatives and muscle relaxants	Chlorzoxazone	Sweden	0.1*
	Midazolam	Slovakia, USA	0.1*
	Xylazine	Portugal	0.02
Stimulants	Benzedrex	USA	Not quantified
	Cathine	USA	Not quantified

	Ephedrine	USA	Not quantified
Synthetic glucocorticoids	Dexamethasone	Portugal, Switzerland	0.4
	Methylprednisolone	Switzerland	1.4*
Vasodilators	Isosorbide	USA	Not quantified
	Sildenafil	Spain	0.1

*Indicates value is the highest average value reported where this is higher than reported maximum values.

8.2 HEALTH EFFECTS OF PHARMACEUTICALS IN HWW

There are several examples of studies available in published literature that have completed human health risk assessments on the presence of pharmaceuticals in and across aquatic environments including drinking water, surface water and groundwater (de Jesus Gaffney et al., 2015; Kumar et al., 2010; Mheidli et al., 2022; Nassiri Koopaei & Abdollahi, 2017; Sanderson, 2011; Simazaki et al., 2015). The majority of studies assessing health risks of low dose exposure in the environment focus on the risk of exposure to trace pharmaceuticals in drinking water and surface water, which is contaminated by wastewater discharges into receiving environments (WHO, 2012).

The aforementioned studies assessing human health risk of pharmaceuticals in water sources have broadly concluded that there is currently no appreciable health risks identified (de Jesus Gaffney et al., 2015; Mheidli et al., 2022; Nassiri Koopaei & Abdollahi, 2017; Sanderson, 2011 ; Schwab et al., 2005; Simazaki et al., 2015; WHO, 2012). Once in drinking water, pharmaceuticals are generally present more than 1000 times below a given minimum therapeutic dose (WHO, 2012). HWW will have higher concentrations as it will not be treated or diluted. However, concentrations of pharmaceuticals detected in HWW are still found in orders of magnitude less than the dose used clinically (Sanderson, 2011; WHO, 2012). For example, ofloxacin was found at the highest concentration of 13.98 mg/L and the oral dose for adults is up to 400 mg twice daily.

Though preliminary assessments for health risks of pharmaceuticals in wastewater may suggest low risk there are several knowledge gaps in the potential health effects of exposure to pharmaceuticals present in HWW (Kumar et al., 2010; WHO, 2012), like many of the contaminants discussed in this report. The effects of chronic low dose exposure, below therapeutic dose levels, are not well understood (Kumar et al., 2010; WHO, 2012). Additionally, it is not clear how pharmaceuticals may interact in wastewater, and whether this would impact the potential public health effects (Schwab et al., 2005; WHO, 2012). Numerous pharmaceuticals have interactions and cannot be taken together when prescribed, it is not clear how this manifests in low doses (Kumar et al., 2010) (Schwab et al., 2005). Also, by products formed from pharmaceuticals may be toxic, while the parent compound is considered ‘safe’ at low levels of exposure (de Jesus Gaffney et al., 2015). Finally, the health risks for sensitive sub-populations, including children and pregnant people, are not clear (WHO, 2012). A current lack of data regarding human health risks does not mean there is no health risk present. Further research is required to address knowledge gaps and develop a deeper understanding of the health risks.

9. RADIOISOTOPES

Radioisotopes are radioactive pharmaceuticals and are used in the medical setting for the diagnosis and treatment of diseases. When used diagnostically, the radioactive label will emit electromagnetic radiation to allow detection of the radionuclide (Vermeulen et al., 2019) Computed Tomography (CT) and Positron Emission Tomography (PET) scans detect the uptake of radionuclides, and the degree of contrast in the image determines the concentration in the target tissues, relative to surrounding tissues (Vermeulen et al., 2019) Additionally, they may be used intraoperatively in procedures, such as identifying sentinel lymph nodes, with small detectors used to detect radiation (Vermeulen et al., 2019). In therapeutic applications, the radionuclide decays and releases ionizing radiation to destroy targeted cells (Vermeulen et al., 2019).

Radiopharmaceuticals are largely used parenterally, with a small number administered through inhalation or oral routes (Vermeulen et al., 2019). Radiopharmaceuticals used for diagnostic purposes require small doses, while therapeutic use requires significantly higher dosages. Radioisotopes have variable half-lives, and excretion mainly occurs through urine. Routes into HWW for radioactive waste will include patient urine and excreta, disposal of medication, or through cleaning areas where radioactive substances may have been used (e.g. sinks) (Piersanti et al., 2018).

The New Zealand Radiation Safety Act 2016 includes dose limits for exposure to ionising radiation. For public exposure the Act states that the dose limits are an effective dose of 1 mSV in a year, or and equivalents dose to the lens of the eye of 15 mSv in a year, or an equivalent dose to the skin of 50 mSv in a year.[5]

9.1 RADIOISOTOPES IN HOSPITAL WASTEWATER

A range of radioisotopes have been detected in untreated HWW. Radioisotopes detected varied between studies, likely contributed to by the different pharmaceuticals available in the countries studied, Additionally, activity levels of each radioisotope varied between studies. Studies reported that it was common practice for patients who had received radiopharmaceuticals effluent to be discharged into the standard sewerage systems (Martínez et al., 2018). Some countries may require the short-term collection of urine until

[5] Radiation Safety Act 2016 No 6 (as at 28 October 2021), Public Act Schedule 3 Dose limits for ionising radiation – New Zealand Legislation

radioactivity has reached a certain level, however this is not required by the International Commission on Radiological Protection.

Piersanti et al (2018) measured the radioactivity of single radionuclides identified in samples of hospital wastewater. The range of radioactivity was scored for each radionuclide identified. Iodine-131, technetium-99m, gallium-67, thallium-201, iodine-123 and indium-111 were all identified in the HWW from 2010-2015. As specific values are not given and the measurements are for individual radionuclides, these have not been included in the table. However, Figure 2 sourced from the article, is included to demonstrate the range of radioactivity found in individual radionuclides. (Piersanti et al., 2019)

Figure 2: Range of radioactivity detected in single radionuclides in hospital wastewater. Sourced from (Piersanti et al., 2018)

Activity range		N. of analysed samples						
		Activity in the range for single radionuclide						for total radionuclides
≥ Bq/l	< Bq/l	^{131}I	^{99m}Tc	^{111}In	^{67}Ga	^{123}I	^{201}Tl	
0	1	331	377	425	70	51	338	3
1	5	43	55	17	386	67	118	17
5	10	15	27	4	21	243	13	154
10	50	51	12	14	8	120	12	214
50	100	17	3	8	1	4	4	33
100	1,000	17	8	13	0	1	1	44
1,000	10,000	9	4	5	0	0	0	18
10,000	50,000	2	0	0	0	0	0	2
50,000	100,000	1	0	0	0	0	0	1

Overall, it appears radioisotopes are found in higher concentrations in HWW compared to municipal. Of note, radioactive iodine is used primarily for the treatment of thyroid disorders. Patients receiving this treatment usually do not stay in hospital, so concentrations of radioactive iodine are lower in hospital wastewater compared to municipal in a Spanish hospital studied (Martínez et al., 2018). Table 11 details the different radioisotopes identified and the average and maximum radioactivity.

Table 11: Summary of studies assessing presence of radionuclides in hospital wastewater.

Radionuclide	Half-life*	Mode(s) of decay*	Average activity (Bq/L)	Max. activity (Bq/L)	Hospital type	Country	Reference
Gallium-67	3.26 days	ɣ, electron capture	ND – 17.3 ± 1.0		General	Spain	Krawczyk et al. (2013)
				16.9 ± 0.3	General	Spain	(Martínez et al., 2018)
Technetium-99m	6 hours	ɣ	148.7 ± 9.8 – 2510 ± 157.6		General	Spain	Krawczyk et al. (2013)
			717	14,151	General + maternity	Kuwait	Mydlarczyk et al. (2022)
				1,268.5 ± 42.0	General	Spain	(Martínez et al., 2018)
Indium-111	2.83 days	ɣ, electron capture	ND – 36.1 ± 4.3		General	Spain	Krawczyk et al. (2013)
Iodine-131	8.02 days	ɣ, β^-	ND – 59.3 ± 2.7		General	Spain	Krawczyk et al. (2013)
			5.5	27.1	General + maternity	Kuwait	Mydlarczyk et al. (2022)

Of note, Martinez et al (2018) completed an exposure assessment for WWTP workers for exposure to radioactive iodine (iodine-131) present in HWW, as this this was present in significantly higher levels than other radioisotopes tested. The assessment concluded that even with worst-case scenario calculations, workers were not at risk of adverse health impacts from the concentrations present in the wastewater with exposure doses not exceeding recommended limit (Martínez et al., 2018). Similar findings are reported in a Swedish dose assessment and modelling study including WWTP workers, however, the concentrations inputted were from municipal wastewater with hospitals feeding into the WWTP (Sundell-Bergman et al., 2009). Estimated doses for iodine-131 for sewage workers were the closest to dose limits, though still below 10 µSv/y (Sundell-Bergman et al., 2009).

The International Atomic Energy Agency provides advice for health workers on the public health risks of radiation exposure from radiopharmaceuticals. Exposure to the public at a potentially harmful dose usually occurs through external exposure from emitted radiation from a treated patient (IAEA, 2017). The agency reports that ingestion of contaminated radioactive bodily fluids, or environmental pathways, including sewerage, would contribute little if any exposure (IAEA, 2017).

9.2 HEALTH EFFECTS OF EXPOSURE TO RADIOISOTOPES

There are clear long term health impacts from radiation exposure, largely established from epidemiological studies from survivors of the Japanese atomic bomb and Chernobyl disaster. Long term impacts include increased risk of cancers, cardiovascular diseases, and microcephaly and restricted childhood growth when exposed in utero (Kamiya et al., 2015; Rühm et al., 2022). These epidemiological studies have focused on high dose exposure to radiation, and evidence is limited, but growing, for low dose (<100mGy) long term health impacts (Kamiya et al., 2015; Rühm et al., 2022). The background population incidence of diseases associated with radiation exposure is high, making it challenging to establish clear epidemiological evidence on low level radiation exposure impacts (Rühm et al., 2022; UNSCEAR, 2010).

Ionising radiation is carcinogenic. There is no threshold value below which there is no risk, and it is assumed that the relationship between exposure dose and risk is linear (UNSCEAR, 2010). However, at lower doses, the relationship between radiation and cancer risk remains unclear within the current evidence base (Kamiya et al., 2015). Current evidence shows a dose of 100mGy is clearly associated with an increased risk of cancer, however some larger and more recent studies, including meta-analyses, have shown an increased risk at lower doses (Hauptmann et al., 2020; Rühm et al., 2022). A 2020 systematic review by the United States National Cancer Centre concluded that despite methodological challenges, recent epidemiological studies support excess solid cancer risk and leukaemia risk from low dose exposure to ionizing radiation, as shown in table 12 (Hauptmann et al., 2020).

Table 12: Meta-analysis of excess relative risks (ERR) at 100 mGy for all solid cancers and leukaemia. Sourced from: (Hauptmann et al., 2020)

Outcome	**No. of studies**	**ERR at 100mGy**	***P***
Adult solid cancer	13	0.029 (0.011, 0.047)	<0.001
Adult leukaemia	14	0.160 (0.070 to 0.250)	<0.001
Childhood leukaemia	6	2.840 (0.370 to 5.320)	0.01

CONCLUSIONS

This review has identified a range of potential public health hazards present in HWW. HWW is clearly a special category of hazardous wastewater given the infectious properties, risk of AMR, higher pharmaceutical load, radioisotopes and chemical substances present in varying concentrations. The presence and concentration of the contaminants discussed will depend on the type of hospital and community it is in as to what specific contaminants are present. Additionally, higher concentrations of contaminants does not equal an increased public health risk. The toxicity of a given contaminant is relative and the concentration causing harm to human health varies. Concentrations of contaminants can vary between studies and will depend on factors such as the treatments available in hospital, and pathogen prevalence in the community feeding into the hospital. The concentrations of specific contaminants, particularly pharmaceuticals, varied significantly between studies by several orders of magnitude in some cases. This highlights that HWW is not a homogenous entity and needs to be assessed contextually. It is likely that contaminants found internationally will have different relevance and significance to public health in New Zealand.

