An economic approach to tackling antimicrobial resistance (AMR)

A thought provoker

Authors

Professor Lin Crase
Professor of Resource Economics, UniSA Business
University of South Australia

Dr Branwen Morgan
Minimising Antimicrobial Resistance Mission
CSIRO

Editorial contributions from
Chris Angwin
Minimising Antimicrobial Resistance Mission
CSIRO

Adapted from work by

Dr Bethany Cooper
Senior Research Fellow, UniSA Business
University of South Australia
bethany.cooper@unisa.edu.au

Professor Harry Clarke
Emeritus Professor, Business School
La Trobe University

Professor Lin Crase
Professor of Resource Economics, UniSA Business
University of South Australia

Dr Ben van den Akker
Lead Wastewater Scientist
SA Water

Professor Erica Donner
Research Director, CRC SAAFE
University of South Australia

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The problem

Antimicrobial drugs work by destroying or hindering the harmful microbes that cause infections (pathogens). However, microbes can rapidly evolve to resist the effects of medicines designed to kill them.

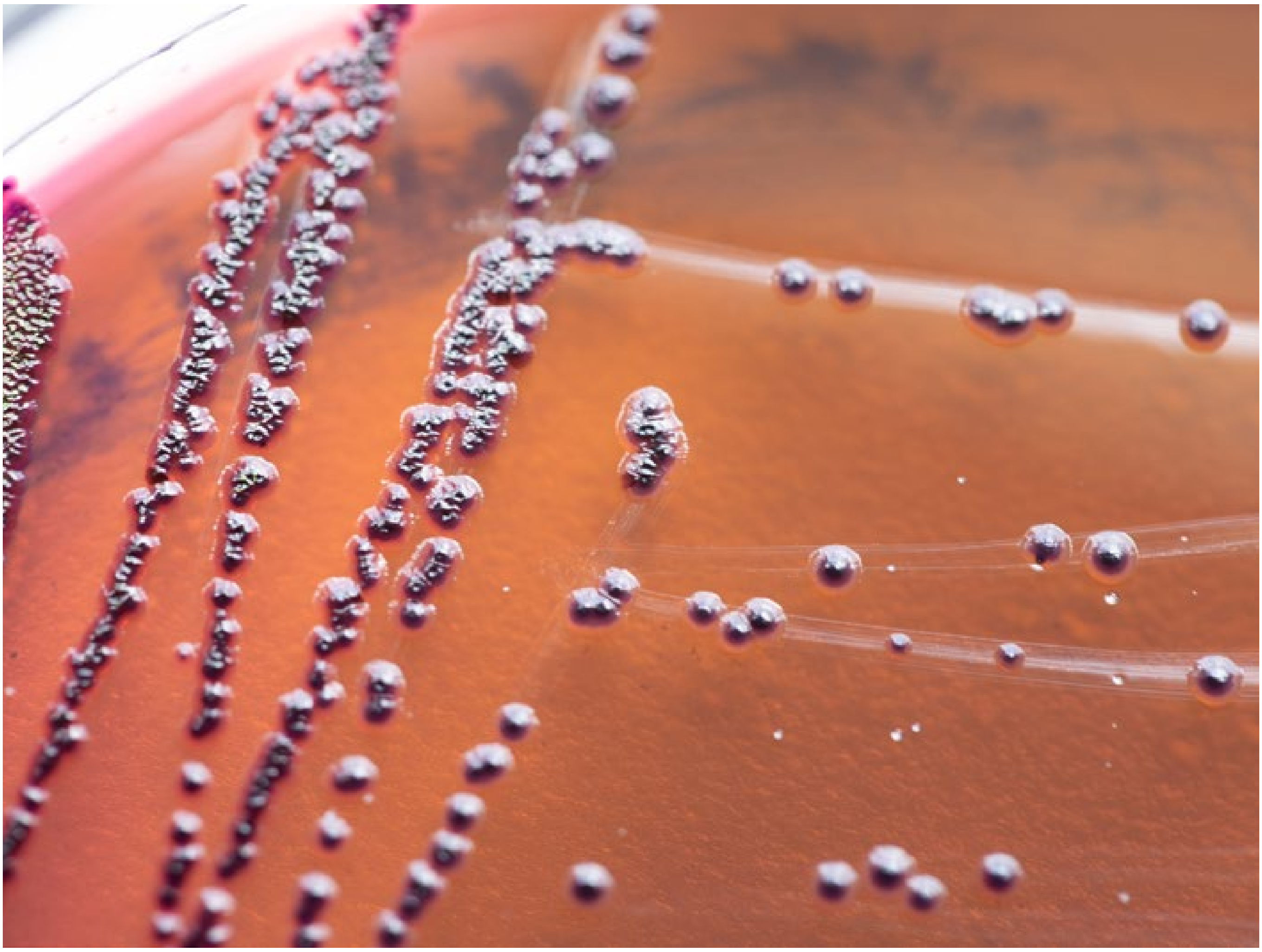
Therefore, over time, antimicrobials become less effective. This process is accelerated by the use and misuse of antimicrobials.

This phenomenon, known as antimicrobial resistance (AMR), is a major international concern.

Although fears about the potential disruption from AMR have existed for decades, mounting evidence of its impacts on human health has elevated its status to a "global health threat"[1].

In 2014, global deaths from AMR were estimated at around 700,000[2]. However, by 2019, the death rate had risen significantly to 1.27 million per year[3].