There is clear knowledge gaps of health impacts for low dose exposure to many of the contaminants identified in HWW. There is a scarcity of epidemiological evidence for chronic low dose exposure for several contaminants including contrast media and pharmaceuticals. Additionally, the interactions between contaminants and how this may alter toxicity are not known. Further research will be required to address knowledge gaps and develop a full understanding of the health risks associated with these contaminants. Ongoing monitoring of available literature surrounding the health risks associated with emerging contaminants would be beneficial.

The potential for disposal of antibiotics directly into HWW, and excretion through patients, is a concerning feature of HWW. The high concentrations of antibiotics present in HWW is a significant public health risk for the development of further antimicrobial resistance in the environment. Of the pharmaceuticals detected in HWW, nine of the top 10 with highest concentrations were antibiotics. Additionally, horizontal gene transfer is possible from AMR with HWW identified as a potential reservoir. AMR is also present in higher proportions in HWW compared to domestic wastewater with several studies showing bacteria present in HWW as resistant to last resort antibiotics.

Te Ao Māori perspectives on HWW are essential to incorporate into a public health assessment of risks of HWW. The effects on hauora not limited to the physical health effects

discussed in each chapter of this report for selected contaminants. The discharge of HWW in waterways, even when treated to meet required standards, is not permitted, and may have profound impacts on hauora, including mental and spiritual wellbeing. Additionally, social and political marginalisation and devaluing of Mātauranga Māori, through the ongoing process of colonisation, has resulted in failure to meet te Tiriti o Waitangi provided rights to tino rangatiratanga for Māori. This has impacted the ability for Māori to have meaningful partnership in wastewater decision making and as shown has implications for health equity.

The aim of this review was to provide a scoping assessment of the potential health hazards present in HWW. Of note, none of the literature identified examining concentrations of HWW contaminants was completed in New Zealand. Therefore, inclusion in the review does not mean that they will be present and constitute a public health risk. Equally, exclusion from the report does not mean that hazardous substances are not present or a risk to public health. There is the potential for health effects from exposure to hospital wastewater across a broad range of contaminants. It would be beneficial to develop a deeper understanding of the concentration of contaminants present in the New Zealand context to be able to comment specifically on the potential effects of contaminants on public health.

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APPENDIX A: DETAILED TABLES OF CONTAMINANTS PRESENT IN HOSPITAL WASTEWATER

Heavy metals detected in hospital wastewater.

Heavy metal	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Aluminium	59	71	Hospital laboratory	Turkey	B. Akin (2016)
Arsenic	10		General	France	(Boillot et al., 2008)
		2	General	Indonesia	Sakina et al. (2023)
	14		General	Mexico	Pérez-Alvarez et al (2018)
	80 ± 8.2		Medical ward	Nigeria	Eze et al (2016)
	60 ± 16.3		Maternity ward	Nigeria	Eze et al (2016)
	140 ± 8.2		Surgical ward	Nigeria	Eze et al (2016)
	3.7	6.5	General	Portugal	Varela et al. (2014)
	1.2	2.3	General	Turkey	Hocaoglu et al. (2021)
Barium		100	General	Indonesia	Sakina et al. (2023)
Cadmium		8	General	Indonesia	Sakina et al. (2023)
	0.8 ± 0.6 - 4.1 ± 3.9		University	Iran	Amouei et al (2015)
	39		General	Mexico	Pérez-Alvarez et al (2018)
	130 ± 16.3		Medical ward	Nigeria	Eze et al (2016)
	40 ± 16.3		Maternity ward	Nigeria	Eze et al (2016)
	50 ± 16.3		Surgical ward	Nigeria	Eze et al (2016)
		7	General	Thailand	Hamjinda et al. (2018)
	2	19	Unspecified	Thailand	Danchaivijitr et al (2005)
	24	31	Hospital laboratory	Turkey	B. Akin (2016)
Chromium		20	General	Indonesia	Sakina et al. (2023)
	30 ± 14 – 38.4 ± 5		University	Iran	Amouei et al (2015)
	51		General	Mexico	Pérez-Alvarez et al (2018)

	90 ± 16.3		Medical ward	Nigeria	Eze et al (2016)
	3 ± 0.8		Maternity ward	Nigeria	Eze et al (2016)
	12 ± 5.2		Surgical ward	Nigeria	Eze et al (2016)
		14	General	Portugal	Varela et al. (2014)
	14	78	Unspecified	Thailand	Danchaivijitr et al (2005)
	73	95	Hospital laboratory	Turkey	B. Akin (2016)
	3.1	7.5	General	Turkey	Hocaoglu et al. (2021)
Cobalt		0.8	General	Indonesia	Sakina et al. (2023)
	2.1 ± 0.12 – 6.7 ± 8.3		University	Iran	Amouei et al (2015)
	0.3	0.4	Hospital laboratory	Turkey	B. Akin (2016)

Heavy metal	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Copper	162		General	France	Boillot et al (2008)
		10	General	Indonesia	Sakina et al. (2023)
	26 ± 1.6 – 62 ± 56		University	Iran	Amouei et al (2015)
	202		General	Mexico	Pérez-Alvarez et al (2018)
		20	General	Thailand	Hamjinda et al. (2018)
	690	854	Hospital laboratory	Turkey	B. Akin (2016)
	42.4	69.6	General	Turkey	Hocaoglu et al. (2021)
Gadolinium		33	General	France	Wiest et al. (2018)
	0.2 – 3.3 (non-weekday – week day)		University	France	J.-P. Goullé et al. (2012)
		55	General	Germany	Kümmerer and Helmers (2000)
	0.1 – 3.3		University	Germany	Künnemeyer et al. (2009)
	20	52.9	General	Turkey	Hocaoglu et al. (2021)
Iron		70	General	Indonesia	Sakina et al. (2023)
	1.6 ± 1.2 – 3.25 ± 2.3		University	Iran	Amouei et al (2015)
		289	General	Thailand	Hamjinda et al. (2018)
Lead	12		General	France	Boillot et al (2008)
	14.6 ± 3.6 - 50 ± 32		University	Iran	A. Amouei et al. (2015)

	123		General	Mexico	Pérez-Alvarez et al (2018)
	83 ± 8.2		Medical ward	Nigeria	(Chukwuebuka Eze et al., 2016)
	20 ± 8.2		Maternity ward	Nigeria	Eze et al (2016)
	60 ± 8.2		Surgical ward	Nigeria	(Chukwuebuka Eze et al., 2016)
		20	General	Portugal	Varela et al. (2014)
		141	General	Thailand	Hamjinda et al. (2018)
	12	55	Unspecified	Thailand	Danchaivijitr et al (2005)
	71	84	Hospital laboratory	Turkey	B. Akin (2016)
	5.2	14.1	General	Turkey	Hocaoglu et al. (2021)
Manganese		40	General	Indonesia	Sakina et al. (2023)
		93	General	Thailand	Hamjinda et al. (2018)
	4	5	Hospital laboratory	Turkey	B. Akin (2016)

Heavy metal	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Mercury	2.9 ± 0.6 – 17.2 ± 16		University	Iran	(Abdoliman Amouei et al., 2015)
	21		General	Mexico	(Itzayana Pérez-Alvarez et al., 2018)
	12 ± 0.8		Medical ward	Nigeria	(Chukwuebuka Eze et al., 2016)
	7 ± 1.6		Maternity ward	Nigeria	(Chukwuebuka Eze et al., 2016)
	9 ± 8.2		Surgical ward	Nigeria	(Chukwuebuka Eze et al., 2016)
	1.2	3.3	General	Portugal	Varela et al. (2014)
	1.6	7.4	General	Turkey	Hocaoglu et al. (2021)
Heavy metal	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Nickel		20	General	Indonesia	Sakina et al. (2023)
	27.4 ± 3 – 36 ± 28		University	Iran	(Abdoliman Amouei et al., 2015)

	170		General	Mexico	(Itzayana Pérez-Alvarez et al., 2018)
		23	General	Thailand	Hamjinda et al. (2018)
	0.7	0.9	Hospital laboratory	Turkey	B. Akin (2016)
	6.7	10.4	General	Turkey	Hocaoglu et al. (2021)
Platinum		3.5	General	Austria	(Kümmerer et al., 1999)
		145	Oncology ward	Austria	(Lenz et al., 2005)
		250	General	EU countries	Mišík et al. (2019)
	0.08 – 0.6 (non-weekday – week day)		University	France	(Goullé et al., 2012)
		3.5	General	Germany	(Kümmerer et al., 1999)
		762	Oncology ward	Iran	(Ghafuria et al., 2018)
	0.2 ± 0.004 – 0.4 ± 0.008		General	Slovenia	Isidori et al. (2016a)
Silver	<LOD – 2.7 (non-weekday – week day)		University	France	(Goullé et al., 2012)
Tin	13.5	27.3	General	Turkey	Hocaoglu et al. (2021)
Zinc	147		General	France	(Boillot et al., 2008)
		90	General	Indonesia	Sakina et al. (2023)
	255 ± 98 - 654 ± 51		University	Iran	(Abdoliman Amouei et al., 2015)
	205		General	Mexico	(Itzayana Pérez-Alvarez et al., 2018)
		623	General	Thailand	Hamjinda et al. (2018)
	4	7	Hospital laboratory	Turkey	B. Akin (2016)
	263	594	General	Turkey	Hocaoglu et al. (2021)

Details of bacterial species identified in hospital wastewater.

Genus	Species identified	Country	Reference
Acinetobacter		China	Guo et al. (2021)
		China	Li et al. (2022)
Actinomyces	*A. calcoaceticus-baumannii* complex	Nigeria	Chukwu et al. (2018)
		Germany	Sib et al. (2020)
Aeromonas	Not further classified.	Thailand	Danchaivijitr et al. (2005b)
		Brazil	Chagas et al. (2011)
		China	Guo et al. (2021)
		China	Ma et al. (2022)
		Scotland	Perry et al. (2021)
	A. sobria	Pakistan	Suliman et al. (2017)
	A. caviae	China	Ma et al. (2022)
Alistipes	Not further classified	Scotland	Perry et al. (2021)
Arcobacter	Not further classified	Netherlands	Buelow et al. (2018)
		China	Li et al. (2022)
		China	Guo et al. (2021)
		Romania	Szekeres et al. (2017)
Bacteroides	Not further classified	Romania	Szekeres et al. (2017)
		China	Li et al. (2022)
		China	Guo et al. (2021)
		Scotland	Perry et al. (2021)
Bifidobacterium	Not further classified	Scotland	Perry et al. (2021)
		China	Guo et al. (2021)
Chromobacterium	*C. violaceum*	Brazil	Chagas et al. (2011)
Chryseobacterium	Not further classified	Scotland	Perry et al. (2021)
		China	Guo et al. (2021)
Citrobacter	Not further classified	China	Li et al. (2022)
	C. freundii	Brazil	Chagas et al. (2011)

Genus	Species identifed	Country	Reference
Clostridium	Not further classified	China	Guo et al. (2021)
Comamonas	Not further classified	Scotland	Perry et al. (2021)
		China	Guo et al. (2021)
Chronobacter	Not further classified	China	Li et al. (2022)
Desulfovibrio	Not further classified	China	Guo et al. (2021)
Enterobacter	Not further classified	Nigeria	Chukwu et al. (2018)
		Pakistan	Shahzad et al. (2021)
		China	Li et al. (2022)
		Brazil	Chagas et al. (2011)
	E. asburiae	Brazil	Chagas et al. (2011)
	E. cloacae	Brazil	Chagas et al. (2011)
Enterococcus	Not further classified	Scotland	Perry et al. (2021)
		Greece	Sakkas et al. (2019)
		China	Li et al. (2022)
		China	Guo et al. (2021)
	E. avium	Poland	Gotkowska-Płachta (2021)
	E. casseliflavus/flavescens	Poland	Gotkowska-Płachta (2021)
	E. durans	Poland	Gotkowska-Płachta (2021)
	E. faecium	Poland	Gotkowska-Płachta (2021)
	E. faecalis	Egypt	Mehanni et al. (2023)
		Pakistan	Suliman et al. (2017)
		Poland	Gotkowska-Płachta (2021)
	E. gallinarum	Poland	Gotkowska-Płachta (2021)
	E. hirae	Poland	Gotkowska-Płachta (2021)
Escherichia	Not further classified	Scotland	Perry et al. (2021)
		China	Li et al. (2022)
		China	Guo et al. (2021)

	E. coli	Nigeria	C. Eze et al. (2016)
		Egypt	Mehanni et al. (2023)
		Greece	Sakkas et al. (2019)
		Pakistan	Shahzad et al. (2021)
		Norway	Paulshus et al. (2019)
		Pakistan	Suliman et al. (2017)
		Germany	Sib et al. (2020)
		Brazil	Chagas et al. (2011)
		Nigeria	Chukwu et al. (2018)
	E. hermannii	Brazil	Chagas et al. (2011)
Genus	**Species identifed**	**Country**	**Reference**
Eubacterium	Not further classified	Scotland	Perry et al. (2021)
		China	Guo et al. (2021)
Haemophilus	*H. influenzae*	Pakistan	Suliman et al. (2017)
Klebsiella	Not further classified	Thailand	Danchaivijitr et al. (2005b)
		China	Li et al. (2022)
		Scotland	Perry et al. (2021)
	K. aerogenes (*Enterobacter aerogenes*)	Pakistan	Suliman et al. (2017)
	K. ornithinolytica	Brazil	Chagas et al. (2011)
	K. oxytoca	South Africa	King et al. (2020)
		Brazil	Chagas et al. (2011)
	K. pneumoniae	Nigeria	C. Eze et al. (2016)
		Pakistan	Suliman et al. (2017)
		Greece	Sakkas et al. (2019)
		Brazil	Chagas et al. (2011)
	K. pneumoniae/oxytoca	South Africa	King et al. (2020)
		Germany	Sib et al. (2020)
	K. terrigena	Brazil	Chagas et al. (2011)

Genus	Species identifed	Country	Reference
Lactobacillus	Not further classified	Scotland	Perry et al. (2021)
Morganella	Not further classified	China	Li et al. (2022)
Mycobacterium	Not further classified	Scotland	Perry et al. (2021)
		China	Li et al. (2022)
	M. tuberculosis	Pakistan	Suliman et al. (2017)
Mycolicibacterium	Not further classified	Scotland	Perry et al. (2021)
Neisseria	Not further classified	Nigeria	Chukwu et al. (2018)
Oscillibacter	Not further classified	Scotland	Perry et al. (2021)
Pantoea	*P. agglomerans*	Brazil	Chagas et al. (2011)
Prevotella	Not further classified	Scotland	Perry et al. (2021)
		China	Li et al. (2022)
		China	Guo et al. (2021)
Proteus	Not further classified	Nigeria	Chukwu et al. (2018)
		China	Li et al. (2022)
	P. mirabilis	Brazil	Chagas et al. (2011)
		Pakistan	Suliman et al. (2017)
	P. vulgaris	Nigeria	C. Eze et al. (2016)
Providencia	Not further classified	China	Li et al. (2022)
	P. stuartii	Pakistan	Suliman et al. (2017)
Pseudomonas	Not further classified	Thailand	Danchaivijitr et al. (2005b)
		China	Li et al. (2022)
		Romania	Szekeres et al. (2017)
		China	Guo et al. (2021)
		Scotland	Perry et al. (2021)
		China	Ma et al. (2022)
	P. aeruginosa	Nigeria	C. Eze et al. (2016)
		Germany	Sib et al. (2020)

		Greece	Sakkas et al. (2019)
		Pakistan	Shahzad et al. (2021)
		Pakistan	Suliman et al. (2017)
		Nigeria	Chukwu et al. (2018)
	P. alcaligenes	China	Ma et al. (2022)
	P. entomophila	China	Ma et al. (2022)
Genus	**Species identifed**	**Country**	**Reference**
Raoultella	Not further classified	China	Li et al. (2022)
Ruminococcus	Not further classified	Romania	Szekeres et al. (2017)
		China	Guo et al. (2021)
		Scotland	Perry et al. (2021)
Salmonella	Not further classified	Nigeria	Chukwu et al. (2018)
		Thailand	Danchaivijitr et al. (2005b)
	S. enterica	Pakistan	Suliman et al. (2017)
	S. enteritidis	Thailand	Danchaivijitr et al. (2005b)
	S. typhi	Nigeria	C. Eze et al. (2016)
		Pakistan	Suliman et al. (2017)
Serratia	Not further classified	Nigeria	Chukwu et al. (2018)
		China	Li et al. (2022)
	S. marcescens	Brazil	Chagas et al. (2011)
		Pakistan	Suliman et al. (2017)
	S. rubidaceae	Brazil	Chagas et al. (2011)
Genus	**Species identifed**	**Country**	**Reference**
Shigella	Not further classified	Nigeria	Chukwu et al. (2018)
		China	Li et al. (2022)
	S. dysentriae	Pakistan	Suliman et al. (2017)
Sphingomonas	Not further classified	Scotland	Perry et al. (2021)

Stenotrophomonas	Not further classified	Scotland	Perry et al. (2021)
	S. maltophilia	China	Ma et al. (2022)
Staphylococcus	Not further classified	China	Li et al. (2022)
	S. aureus	Nigeria	C. Eze et al. (2016)
		Greece	Sakkas et al. (2019)
		Pakistan	Shahzad et al. (2021)
		Pakistan	Suliman et al. (2017)
		Nigeria	Chukwu et al. (2018)
	S. epidermidis	Nigeria	Chukwu et al. (2018)
		China	Ma et al. (2022)
		Pakistan	Suliman et al. (2017)
		Pakistan	Shahzad et al. (2021)
	S. haemolyticus	Egypt	Mehanni et al. (2023)
Streptococcus	Not further classified	Netherlands	Buelow et al. (2018)
		China	Guo et al. (2021)
	S. pyogenes	Pakistan	Shahzad et al. (2021)
Subdoligranulum	Not further classified	China	Guo et al. (2021)
Vibrio	Not further classified	Thailand	Danchaivijitr et al. (2005b)
	V. chloerae	Thailand	Danchaivijitr et al. (2005b)
		South Africa	(Mavhungu et al., 2023)
	V. parahemolyticus	Thailand	Danchaivijitr et al. (2005b)
		South Africa	(Mavhungu et al., 2023)
Genus	**Species identifed**	**Country**	**Reference**
Yokenella	Not further classified	China	Li et al. (2022)

Detailed summary of pharmaceuticals detected in hospital wastewater.

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
ACE inhibitors	Enalapril	0.2 ± 0.01 - 0.4 ± 0.06		General	Mexico	Hernández-Tenorio et al. (2021)
		0.2	0.3	General	Spain	Bijlsma et al. (2021)
		0.1±0.1	0.2	General	Turkey	Gönder et al. (2021)
Adrenergic agonists	Etilefrine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Alpha blockers	Tamsulosin	0.002 ± 0.0003 - 0.003 ± 0.0003	0.003	University/General	Portugal	Santos et al. (2013)
		0.002 ± 0.0002	0.002	Paediatric	Portugal	Santos et al. (2013)
		0.002 ± 0.0002	0.002	Maternity	Portugal	Santos et al. (2013)
Anaesthetics	Bupivacaine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Ketamine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Levomenthol	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Lidocaine	0.8		General	Sweden	Sörengård et al. (2019)
		9.1 ± 8.1		General	Switzerland	Kovalova et al. (2012)
		2.12±2.93	8.1	General	Turkey	Gönder et al. (2021)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Propofol	Not quantified		Paediatric/ General	USA	Meza et al. (2020)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Analgesics and anti-inflammatories	Aceclofenac	<0.05		General	Sweden	Sörengård et al. (2019)
	Acetaminophen	211.9		University	Cameroon	Mayoudom et al. (2018)
		675		University	Switzerland	Daouk et al. (2016)
		10.8 - 78.1	46.6	General	Colombia	Botero-Coy et al. (2018)
		37.5		Psychiatric	France	Mazzitelli et al. (2018)
			1,510	General	France	Wiest et al. (2018)
		17	47.7	General	Japan	Azuma et al. (2019)
		9.7 ± 0.4 -51.2 ± 4.2		General	Mexico	Hernández-Tenorio et al. (2021)
		2.7 ± 0.02		General	Mexico	I. Pérez-Alvarez et al. (2018)
		18.2 ± 15.5	57.1	Paediatric	Portugal	Santos et al. (2013)
		9.2 ± 4.6	14.0	Maternity	Portugal	Santos et al. (2013)
		24.7 ± 12.2 - 27.7 ± 16.1	58.9	University/General	Portugal	Santos et al. (2013)
		27.2	44.3	University	Spain	(Mendoza et al., 2015)
		134	158.8	General	Spain	Bijlsma et al. (2021)
		<0.05		General	Sweden	Sörengård et al. (2019)
		107.0 ± 85.7		General	Switzerland	Kovalova et al. (2012)
		7.4 - 65		General	Turkey	Yilmaz et al. (2017)
		108.25±56.63	210	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Analgesics and anti-inflammatories	Anileridin	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Celecoxib	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Codeine	0.1		General	Germany	Kraus (2014)
		0.3 ± 0.3 - 0.5 ± 0.9	2.8	University/General	Portugal	Santos et al. (2013)
		0.07 ± 0.1	0.4	Paediatric	Portugal	Santos et al. (2013)
		0.4 ± 0.9	2.8	Maternity	Portugal	Santos et al. (2013)
		0.1 - 0.2		General	Slovakia	Bírošová et al. (2020)
		0.04		Oncology	Slovakia	Bírošová et al. (2020)
		0.4		General	Sweden	Sörengård et al. (2019)
	Diclofenac	1.1 - 3.0	5.84	General	Colombia	Botero-Coy et al. (2018)
			1.1	General	France	Wiest et al. (2018)
		3.5		General	Germany	Kraus (2014)
		0.6 ± 0.3		General	Mexico	I. Pérez-Alvarez et al. (2018)
		<LOQ - 0.08 ± 0.06	0.2	University/General	Portugal	Santos et al. (2013)
		0.05 ± 0.05	0.2	Paediatric	Portugal	Santos et al. (2013)
		0.05 ± 0.03	0.1	Maternity	Portugal	Santos et al. (2013)
		0.6	0.7	University	Spain	(Mendoza et al., 2015)
		0.5 - 4.0	8.0	General	Sri Lanka	Goswami et al. (2022)
		0.3		General	Sweden	Sörengård et al. (2019)

		0.8 ± 0.2		General	Switzerland	Kovalova et al. (2012)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Analgesics and anti-inflammatories	Diclofenac		0.008	General	Tunisia	Afsa et al. (2020)
		0.1 - 11		General	Turkey	Yilmaz et al. (2017)
		1.23±0.53	2.3	General	Turkey	Gönder et al. (2021)
		0.3	0.4	General	Spain	Bijlsma et al. (2021)
	Dihydrocodeine	0.1		General	Germany	Kraus (2014)
	Ethenzamide	0.05	0.1	General	Japan	Azuma et al. (2019)
	Glucosamine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Ibuprofen	141		University	Cameroon	Mayoudom et al. (2018)
			17	General	France	Wiest et al. (2018)
		26.6		General	Germany	Kraus (2014)
		0.8	1.8	General	Japan	Azuma et al. (2019)
		ND - 3.3 ± 0.4		General	Mexico	Hernández-Tenorio et al. (2021)
		0.6 ± 0.4		General	Mexico	I. Pérez-Alvarez et al. (2018)
		2.0 ± 2.1 - 3.1 ± 4.2	11.3	University/General	Portugal	Santos et al. (2013)
		7.1 ± 12.0	38.1	Paediatric	Portugal	Santos et al. (2013)
		7.7 ± 5.3	16.6	Maternity	Portugal	Santos et al. (2013)
		1.4	2.2	University	Spain	Mendoza et al. (2015)
		1.4 - 3.0	7.3	General	Sri Lanka	Goswami et al. (2022)
		1.2		General	Sweden	Sörengård et al. (2019)
		0.09 - 0.6		General	Turkey	Yilmaz et al. (2017)

		3.139±3.17	8	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Analgesics and anti-inflammatories	Indomethacin	0.07	0.1	General	Japan	Azuma et al. (2019)
		ND - LOQ	0.2	University/General	Portugal	Santos et al. (2013)
		<LOD	0.08	Maternity	Portugal	Santos et al. (2013)
		<LOQ	<LOQ	University	Spain	
		0.01 - 0.06	0.3	General	Sri Lanka	Goswami et al. (2022)
		0.07 ± 0.08		General	Switzerland	Kovalova et al. (2012)
			0.01	General	Tunisia	Afsa et al. (2020)
	Ketoprofen		20	General	France	Wiest et al. (2018)
		0.1 ± 0.07 - 1.1 ± 1.3	3.3	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.03	0.2	Paediatric	Portugal	Santos et al. (2013)
		0.1 ± 0.07	0.3	Maternity	Portugal	Santos et al. (2013)
		2.5	4.2	University	Spain	(Mendoza et al., 2015)
			18.1	General	Tunisia	Afsa et al. (2020)
		0.08 - 1.5		General	Turkey	Yilmaz et al. (2017)
	Loxoprofen	20.1	65.3	General	Japan	Azuma et al. (2019)
	Meclofenamic acid	<0.05		General	Sweden	Sörengård et al. (2019)
	Mefenamic acid	0.9 - 3.6	12.1	General	Sri Lanka	Goswami et al. (2022)
		0.007		General	Sweden	Sörengård et al. (2019)
		6.1 ± 1.8		General	Switzerland	Kovalova et al. (2012)
		0.21 ± 0.24	0.58	General	Turkey	Gönder et al. (2021)

		0.02		General	Turkey	Yilmaz et al. (2017)
	Methadone	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Morphine	0.08		General	Germany	Kraus (2014)
		3.7 ± 1.8		General	Switzerland	Kovalova et al. (2012)
	Naproxen	2.7 - 5.7	4.2	General	Colombia	Botero-Coy et al. (2018)
		0.05		General	Germany	Kraus (2014)
		5.9 ± 1.0 - 10.6 ± 0.6		General	Mexico	Hernández-Tenorio et al. (2021)
		1.8 ± 0.2		General	Mexico	I. Pérez-Alvarez et al. (2018)
		0.6 ± 1.3 - 1.8 ± 2.1	6.0	University/General	Portugal	Santos et al. (2013)
		0.7 ± 1.9	5.6	Paediatric	Portugal	Santos et al. (2013)
		0.5 ± 0.6	1.6	Maternity	Portugal	Santos et al. (2013)
		2.2	7.1	University	Spain	Mendoza et al. (2015)
		2.9	2.9	General	Spain	Bijlsma et al. (2021)
		1.2		General	Sweden	Sörengård et al. (2019)
		0.5 - 1.8		General	Turkey	Yilmaz et al. (2017)
		12.0 ± 8.9	30	General	Turkey	Gönder et al. (2021)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Analgesics and anti-inflammatories	Oxycodone	0.1		General	Germany	Kraus (2014)
		<LOQ	0.02	Paediatric	Portugal	Santos et al. (2013)
		<LOQ	0.01	Maternity	Portugal	Santos et al. (2013)
		0.1		General	Slovakia	Bírošová et al. (2020)

		0.3		General	Sweden	Sörengård et al. (2019)
	Phenazone	0.08 ± 0.03 - 0.1 ± 0.07	0.3	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.01	Paediatric	Portugal	Santos et al. (2013)
		0.01 ± 0.02	0.06	Maternity	Portugal	Santos et al. (2013)
		0.1	0.4	General	Spain	Bijlsma et al. (2021)
		0.002		General	Sweden	Sörengård et al. (2019)
		0.2 ± 0.08		General	Switzerland	Kovalova et al. (2012)
			0.05	General	Tunisia	Afsa et al. (2020)
		< 0.01 - 0.06		General	Turkey	Yilmaz et al. (2017)
		0.09±0.06	0.17	General	Turkey	Gönder et al. (2021)
	Phenylbutazone		0.2	General	Tunisia	Afsa et al. (2020)
	Piroxicam	ND - 0.009 ± 0.02	0.05	University/General	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
	Propyphenazone	<LOQ	0.002	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.002	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
		0.02	0.04	University	Spain	Mendoza et al. (2015b)
		0.009		General	Turkey	Yilmaz et al. (2017)
		<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Analgesics and anti-inflammatories	Salicylic acid		62	General	France	Wiest et al. (2018)
		1.3 ± 0.8 - 1.8 ± 0.8	2.8	University/General	Portugal	Santos et al. (2013)
		1.3 ± 1.5	4.7	Paediatric	Portugal	Santos et al. (2013)

		1.3 ± 1.5	4.6	Maternity	Portugal	Santos et al. (2013)
			0.1	General	Tunisia	Afsa et al. (2020)
	Sulindac	<0.003		General	Sweden	Sörengård et al. (2019)
	Tramadol	76		University	Cameroon	Mayoudom et al. (2018)
		0.4 - 12.6		General	Slovakia	Bírošová et al. (2020)
		9.6		Oncology	Slovakia	Bírošová et al. (2020)
		1.5	1.8	General	Spain	Bijlsma et al. (2021)
		ND - 2.0	5.0	General	Sri Lanka	Goswami et al. (2022)
		0.7		General	Sweden	Sörengård et al. (2019)
		1.0 ± 0.3		General	Switzerland	Kovalova et al. (2012)
		1.3 ± 1.2	3.9	General	Turkey	Gönder et al. (2021)
Antiandrogens	Bicalutamide	0.1		General	Sweden	Sörengård et al. (2019)
		0.02±0.02	<LOQ –0.07	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Antibiotics	Amoxicillin		1.4	General	China	Yao et al. (2021)

		5.9 ± 1.2	7.9	General	Iran	Shokoohi et al. (2017)
		ND - 0.8 ± 0.2		General	Qatar	Al-Maadheed et al. (2019)
		1.3	2.4	General	Thailand	Hamjinda et al. (2018)
	Ampicillin		0.7	General	China	Yao et al. (2021)
		0.2 ± 0.01		Hospital wards	Kenya	Ngigi et al. (2019)
		0.2 ± 0.01		Hospital laboratory	Kenya	Ngigi et al. (2019)
		53.1 ± 0.08		Oncology hospital	Romania	Szekeres et al. (2017)
		8.1 ± 0.05 - 15.6 ± 0.05		General	Romania	Szekeres et al. (2017)
		0.41±1.13	3.2	General	Turkey	Gönder et al. (2021)
	Azithromycin	0.4		University	Cameroon	Mayoudom et al. (2018)
		200.9		Inpatients	China	Cai et al. (2022)
		<LOQ - 26.1	11	General	Colombia	Botero-Coy et al. (2018)
		0.1	0.5	General	Japan	Azuma et al. (2019)
		1.9 ± 1.3 - 3.7 ± 2.3	7.4	University/General	Portugal	Santos et al. (2013)
		0.09 ± 0.1	0.4	Paediatric	Portugal	Santos et al. (2013)
		0.8 ± 0.9	2.7	Maternity	Portugal	Santos et al. (2013)
		1.0 - 1.4		General	Slovakia	Bírošová et al. (2020)
		0.3		Oncology	Slovakia	Bírošová et al. (2020)
		<0.005		General	Sweden	Sörengård et al. (2019)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Antibiotics	Azithromycin	0.1 ± 0.2		General	Switzerland	Kovalova et al. (2012)
		< 0.01 - 0.4		General	Turkey	Yilmaz et al. (2017)
		1.06±1.05	2.5	General	Turkey	Gönder et al. (2021)
		0.2 ± 0.01 - 19.5 ± 0.007	162.5 ± 0.01	General/University /Paediatric	Turkey	Aydin et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Cefalotin		0.1	General	China	Yao et al. (2021)
	Cefazolin		5.0	General	China	Yao et al. (2021)
		<LOQ	< LOQ	General	Turkey	Gönder et al. (2021)
	Cefdinir	0.02	0.07	General	Japan	Azuma et al. (2019)
	Cefepime		540.4	General	China	Yao et al. (2021)
		5.2 ± 0.2 - 8.5 ± 0.4		General	Romania	Szekeres et al. (2017)
	Cefixime	10.9 ± 1.2	12.4	General	Iran	Shokoohi et al. (2017)
	Cefotaxime	<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
	Cefoxitin		9.0	General	China	Yao et al. (2021)
	Cefradine		2.4	General	China	Yao et al. (2021)
	Ceftazidime		31.2	General	China	Yao et al. (2021)
		3.7 ± 0.03		Oncology hospital	Romania	Szekeres et al. (2017)
		ND - 10.5 ± 0.6		General	Romania	Szekeres et al. (2017)
		1.6		General	Turkey	Yilmaz et al. (2017)
	Cephalexin		0.9	General	China	Yao et al. (2021)

		<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
	Chloramphenicol	0.2		General	Sweden	Sörengård et al. (2019)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Antibiotics	Chlortetracycline	0.0009 ± 0.00009 - 0.01 ± 0.002	0.02 ± 0.001	General/University /Paediatric	Turkey	Aydin et al. (2019)
	Ciprofloxacin	24		University	Cameroon	Mayoudom et al. (2018)
		180.6		Inpatients	China	Cai et al. (2022)
		5.6 - 20.2	13.6	General	Colombia	Botero-Coy et al. (2018)
			179	General	France	Bergé et al. (2018)
		10.7	14.7	General	Iran	Shokoohi et al. (2020)
		0.03	0.06	General	Japan	Azuma et al. (2019)
		2.7		General	Netherlands	Paulus et al. (2019b)
	Ciprofloxacin		178	University/General	Nigeria	Ajibola et al. (2021)
		3.7 ± 3.8 - 11.6 ± 11.3	38.7	University/General	Portugal	Santos et al. (2013)
		0.5 ± 0.4	1.3	Paediatric	Portugal	Santos et al. (2013)
		0.6 ± 0.6	2.0	Maternity	Portugal	Santos et al. (2013)
		0.9	2.5	General	Portugal	Varela et al. (2014)
		0.3 ± 0.1 - 2.0 ± 1.5		General	Qatar	Al-Maadheed et al. (2019)
		1.8 - 2.6		General	Slovakia	Bírošová et al. (2020)
		5.4		Oncology	Slovakia	Bírošová et al. (2020)
		165.6	680	General	Spain	Bijlsma et al. (2021)

		32.0 ± 14.1		General	Switzerland	Kovalova et al. (2012)
		9.6	24.0	General	Thailand	Hamjinda et al. (2018)
		1.9 - 24		General	Turkey	Yilmaz et al. (2017)
		3.48±2.72	8.6	General	Turkey	Gönder et al. (2021)
		0.08 ± 0.006 - 3.1 ± 0.01	19.7 ± 0.01	General/University /Paediatric	Turkey	Aydin et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Clarithromycin	0.09		University	Cameroon	Mayoudom et al. (2018)
		218.1		Inpatients	China	Cai et al. (2022)
		0.1 - 26.8	12.9	General	Colombia	Botero-Coy et al. (2018)
		1.2 ± 0.7		General	Germany	Kraus (2014)
		0.4	1.4	General	Japan	Azuma et al. (2019)
		0.006		General	Netherlands	Paulus et al. (2019b)
		0.008 ± 0.02 - 0.06 ± 0.07	0.2	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.3	1.0	Paediatric	Portugal	Santos et al. (2013)
		0.03 ± 0.06	0.2	Maternity	Portugal	Santos et al. (2013)
		0.2	0.5	University	Spain	Mendoza et al. (2015b)
		0.05	0.07	General	Spain	Bijlsma et al. (2021)
		0.004		General	Sweden	Sörengård et al. (2019)

		2.6 ± 1.6		General	Switzerland	Kovalova et al. (2012)
		0.06 - 15		General	Turkey	Yilmaz et al. (2017)
		5.34±2.35	8.4	General	Turkey	Gönder et al. (2021)
		0.2 ± 0.01 - 19.3 ± 0.008	159.7 ± 0.004	General/University /Paediatric	Turkey	Aydin et al. (2019)
	Clavulanic acid	ND - 41.2 ± 3.9		General	Qatar	Al-Maadheed et al. (2019)
	Clindamycin	8.3 - 24.1	16.6	General	Colombia	Botero-Coy et al. (2018)
		0.1	0.2	General	Spain	Bijlsma et al. (2021)
		0.3		General	Sweden	Sörengård et al. (2019)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Antibiotics	Clindamycin	1.0 ± 0.9		General	Switzerland	Kovalova et al. (2012)
		< 0.01 - 0.04		General	Turkey	Yilmaz et al. (2017)
		0.1±0.1	0.1	General	Turkey	Gönder et al. (2021)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Dicloxacillin	17.3 ± 0.3		Hospital laboratory	Kenya	Ngigi et al. (2019)
	Doxycyline	0.008 ± 0.002 - 0.01 ± 0.003	0.06 ± 0.003	General/University /Paediatric	Turkey	Aydin et al. (2019)
			0.7	General	Portugal	Varela et al. (2014)
	Erythromycin	7		University	Cameroon	Mayoudom et al. (2018)
		0.3 - 1.9	1.1	General	Colombia	Botero-Coy et al. (2018)
		0.08		General	Netherlands	Paulus et al. (2019b)
		<LOQ - 0.2 ± 0.4	1.1	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.3	0.9	Paediatric	Portugal	Santos et al. (2013)
		1.4 ± 2.4	7.5	Maternity	Portugal	Santos et al. (2013)
		ND - 5.2 ± 1.6		General	Qatar	Al-Maadheed et al. (2019)
		7.5 ± 0.4		Oncology hospital	Romania	Szekeres et al. (2017)
		0.04 - 0.07		General	Slovakia	Bírošová et al. (2020)
	Erythromycin	0.02		Oncology	Slovakia	Bírošová et al. (2020)

		0.7	3.1	General	Spain	Bijlsma et al. (2021)
		0.5		General	Sweden	Sörengård et al. (2019)
		0.2	0.6	General	Thailand	Hamjinda et al. (2018)
		0.3 ± 0.3	0.84	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Antibiotics	Erythromycin	0.01 ± 0.02 - 0.009 ± 0.002	0.1 ± 0.00002	General/University /Paediatric	Turkey	Aydin et al. (2019)
	Gentamicin	ND - 7.9 ± 0.2		General	Romania	Szekeres et al. (2017)
	Imipenem	ND - 14.4 ± 0.4		General	Romania	Szekeres et al. (2017)
		25.5 ± 2.9	29.1	General	Iran	Shokoohi et al. (2017)
	Levofloxacin	0.5	0.7	General	Japan	Azuma et al. (2019)
	Lincomycin	66.9		Inpatients	China	Cai et al. (2022)
		0.2	0.2	General	Thailand	Hamjinda et al. (2018)
	Lomefloxacin	2.3		Inpatients	China	Cai et al. (2022)
	Meropenem		0.2	General	China	Yao et al. (2021)
	Metronidazole	2.4 - 3.5	3	General	Colombia	Botero-Coy et al. (2018)
		0.8	1.3	General	Iran	Shokoohi et al. (2020)
		0.004		General	Netherlands	Paulus et al. (2019b)
		0.2 ± 0.5 - 1.6 ± 4.0	12.3	University/General	Portugal	Santos et al. (2013)
		0.6 ± 1.4	4.3	Paediatric	Portugal	Santos et al. (2013)

		0.8 ± 1.6	5.0	Maternity	Portugal	Santos et al. (2013)
		1.0 ± 0.3 - 5.5 ± 1.7		General	Qatar	Al-Maadheed et al. (2019)
		5		General	Sweden	Sörengård et al. (2019)
		3.4 ± 1.3		General	Switzerland	Kovalova et al. (2012)
	Metronidazole	< 0.03 - 3		General	Turkey	Yilmaz et al. (2017)
		0.86 ± 0.60	1.8	General	Turkey	Gönder et al. (2021)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Nalidixic acid	<LOQ	<LOQ	General	Belgium	Lorenzo et al. (2018)
	Norfloxacin		0.6	General	China	Yao et al. (2021)
		2201.9		Inpatients	China	Cai et al. (2022)
		0.9 - 10.1	4.1	General	Colombia	Botero-Coy et al. (2018)
		0.02		General	Netherlands	Paulus et al. (2019b)
			561	University/General	Nigeria	Ajibola et al. (2021)
		8.3	14.8	General	Spain	Bijlsma et al. (2021)
		5.9 ± 3.4		General	Switzerland	Kovalova et al. (2012)
		12.1	24.0	General	Thailand	Hamjinda et al. (2018)
		0.1 ± 0.2	0.4	General	Turkey	Gönder et al. (2021)
	Ofloxacin		49.5	General	China	Yao et al. (2021)
		13,987		Inpatients	China	Cai et al. (2022)

		6.3	13.4	General	Iran	Shokoohi et al. (2020)
		0.3		General	Netherlands	Paulus et al. (2019b)
			152	University/General	Nigeria	Ajibola et al. (2021)
		7.3 ± 3.7 - 12.2 ± 6.8	24.8	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.2	0.7	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
		0.6	1.4	General	Portugal	Varela et al. (2014)
		3.5	4.8	University	Spain	Mendoza et al. (2015b)
		0.08 - 200		General	Turkey	Yilmaz et al. (2017)
		1.0 ± 0.7	1.9	General	Turkey	Gönder et al. (2021)
	Oxacillin	0.2 ± 0.01		Hospital wards	Kenya	Ngigi et al. (2019)
		0.1 ± 0.0		Hospital laboratory	Kenya	Ngigi et al. (2019)
	Oxytetracycline	0.001 ± 0.0004 ± 0.02 ± 0.001	0.03 ± 0.002	General/University /Paediatric	Turkey	Aydin et al. (2019)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Penicillin	ND - 0.1 ± 0.07		General	Qatar	Al-Maadheed et al. (2019)
	Penicillin G	3.8 ± 0.03		General	Mexico	I. Pérez-Alvarez et al. (2018)
		0.9	1.4	General	Portugal	Varela et al. (2014)
	Penicillin V	0.4 ± 0.01		General	Mexico	I. Pérez-Alvarez et al. (2018)
			0.6	General	Portugal	Varela et al. (2014)
	Piperacillin	7.8 ± 0.2		Oncology hospital	Romania	Szekeres et al. (2017)
	Rifaximin	Not quantified		Paediatric/	USA	Meza et al. (2020)

				General		
	Ronidazole	<LOD	<LOQ	University/General	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
	Roxithromycin	125.1		Inpatients	China	Cai et al. (2022)
		0.03 ± 0.03		General	Germany	Kraus (2014)
		<0.0005		General	Sweden	Sörengård et al. (2019)
		0.02		General	Switzerland	Kovalova et al. (2012)
		0.9	1.6	General	Thailand	Hamjinda et al. (2018)
		0.2±0.1	0.3	General	Turkey	Gönder et al. (2021)
	Spectinomycin	0.3 ± 0.0		Hospital wards	Kenya	Ngigi et al. (2019)
		0.2 ± 0.0		Hospital laboratory	Kenya	Ngigi et al. (2019)
	Spiramycin	1.6 ± 0.02		Hospital wards	Kenya	Ngigi et al. (2019)
		0.4 ± 0.0		Hospital laboratory	Kenya	Ngigi et al. (2019)
	Sulfachloropyridazine	0.02		General	Netherlands	Paulus et al. (2019b)
	Sulfaclozine	0.04		General	Netherlands	Paulus et al. (2019b)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Sulfadiazine	3.4 ± 0.07		Hospital wards	Kenya	Ngigi et al. (2019)
		0.02		General	Netherlands	Paulus et al. (2019b)
		0.06	0.1	University	Spain	(Mendoza et al., 2015)

		<LOQ	0.004	General	Spain	Bijlsma et al. (2021)
		1.9 ± 4.0		General	Switzerland	Kovalova et al. (2012)
			39.3	General	Tunisia	Afsa et al. (2020)
		< 0.01 - 0.2		General	Turkey	Yilmaz et al. (2017)
		0.2 ± 0.4	1.1	General	Turkey	Gönder et al. (2021)
	Sulfadimethoxine	2.7		General	Germany	Kraus (2014)
			0.004	General	Tunisia	Afsa et al. (2020)
	Sulfadimethoxine	<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
	Sulfaguanidine		0.3	General	Tunisia	Afsa et al. (2020)
	Sulfamerazine	0.01		General	Netherlands	Paulus et al. (2019b)
	Sulfamethazine	15.7 ± 0.4		Hospital wards	Kenya	Ngigi et al. (2019)
			1.7	General	Portugal	Varela et al. (2014)
		<LOD	<LOQ	University	Spain	(Mendoza et al., 2015)
			0.02	General	Tunisia	Afsa et al. (2020)
		<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
		0.0006 ± 0.0002 - 0.001 ± 0.0003	0.009 ± 0.0002	General/University /Paediatric	Turkey	Aydin et al. (2019)
	Sulfamethizole		1.1	General	Tunisia	Afsa et al. (2020)
	Sulfamethoxazole	18.4	66.4	General	Belgium	Lorenzo et al. (2018)
		0.2		University	Cameroon	Mayoudom et al. (2018)
		1429.3		Inpatients	China	Cai et al. (2022)
		<LOQ - 1.3	0.9	General	Colombia	Botero-Coy et al. (2018)
			26	General	France	Wiest et al. (2018)

		1.5	4.0	General	Iran	Shokoohi et al. (2020)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Sulfamethoxazole	20.6 ± 0.4		Hospital wards	Kenya	Ngigi et al. (2019)
		0.6 ± 0.1 - 3.3 ± 0.6		General	Mexico	Hernández-Tenorio et al. (2021)
		0.4		General	Netherlands	Paulus et al. (2019b)
		1.9 ± 1.7 - 3.0 ± 3.0	8.7	University/General	Portugal	Santos et al. (2013)
		0.4 ± 0.4	1.3	Paediatric	Portugal	Santos et al. (2013)
		0.09 ± 0.2	0.7	Maternity	Portugal	Santos et al. (2013)
		0.9	1.5	General	Portugal	Varela et al. (2014)
		6.1 ± 0.2		Oncology hospital	Romania	Szekeres et al. (2017)
		0.6	1.0	General	Spain	Bijlsma et al. (2021)
		1.5		General	Sweden	Sörengård et al. (2019)
		3.5 ± 4.6		General	Switzerland	Kovalova et al. (2012)
		2.9	6.4	General	Thailand	Hamjinda et al. (2018)
			0.02	General	Tunisia	Afsa et al. (2020)
		< 0.01 - 8.5		General	Turkey	Yilmaz et al. (2017)
		15.7 ± 9.1	35	General	Turkey	Gönder et al. (2021)
		0.002 ± 0.0005 - 0.04 ± 0.005	0.4 ± 0.001	General/University /Paediatric	Turkey	Aydin et al. (2019)
	Sulfamethoxypyridazine	18.2		Inpatients	China	Cai et al. (2022)
		0.006		General	Netherlands	Paulus et al. (2019b)
			0.04	General	Tunisia	Afsa et al. (2020)

	Sulfamonomethoxine	0.01		General	Netherlands	Paulus et al. (2019b)
	Sulfanilamide	7.7 ± 0.2		Hospital wards	Kenya	Ngigi et al. (2019)
	Sulfapyridine	0.05		General	Netherlands	Paulus et al. (2019b)
		0.3		General	Switzerland	Kovalova et al. (2012)
		< 0.01 - 0.05		General	Turkey	Yilmaz et al. (2017)
		1.9 ± 1.2	4.3	General	Turkey	Gönder et al. (2021)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Sulfathiazole		0.01	General	Tunisia	Afsa et al. (2020)
			0.3	General	Portugal	Varela et al. (2014)
	Sulfisoxazole	1.1		General	Netherlands	Paulus et al. (2019b)
			0.1	General	Tunisia	Afsa et al. (2020)
	Tazobactam	ND - 10.3 ± 0.08		General	Romania	Szekeres et al. (2017)
	Tetracycline	1.0	1.2	General	Belgium	Lorenzo et al. (2018)
		0.8	1.2	General	Iran	Shokoohi et al. (2020)
		1.1	2.1	General	Portugal	Varela et al. (2014)
		ND - 0.2 ± 0.01		General	Qatar	Al-Maadheed et al. (2019)
		ND - 1.3 ± 0.07		General	Romania	Szekeres et al. (2017)
		<0.5		General	Sweden	Sörengård et al. (2019)
		1.4	2.4	General	Thailand	Hamjinda et al. (2018)

	Trimethoprim	0.3		University	Cameroon	Mayoudom et al. (2018)
			0.5	General	China	Yao et al. (2021)
		493.8		Inpatients	China	Cai et al. (2022)
		0.06 - 1.7	0.9	General	Colombia	Botero-Coy et al. (2018)
		0.4		General	Germany	Kraus (2014)
		1.1	3.1	General	Iran	Shokoohi et al. (2020)
		6.6 ± 0.1		Hospital wards	Kenya	Ngigi et al. (2019)
		0.06		General	Netherlands	Paulus et al. (2019b)
		0.5 ± 0.4 - 1.8 ± 1.3	4.0	University/General	Portugal	Santos et al. (2013)
		0.3 ± 0.3	1.1	Paediatric	Portugal	Santos et al. (2013)
		0.01 ± 0.04	0.1	Maternity	Portugal	Santos et al. (2013)
		13.1 ± 0.09		Oncology hospital	Romania	Szekeres et al. (2017)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antibiotics	Trimethoprim	ND - 30.4 ± 0.8		General	Romania	Szekeres et al. (2017)
		3.2	4.8	University	Spain	(Mendoza et al., 2015)
		0.7		General	Sweden	Sörengård et al. (2019)
		0.9 ± 0.9		General	Switzerland	Kovalova et al. (2012)
		0.5	1.6	General	Thailand	Hamjinda et al. (2018)
		< 0.01 - 2.2		General	Turkey	Yilmaz et al. (2017)
		3.6 ± 1.4	6.4	General	Turkey	Gönder et al. (2021)

		0.009 ± 0.003 - 0.03 ± 0.005	0.3 ± 0.002	General/University /Paediatric	Turkey	Aydin et al. (2019)
		0.3	1.3	General	Spain	Bijlsma et al. (2021)
	Vancomycin		7.4	General	France	Wiest et al. (2018)
		5.0 ± 0.1		Oncology hospital	Romania	Szekeres et al. (2017)
		ND - 14.0 ± 0.4		General	Romania	Szekeres et al. (2017)
Anticoagulants	Coumarin	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Warfarin	0.005 ± 0.002 - 0.006 ± 0.002	0.008	University/General	Portugal	Santos et al. (2013)
		0.001 ± 0.0007	0.003	Paediatric	Portugal	Santos et al. (2013)
		0.002 ± 0.0007	0.002	Maternity	Portugal	Santos et al. (2013)
		0.001 - 0.02	0.04	General	Sri Lanka	Goswami et al. (2022)
Anticonvulsants	Lamotrigine	0.6		General	Sweden	Sörengård et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Levetiracetam	11.0 ± 6.5		General	Switzerland	Kovalova et al. (2012)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Anticonvulsants	Oxcarbazepine	0.8 ± 0.1 - 1.6 ± 0.2		General	Mexico	Hernández-Tenorio et al. (2021)
		0.03		General	Turkey	Yilmaz et al. (2017)
	Phenytoin	0.03 - 2.2	6.1	General	Sri Lanka	Goswami et al. (2022)
	Primidone	2.1		General	Germany	Kraus (2014)
		0.07	0.07	General	Spain	Bijlsma et al. (2021)

		<0.5		General	Sweden	Sörengård et al. (2019)
		0.4 ± 0.4		General	Switzerland	Kovalova et al. (2012)
	Valproic acid	0.5		General	Sweden	Sörengård et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Antidiabetics	Glibenclamide	1.9 ± 0.02		General	Mexico	I. Pérez-Alvarez et al. (2018)
			0.04	General	Tunisia	Afsa et al. (2020)
	Metformin	154		University	Cameroon	Mayoudom et al. (2018)
		1.3 ± 0.02		General	Mexico	I. Pérez-Alvarez et al. (2018)
		1.0 ± 0.9 - 1.3 ± 1.1	3.8	University/General	Portugal	Santos et al. (2013)
		0.2 ± 0.2	0.7	Paediatric	Portugal	Santos et al. (2013)
		1.2 ± 1.3	4.0	Maternity	Portugal	Santos et al. (2013)
		34.3 ± 8.0	48	General	Turkey	Gönder et al. (2021)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Antifungals	Climbazole	0.09		General	Sweden	Sörengård et al. (2019)
	Econazole		0.018	General	France	Wiest et al. (2018)
	Fluconazole	0.2		General	Netherlands	Paulus et al. (2019b)
		13		General	Sweden	Sörengård et al. (2019)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference

Antifungals	Fluconazole	3.4 ± 1.6		General	Switzerland	Kovalova et al. (2012)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Thiabendazole	<LOQ - 0.06 ± 0.2	0.5	University/General	Portugal	Santos et al. (2013)
		0.4 ± 0.6	1.7	Paediatric	Portugal	Santos et al. (2013)
		0.03 ± 0.04	0.1	Maternity	Portugal	Santos et al. (2013)
		0.004		General	Sweden	Sörengård et al. (2019)
	Voriconazole	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Antihistamines	Benadryl	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Cetirizine	1.3		Psychiatric	France	Mazzitelli et al. (2018)
		0.5		General	Sweden	Sörengård et al. (2019)
		0.5 - 0.7	1.5	General	Sri Lanka	Goswami et al. (2022)
	Chlorpheniramine	0.08 - 0.1	0.3	General	Sri Lanka	Goswami et al. (2022)
	Desloratadine	0.003 ± 0.003	0.01	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.001	Paediatric	Portugal	Santos et al. (2013)
		0.0002 ± 0.0005	0.001	Maternity	Portugal	Santos et al. (2013)
	Diphenhydramine	0.4		University	Cameroon	Mayoudom et al. (2018)
		0.006 - 0.02	0.07	General	Sri Lanka	Goswami et al. (2022)
	Fexofenadine	0.4		General	Sweden	Sörengård et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)

	Hydroxyzine	0.02		Psychiatric	France	Mazzitelli et al. (2018)
	Levocetirizine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Loratadine	ND - 0.3 ± 0.06		General	Mexico	Hernández-Tenorio et al. (2021)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antihypertensives	Amlodipine	0.04 ± 0.03 - 0.09 ± 0.06	0.2	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.05	Paediatric	Portugal	Santos et al. (2013)
		0.04 ± 0.03	0.1	Maternity	Portugal	Santos et al. (2013)
		0.005 - 0.03	0.05	General	Sri Lanka	Goswami et al. (2022)
	Irbesartan	0.03 - 1.4	0.6	General	Colombia	Botero-Coy et al. (2018)
		0.5 ± 0.6	2.1	University/General	Portugal	Santos et al. (2013)
		0.5 ± 0.6	1.8	Paediatric	Portugal	Santos et al. (2013)
		0.7 ± 1.2	3.9	Maternity	Portugal	Santos et al. (2013)
		0.2	0.3	General	Spain	Bijlsma et al. (2021)
		0.03		General	Sweden	Sörengård et al. (2019)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Losartan	1.2 - 7.7	4.5	General	Colombia	Botero-Coy et al. (2018)
		0.04		Psychiatric	France	Mazzitelli et al. (2018)
		0.3	0.8	General	Japan	Azuma et al. (2019)
		2.4 ±0.1 - 3.2 ± 0.3		General	Mexico	Hernández-Tenorio et al. (2021)

		0.2 ± 0.1 - 0.3 ± 0.3	0.9	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.1	0.3	Paediatric	Portugal	Santos et al. (2013)
		0.09 ± 0.09	0.3	Maternity	Portugal	Santos et al. (2013)
		0.3	0.8	General	Spain	Bijlsma et al. (2021)
		0.5 - 1.6	3.6	General	Sri Lanka	Goswami et al. (2022)
		0.6		General	Sweden	Sörengård et al. (2019)
		1.1 ± 0.7	2.6	General	Turkey	Gönder et al. (2021)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antihypertensives	Olmesartan	0.08	0.2	General	Japan	Azuma et al. (2019)
		0.06	0.2	General	Japan	Azuma et al. (2019)
	Ramipril	0.006		General	Sweden	Sörengård et al. (2019)
	Valsartan	0.04 - 2.3	1.4	General	Colombia	Botero-Coy et al. (2018)
		1.6 ± 1.3 - 8.9 ± 7.4	19.8	University/General	Portugal	Santos et al. (2013)
		1.9 ± 3.8	11.7	Paediatric	Portugal	Santos et al. (2013)
		1.8 ± 2.4	7.8	Maternity	Portugal	Santos et al. (2013)
		0.4 - 7.1		General	Slovakia	Bírošová et al. (2020)
		0.7		Oncology	Slovakia	Bírošová et al. (2020)
		2.9	5.9	General	Spain	Bijlsma et al. (2021)
		0.4		General	Sweden	Sörengård et al. (2019)
		3.0 ± 1.3		General	Switzerland	Kovalova et al. (2012)
Antiparasitics	Albendazole	ND - 0.004 ± 0.009	0.03	University/General	Portugal	Santos et al. (2013)

		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
	Crotamiton	0.07	0.2	General	Japan	Azuma et al. (2019)
	Levamisole	ND - 0.006 ± 0.01	0.04	University/General	Portugal	Santos et al. (2013)
		0.02 ± 0.06	0.2	Paediatric	Portugal	Santos et al. (2013)
		0.03 ± 0.03	0.07	Maternity	Portugal	Santos et al. (2013)
	Pyrimethamine	0.0002		General	Sweden	Sörengård et al. (2019)
Antiplatelet agents	Clopidogrel	0.1 ± 0.05 - 0.2 ± 0.1	0.4	University/General	Portugal	Santos et al. (2013)
		0.03 ± 0.06	0.2	Paediatric	Portugal	Santos et al. (2013)
		0.03 ± 0.06	0.2	Maternity	Portugal	Santos et al. (2013)
Antivirals	Aciclovir	0.06	0.1	General	Japan	Azuma et al. (2019)
	Famciclovir	0.02	0.06	General	Japan	Azuma et al. (2019)
	Nevirapine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Antivirals	Oseltamivir	0.03 ± 0.02		General	Switzerland	Kovalova et al. (2012)
	Penciclovir	0.009	0.03	General	Japan	Azuma et al. (2019)
	Ritonavir	0.1 ± 0.09		General	Switzerland	Kovalova et al. (2012)
	Valaciclovir	0.008	0.02	General	Japan	Azuma et al. (2019)
Artificial sweeteners	Sucralose	13.1		University	Cameroon	Mayoudom et al. (2018)
		<0.05		General	Sweden	Sörengård et al. (2019)
β–Blockers	Acebutolol	0.1		Psychiatric	France	Mazzitelli et al. (2018)
	Atenolol	0.4		University	Cameroon	Mayoudom et al. (2018)
		0.06		Psychiatric	France	Mazzitelli et al. (2018)

			39	General	France	Wiest et al. (2018)
		0.2 ± 0.02 - 0.4 ± 0.05		General	Mexico	Hernández-Tenorio et al. (2021)
		0.2 ± 0.0001		General	Mexico	I. Pérez-Alvarez et al. (2018)
		0.6 ± 0.4 - 0.7 ± 0.6	2.0	University/General	Portugal	Santos et al. (2013)
		1.1 ± 2.6	8.0	Paediatric	Portugal	Santos et al. (2013)
		1.1 ± 1.9	5.9	Maternity	Portugal	Santos et al. (2013)
		0.006 - 11.7		General	Slovakia	Bírošová et al. (2020)
		0.07		Oncology	Slovakia	Bírošová et al. (2020)
		1.4	2.3	University	Spain	(Mendoza et al., 2015)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
β–Blockers	Atenolol	0.6		General	Sweden	Sörengård et al. (2019)
		2.3 ± 0.6		General	Switzerland	Kovalova et al. (2012)
			12.9	General	Tunisia	Afsa et al. (2020)
		0.7 ± 0.4	1.5	General	Turkey	Gönder et al. (2021)
	Bisoprolol	0.1		Psychiatric	France	Mazzitelli et al. (2018)
		0.2		General	Sweden	Sörengård et al. (2019)
	Bisoprolol	0.05 ± 0.02	0.09	General	Turkey	Gönder et al. (2021)
	Carazolol	0.006 ± 0.0002 - 0.007 ± 0.0004	0.007	University/General	Portugal	Santos et al. (2013)

		0.006 ± 0.0004	0.007	Paediatric	Portugal	Santos et al. (2013)
		0.006 ± 0.0004	0.007	Maternity	Portugal	Santos et al. (2013)
	Carvedilol	ND - 0.005	0.02	General	Sri Lanka	Goswami et al. (2022)
	Metoprolol	2.0 ± 0.3		General	Mexico	I. Pérez-Alvarez et al. (2018)
		0.04 ± 0.09 - 0.06 ± 0.1	0.4	University/General	Portugal	Santos et al. (2013)
		0.02 ± 0.05	0.2	Paediatric	Portugal	Santos et al. (2013)
		<LOQ	0.005	Maternity	Portugal	Santos et al. (2013)
		0.05	0.09	University	Spain	(Mendoza et al., 2015)
		<LOQ	0.03	General	Spain	Bijlsma et al. (2021)
		0.8		General	Sweden	Sörengård et al. (2019)
		1.3 ± 0.3		General	Switzerland	Kovalova et al. (2012)
			0.03	General	Tunisia	Afsa et al. (2020)
		0.2 - 5		General	Turkey	Yilmaz et al. (2017)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
β–Blockers	Metoprolol	1.2 ± 0.5	2.2	General	Turkey	Gönder et al. (2021)
	Propranolol	0.3		University	Cameroon	Mayoudom et al. (2018)
		0.06		Psychiatric	France	Mazzitelli et al. (2018)
			3.8	General	France	Wiest et al. (2018)
		0.02 ± 0.02	0.08	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.3	0.8	Paediatric	Portugal	Santos et al. (2013)
		0.07 ± 0.08	0.2	Maternity	Portugal	Santos et al. (2013)
		0.3	0.6	University	Spain	(Mendoza et al., 2015)

		0.02 - 0.1	0.2	General	Sri Lanka	Goswami et al. (2022)
		0.2		General	Sweden	Sörengård et al. (2019)
	Propranolol	0.1 ± 0.04		General	Switzerland	Kovalova et al. (2012)
			0.004	General	Tunisia	Afsa et al. (2020)
		0.09 ± 0.09	0.26	General	Turkey	Gönder et al. (2021)
	Sotalol	0.3		Psychiatric	France	Mazzitelli et al. (2018)
		0.06 ± 0.04 - 0.09 ± 0.1	0.3	University/General	Portugal	Santos et al. (2013)
		0.02 ± 0.06	0.2	Maternity	Portugal	Santos et al. (2013)
		0.2	0.8	University	Spain	Mendoza et al. (2015b)
		0.2		General	Sweden	Sörengård et al. (2019)
		0.7 ± 0.6		General	Switzerland	Kovalova et al. (2012)
		0.3 ± 0.2	0.64	General	Turkey	Gönder et al. (2021)
	Timolol		0.02	General	Tunisia	Afsa et al. (2020)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Brochodilators	Salbutamol	0.1 ± 0.05 - 0.4 ± 0.8	2.6	University/General	Portugal	Santos et al. (2013)
		0.08 ± 0.09	0.3	Paediatric	Portugal	Santos et al. (2013)
		0.007 ± 0.01	0.04	Maternity	Portugal	Santos et al. (2013)
			0.2	General	Tunisia	Afsa et al. (2020)
		0.04	0.06	General	Spain	Bijlsma et al. (2021)

		0.3		General	Sweden	Sörengård et al. (2019)
	Theophylline	1.3		Psychiatric	France	Mazzitelli et al. (2018)
		3.5	6.4	General	Japan	Azuma et al. (2019)
Calcium channel blockers	Diltiazem	0.4 ± 0.3 - 0.8 ± 0.3	1.5	University/General	Portugal	Santos et al. (2013)
		0.06 ± 0.05	0.2	Paediatric	Portugal	Santos et al. (2013)
		0.05 ± 0.1	0.3	Maternity	Portugal	Santos et al. (2013)
		0.02 - 0.4	0.4	General	Sri Lanka	Goswami et al. (2022)
		0.006		General	Sweden	Sörengård et al. (2019)
	Verapamil	0.007 ± 0.003 - 0.01 ± 0.02	0.7	University/General	Portugal	Santos et al. (2013)
		0.005 ± 0.0006	0.006	Paediatric	Portugal	Santos et al. (2013)
		0.005 ± 0.0007	0.007	Maternity	Portugal	Santos et al. (2013)
		0.03 ± 0.02		General	Switzerland	Kovalova et al. (2012)
Dehydropeptidase inhibitors	Cilastatin	1.0 ± 1.0		General	Switzerland	Kovalova et al. (2012)
		< 0.01 - 4.1		General	Turkey	Yilmaz et al. (2017)
		4.3 ± 4.2	13	General	Turkey	Gönder et al. (2021)
Diuretics	Amiloride	<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Diuretics	Furosemide	11.1 ± 5.7 - 12.0 ± 6.3	22.3	University/General	Portugal	Santos et al. (2013)
		5.4 ± 10.2	32.6	Paediatric	Portugal	Santos et al. (2013)
		3.6 ± 3.7	10.0	Maternity	Portugal	Santos et al. (2013)

		10.4	14.7	University	Spain	Mendoza et al. (2015b)
		1.4		General	Sweden	Sörengård et al. (2019)
		2.0 ± 0.6		General	Switzerland	Kovalova et al. (2012)
			0.09	General	Tunisia	Afsa et al. (2020)
		< 0.1 - 1.9		General	Turkey	Yilmaz et al. (2017)
	Hydrochlorothiazide	0.8 ± 0.1	0.7	University/General	Portugal	Santos et al. (2013)
		0.6 ± 0.2	0.8	Paediatric	Portugal	Santos et al. (2013)
		0.5 ± 0.3	1.0	Maternity	Portugal	Santos et al. (2013)
		1.1	1.7	University	Spain	(Mendoza et al., 2015)
		0.5		General	Sweden	Sörengård et al. (2019)
		2.0 ± 0.5		General	Switzerland	Kovalova et al. (2012)
			2.1	General	Tunisia	Afsa et al. (2020)
Hormones	17-α-Estradiol	0.01 ± 0.009	0.03	General	Turkey	Gönder et al. (2021)
	17-α-Ethinylestradiol	0.2 ± 0.3	0.7	General	Turkey	Gönder et al. (2021)
	17-β-Estradiol	0.05 ± 0.04	0.1	General	Turkey	Gönder et al. (2021)
	Androstanedione	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Cortisone	0.9 ± 1.7	4.4	General	Turkey	Gönder et al. (2021)
	Estriol	0.9 ± 0.8	2.2	General	Turkey	Gönder et al. (2021)
	Estrone	0.08 ± 0.07	0.2	General	Turkey	Gönder et al. (2021)

	Hexestrol	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Hydrocortisone	0.1 ± 0.1	0.3	General	Turkey	Gönder et al. (2021)
	Prasterone	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Testosterone cypionate	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Testosterone propionate	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Histamine H_2 receptor antagonist	Cimetidine	34		University	Cameroon	Mayoudom et al. (2018)
		0.005 ± 0.008 - 0.06 ± 0.2	0.5	University/General	Portugal	Santos et al. (2013)
		<LOD	0.002	Paediatric	Portugal	Santos et al. (2013)
		<LOQ	0.002	Maternity	Portugal	Santos et al. (2013)
	Famotidine	0.004 ± 0.004 - 0.03 ± 0.07	0.2	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.001	Paediatric	Portugal	Santos et al. (2013)
		<LOQ	0.003	Maternity	Portugal	Santos et al. (2013)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Histamine H_2 receptor antagonist	Famotidine		15.2	General	Tunisia	Afsa et al. (2020)
	Ranitidine	2.2 ± 4.2 - 4.2 ± 6.4	19.8	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.3	0.9	Paediatric	Portugal	Santos et al. (2013)
		0.5 ± 1.0	3.4	Maternity	Portugal	Santos et al. (2013)
		1.8		General	Sweden	Sörengård et al. (2019)
		1.6 ± 0.8		General	Switzerland	Kovalova et al. (2012)
		1.9±0.6	2.9	General	Turkey	Gönder et al. (2021)

Immunosuppressive agents	Mycophenolate	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Lipid regulators	Atorvastatin	ND - 0.01 ± 0.02	0.06	University/General	Portugal	Santos et al. (2013)
		0.01 ± 0.02	0.07	Maternity	Portugal	Santos et al. (2013)
		0.3	0.7	General	Spain	Bijlsma et al. (2021)
		0.5 - 2.2	4.1	General	Sri Lanka	Goswami et al. (2022)
		0.3		General	Sweden	Sörengård et al. (2019)
		0.92±0.74	2.4	General	Turkey	Gönder et al. (2021)
	Bezafibrate	5.5		General	Germany	Kraus (2014)
		0.09 ± 0.2 - 0.3 ± 0.5	1.4	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.02	Paediatric	Portugal	Santos et al. (2013)
		0.08 ± 0.09	0.2	Maternity	Portugal	Santos et al. (2013)
		0.1	0.3	University	Spain	(Mendoza et al., 2015)
		0.1		General	Sweden	Sörengård et al. (2019)
	Bezafibrate	0.06 ± 0.08		General	Switzerland	Kovalova et al. (2012)
		<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
	Fenofibrate	0.1	0.1	University	Spain	(Mendoza et al., 2015)
		0.04		General	Turkey	Yilmaz et al. (2017)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Lipid regulators	Fenofibric acid	0.1 - 0.9	2.7	General	Sri Lanka	Goswami et al. (2022)
	Fluvastatin	ND - <LOQ	0.03	University/General	Portugal	Santos et al. (2013)
	Gemfibrozil	ND - 0.03 ± 0.09	0.3	University/General	Portugal	Santos et al. (2013)

		0.1 ± 0.4	1.1	Paediatric	Portugal	Santos et al. (2013)
		0.04 ± 0.07	0.2	Maternity	Portugal	Santos et al. (2013)
		0.003 - 0.05	0.1	General	Sri Lanka	Goswami et al. (2022)
	Pravastatin	0.08 ± 0.1 - 0.3 ± 0.4	1.2	University/General	Portugal	Santos et al. (2013)
		0.3 ± 0.7	2.1	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
	Rosuvastatin	0.36±0.13	0.64	General	Turkey	Gönder et al. (2021)
	Simvastatin	6.7±9.8	24	General	Turkey	Gönder et al. (2021)
Melanin synthesis inhibitors	Mequinol	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Phytochemicals	Berberine	0.05	0.08	General	Japan	Azuma et al. (2019)
	Daidzein	1.3	2.1	General	Japan	Azuma et al. (2019)
		0.6		General	Sweden	Sörengård et al. (2019)
	Daidzin	0.05	0.2	General	Japan	Azuma et al. (2019)
	Genistein	0.8	1.0	General	Japan	Azuma et al. (2019)
		0.6		General	Sweden	Sörengård et al. (2019)
	Genistin	0.1	0.4	General	Japan	Azuma et al. (2019)
	Glycitein	0.6	1.4	General	Japan	Azuma et al. (2019)
	Glycitin	0.03	0.07	General	Japan	Azuma et al. (2019)
	Puerarin	0.6	2.6	General	Japan	Azuma et al. (2019)
Proton pump inhibitors	Omeprazole	ND - 0.8 ± 0.1		General	Mexico	Hernández-Tenorio et al. (2021)
	Pantoprazole	0.1	0.2	General	Spain	Bijlsma et al. (2021)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Psychiatric drugs	Alprazolam	0.04 ± 0.01 - 0.1 ± 0.04	0.2	University/General	Portugal	Santos et al. (2013)

		0.03 ± 0.04	0.1	Paediatric	Portugal	Santos et al. (2013)
		0.05 ± 0.03	0.1	Maternity	Portugal	Santos et al. (2013)
		<LOQ	<LOQ	General	Spain	Bijlsma et al. (2021)
		ND - 0.004	0.01	General	Sri Lanka	Goswami et al. (2022)
	Amitriptyline		0.09	General	Tunisia	Afsa et al. (2020)
	Azaperol	<LOD	<LOQ	University/General	Portugal	Santos et al. (2013)
	Azaperone	<LOQ	0.004	University/General	Portugal	Santos et al. (2013)
		<LOQ	<LOQ	Paediatric	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
	Benperidol	0.02 ± 0.02	0.05	General	Turkey	Gönder et al. (2021)
	Carbamazepine	0.9		University	Cameroon	Mayoudom et al. (2018)
		0.07 - 1.4	6	General	Colombia	Botero-Coy et al. (2018)
		2		Psychiatric	France	Mazzitelli et al. (2018)
			12	General	France	Wiest et al. (2018)
		0.6		General	Germany	Kraus (2014)
		0.04	0.06	General	Japan	Azuma et al. (2019)
		0.7 ± 0.4 - 0.8 ± 0.2	1.1	University/General	Portugal	Santos et al. (2013)
		0.3 ± 0.7	2.0	Paediatric	Portugal	Santos et al. (2013)
		0.07 ± 0.1	0.3	Maternity	Portugal	Santos et al. (2013)
		0.5 - 1.2		General	Slovakia	Bírošová et al. (2020)
		0.05		Oncology	Slovakia	Bírošová et al. (2020)
		0.3	0.6	University	Spain	(Mendoza et al., 2015)

Therapeutic group	Drug	Average conc. (µg/L)	Max. conc. (µg/L)	Hospital type	Country	Reference
Psychiatric drugs	Carbamazepine	0.5 - 1.3	3.2	General	Sri Lanka	Goswami et al. (2022)
		0.3		General	Sweden	Sörengård et al. (2019)
		0.2 ± 0.1		General	Switzerland	Kovalova et al. (2009)
			4.5	General	Tunisia	Afsa et al. (2020)
		0.09 - 1.2		General	Turkey	Yilmaz et al. (2017)
		1.4 ± 0.7	2.5	General	Turkey	Gönder et al. (2021)
	Chlorpromazine	0.5 ± 0.03		Psychiatric wing	Brazil	Reichert et al. (2019)
		ND - 0.02	0.05	General	Sri Lanka	Goswami et al. (2022)
	Chlorprothixene	0.02±0.02	0.05	General	Turkey	Gönder et al. (2021)
	Citalopram	0.2		Psychiatric	France	Mazzitelli et al. (2018)
		0.06 ± 0.05 - 0.1 ± 0.09	0.2	University/General	Portugal	Santos et al. (2013)
		0.2 ± 0.3	0.9	Paediatric	Portugal	Santos et al. (2013)
		0.1 ± 0.2	0.5	Maternity	Portugal	Santos et al. (2013)
		0.09 - 1.3		General	Slovakia	Bírošová et al. (2020)
		0.7		Oncology	Slovakia	Bírošová et al. (2020)
		0.03 - 0.09		General	Turkey	Yilmaz et al. (2017)
		0.1 ± 0.08	0.29	General	Turkey	Gönder et al. (2021)
	Clozapine	0.6 ± 0.05 - 1.0 ± 0.04		Psychiatric wing	Brazil	Reichert et al. (2019)

		0.7 ± 0.02 - 1.0 ± 0.05		Emergency ward	Brazil	Reichert et al. (2019)
		0.1 ± 0.2	0.46	General	Turkey	Gönder et al. (2021)
	Cyamemazine	0.3		Psychiatric	France	Mazzitelli et al. (2018)
	Desvenlafaxine	0.6		General	Sweden	Sörengård et al. (2019)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Psychiatric drugs	Diazepam	0.1		Psychiatric	France	Mazzitelli et al. (2018)
		ND		General	Germany	Kraus (2014)
		0.01 ± 0.008 - 0.02 ± 0.007	0.03	University/General	Portugal	Santos et al. (2013)
		<LOD	0.03	Paediatric	Portugal	Santos et al. (2013)
		0.02 ± 0.02	0.05	Maternity	Portugal	Santos et al. (2013)
		0.03	0.05	University	Spain	(Mendoza et al., 2015)
		ND - 0.03	0.05	General	Sri Lanka	Goswami et al. (2022)
		0.006		General	Sweden	Sörengård et al. (2019)
		0.07		General	Switzerland	Kovalova et al. (2009)
	Doxepin	0.1		General	Germany	Kraus (2014)
	Fluoxetine	0.02		Psychiatric	France	Mazzitelli et al. (2018)
		0.03 ± 0.009 - 0.07 ± 0.04	0.1	University/General	Portugal	Santos et al. (2013)
		0.02 ± 0.02	0.04	Paediatric	Portugal	Santos et al. (2013)
		0.04 ± 0.05	0.1	Maternity	Portugal	Santos et al. (2013)

		0.007 - 0.03	0.04	General	Sri Lanka	Goswami et al. (2022)
		0.04		General	Sweden	Sörengård et al. (2019)
			0.8	General	Tunisia	Afsa et al. (2020)
	Escitalopram	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Gabapentin	14.7	23.0	General	Spain	Bijlsma et al. (2021)
		19.4 ± 24.2		General	Switzerland	Kovalova et al. (2009)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Psychiatric drugs	Haloperidol	< 1.4 - 2.7 ± 0.04		Psychiatric wing	Brazil	Reichert et al. (2019)
		< 1.4 - 2.3 ± 0.1		Emergency ward	Brazil	Reichert et al. (2019)
		0.0005 - 0.02	0.06	General	Sri Lanka	Goswami et al. (2022)
		0.05 ± 0.04	0.12	General	Turkey	Gönder et al. (2021)
	Lorazepam	0.4		Psychiatric	France	Mazzitelli et al. (2018)
		0.3 ± 0.1 - 0.4 ± 0.4	1.3	University/General	Portugal	Santos et al. (2013)
		0.1 ± 0.09	0.3	Paediatric	Portugal	Santos et al. (2013)
		0.3 ± 0.2	0.6	Maternity	Portugal	Santos et al. (2013)
		0.6	0.8	University	Spain	(Mendoza et al., 2015)
		0.2	0.3	General	Spain	Bijlsma et al. (2021)

		0.002 - 0.009	0.02	General	Sri Lanka	Goswami et al. (2022)
	Melperone	0.01 ± 0.01	0.02	General	Turkey	Gönder et al. (2021)
	Memantine	0.02		General	Sweden	Sörengård et al. (2019)
	Meprobamate	0.2		Psychiatric	France	Mazzitelli et al. (2018)
	Mirtazapine	0.2		General	Sweden	Sörengård et al. (2019)
		0.2 ± 0.3	0.8	General	Turkey	Gönder et al. (2021)
	Nordazepam	0.02		General	Germany	Kraus (2014)
	Norfluoxetine	0.003		Psychiatric	France	Mazzitelli et al. (2018)
		0.02 ± 0.02	0.05	University/General	Portugal	Santos et al. (2013)
		0.01 ± 0.009	0.03	Paediatric	Portugal	Santos et al. (2013)
		0.03 ± 0.03	0.09	Maternity	Portugal	Santos et al. (2013)
		ND - 0.01	0.03	General	Sri Lanka	Goswami et al. (2022)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Psychiatric drugs	Olanzapine	< 0.3 - 0.3 ± 0.02		Psychiatric wing	Brazil	Reichert et al. (2019)
		< 0.3 - 0.5 ± 0.03		Emergency ward	Brazil	Reichert et al. (2019)
		0.03 ± 0.04 - 0.2 ± 0.3	0.8	University/General	Portugal	Santos et al. (2013)
		0.04 ± 0.1	0.3	Paediatric	Portugal	Santos et al. (2013)
		0.002 ± 0.004	0.01	Maternity	Portugal	Santos et al. (2013)
		0.02 ± 0.01	LOQ	General	Turkey	Gönder et al. (2021)

	Oxazepam	7		Psychiatric	France	Mazzitelli et al. (2018)
		3.8		General	Germany	Kraus (2014)
		0.03 - 0.3		General	Slovakia	Bírošová et al. (2020)
		0.07		Oncology	Slovakia	Bírošová et al. (2020)
		0.004 - 0.09	0.2	General	Sri Lanka	Goswami et al. (2022)
		0.4		General	Sweden	Sörengård et al. (2019)
		1.1 ± 0.3		General	Switzerland	Kovalova et al. (2009)
		0.04		General	Turkey	Yilmaz et al. (2017)
	Paroxetine	<LOD	<LOQ	University/General	Portugal	Santos et al. (2013)
		0.3	0.9	University	Spain	Mendoza et al. (2015b)
	Pipamperone	0.03±0.03	0.07	General	Turkey	Gönder et al. (2021)
	Quetiapine	0.002 - 0.04	0.2	General	Sri Lanka	Goswami et al. (2022)
	Risperidone	< 0.9 - 1.0 ± 0.06		Psychiatric wing	Brazil	Reichert et al. (2019)
		0.1 ± 0.3	0.77	General	Turkey	Gönder et al. (2021)

Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**
Psychiatric drugs	Sertraline	0.01		Psychiatric	France	Mazzitelli et al. (2018)
		<LOD	<LOQ	University/General	Portugal	Santos et al. (2013)
		<LOD	<LOQ	Paediatric	Portugal	Santos et al. (2013)

		<LOD	<LOQ	Maternity	Portugal	Santos et al. (2013)
		0.006 - 0.02	0.09	General	Sri Lanka	Goswami et al. (2022)
		0.08		General	Sweden	Sörengård et al. (2019)
	Sulpiride	2.1	7.3	General	Japan	Azuma et al. (2019)
	Temazepam	0.02		General	Germany	Kraus (2014)
	Trazodone	0.01 ± 0.01 - 0.02 ± 0.01	0.05	University/General	Portugal	Santos et al. (2013)
		0.008 ± 0.01	0.04	Paediatric	Portugal	Santos et al. (2013)
		0.01 ± 0.01	0.04	Maternity	Portugal	Santos et al. (2013)
	Venlafaxine	<LOQ - 0.07	0.03	General	Colombia	Botero-Coy et al. (2018)
		0.2 ± 0.2 - 0.3 ± 0.3	0.9	University/General	Portugal	Santos et al. (2013)
		0.2 ± 0.3	1.0	Paediatric	Portugal	Santos et al. (2013)
		0.5 ± 0.6	1.9	Maternity	Portugal	Santos et al. (2013)
		1	1.5	General	Spain	Bijlsma et al. (2021)
		0.4		General	Sweden	Sörengård et al. (2019)
		0.8 ± 0.3		General	Switzerland	Kovalova et al. (2009)
	Venlaxafine	0.02 - 0.2		General	Turkey	Yilmaz et al. (2017)
		0.2 ± 0.1	0.38	General	Turkey	Gönder et al. (2021)
		0.3 - 2.4		General	Slovakia	Bírošová et al. (2020)
		0.6		Oncology	Slovakia	Bírošová et al. (2020)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Therapeutic group	**Drug**	**Average conc. (µg/L)**	**Max. conc. (µg/L)**	**Hospital type**	**Country**	**Reference**

Psychiatric drugs	Zuclopenthixol	0.2 ± 0.4	0.88	General	Turkey	Gönder et al. (2021)
Sedatives and muscle relaxants	Chlorzoxazone	0.1		General	Sweden	Sörengård et al. (2019)
	Midazolam	0.1		General	Slovakia	Bírošová et al. (2020)
		Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Xylazine	<LOQ	0.01	Paediatric	Portugal	Santos et al. (2013)
		<LOD	0.02	Maternity	Portugal	Santos et al. (2013)
Selective estrogen receptor modulators	Tamoxifen	<LOQ	<LOQ	General	Turkey	Gönder et al. (2021)
Stimulants	Benzedrex	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Cathine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Ephedrine	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
Synthetic glucocorticoids	Dexamethasone	0.03 ± 0.02 - 0.1 ± 0.09	0.4	University/General	Portugal	Santos et al. (2013)
		<LOQ	0.03	Paediatric	Portugal	Santos et al. (2013)
		0.07 ± 0.1	0.3	Maternity	Portugal	Santos et al. (2013)
		0.1 ± 0.01		General	Switzerland	Kovalova et al. (2009)
	Methylprednisolone	1.4 ± 0.8		General	Switzerland	Kovalova et al. (2009)
Vasodilators	Isosorbide	Not quantified		Paediatric/ General	USA	Meza et al. (2020)
	Sildenafil	0.1	0.1	University	Spain	(Mendoza et al., 2015)

Where a range of average concentrations is given, this represents the range of averages for discharges from multiple hospitals or multiple sampling periods.

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