By 2050 this is expected to increase to 50 million deaths per year[2] and cause an increase in global AMR healthcare costs from $300 billion to greater than $1 trillion per annum[4].



1 World Health Organization (WHO) (2015) Global Action Plan on Antimicrobial Resistance, available at www.who.int/publications/i/item/9789241509763
2 O'Neill J. (2014) Tackling drug-resistant infections globally – Final report and recommendations, The Review of Antimicrobial Resistance, amr-review.org/.
3 Antimicrobial Resistance Collaborators (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, Lancet; 399: 629–55
4 WHO. 2019. "Ten threats to global health in 2019", Newsroom, www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019

One Health

Initially, concerns about AMR were focused on human misuse of antimicrobials. In 1945, Alexander Fleming himself observed that the antibiotic he discovered, penicillin, could lose effectiveness due to the evolutionary process of antimicrobial resistance[5].

Now, we understand AMR in a broader context, considering humans alongside animals, food production and the environment.

There has been a strong focus on use of antibiotics in animal production particularly, building directly on the links between animal and human health, dating from the 19th Century.

Subsequently, emphasis has shifted to include wider environmental influences and the notion of 'One Health' has been used to characterise the complexity of the challenge.

One Health is premised on the idea that human, animal, and environmental health are interlinked and that actions to reduce AMR need to be coordinated across these domains.

The least-well understood component of the One Health perspective on AMR is the role that the environment plays in eventual clinical presentations.

Despite very few antimicrobial active pharmaceutical ingredients (APIs) being manufactured in Australia, the release of unmetabolised or partially metabolised antimicrobials into water and the environment is acknowledged as a driving force of AMR.

Some antimicrobials are packaged in Australia and many are delivered/formulated in animal feed. **Currently, there are no Australian regulations for pharmaceutical levels in waste discharges (hospital or household).**

The only Australian 'regulation' or guideline that mentions antimicrobials is the Water Quality Guidelines for recycled drinking water 2008. This has default guidance values for antimicrobials and chemicals.

The problem is that pharmaceuticals (unlike chemicals) are not included in most regulations and guidelines related to waste in Australia and globally. Furthermore, specific guidelines or regulations on hospital waste/wastewater treatment plants do not consider antimicrobials.

Regulations dealing with medical waste (infectious, hazardous, radioactive, and general) do not cover drugs/antimicrobials entering the sewage waste system (urine/faeces). The only reference to pharmaceuticals is under hazardous waste disposal of unused medications.

Globally, there is an increased focus on the removal of pharmaceutical residues from wastewater. In the Netherlands, the government adopted the 'Chain Approach Medicine Residues from Water' policy.

The chain approach has recently been nominated by the 'World Future Council' for the Future Policy Award 2021. The Dutch Consortium on Antibiotics and Pharmaceutical Residues from Water consisting of a 'coalition of doing' acts in accordance with this chain approach specifically focuses on the removal of antibiotic residues from water.

5 Spellberg B, Gilbert DN. (2014) The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett. Clin Infect Dis. 59

Why different perspectives are needed

While tackling AMR through wastewater has clear merit on some fronts, the complexity and unknown aspects of AMR make it difficult to identify definitive solutions.

Accordingly, bringing different perspectives to bear when contemplating actions is helpful. This is a core principle embedded in the One Health approach.

In addition to recognising that humans are one aspect of the ecosystem, it is important to also recognise that human behaviours in that environment are not fixed, and that can result in feedback effects, both positive and negative.

For instance, the price of alternatives to antimicrobials used in some settings (e.g. vaccination) could change, resulting in less (or more) use of antimicrobials.

International travel could become more accessible and affordable, accelerating the spread of AMR across countries. In these circumstances, understanding social sciences, like economics, offers an alternative lens for formulating solutions.

Economic approaches to AMR

Economics has several appealing aspects that can help decision-making. First, most economic analysis is concerned with change at the margin. That is, choices are considered and compared based on the net benefits of taking one action over another. This feature has resulted in a widely-used approach known as **cost-benefit analysis** (see case analysis on page 8).

Cost-benefit analysis usually follows four rudimentary steps: (1) establish the scope of benefits and costs that attend a choice – ideally keeping the scope similar for both; (2) measure benefits and costs with the same metric, usually dollars; (3) discount future benefits and costs so that all values are expressed in current terms; (4) apply a decision rule, for instance choosing the alternative that delivers greatest net benefits.

While appearing straightforward the application of cost-benefit analysis to specific choices can be challenging, particularly when information is incomplete.

The second appealing aspect of economics is that it has established mechanisms for dealing with choices when information is not fully available. Here, economics makes a distinction between the idea of **'risk'** and **'uncertainty'**. Risk in economics relates to a decision that has a probabilistic outcome.

In contrast, uncertainty pertains to situations where the gaps in knowledge are so severe that a probability distribution is not available. In practice, many choices sit along this spectrum and expert judgement or community preference are used to shape the choice.

Where a probability is assigned to an outcome the standard steps in a cost-benefit analysis can still be applied by invoking **expected utility theory.** For instance, if a project has an 80 per cent chance of delivering a benefit of $100 million dollars, this is weighted at $80 million and included in the cost-benefit framework.

However, once this type of calculation enters the analysis it is important to also consider risk preferences. In the previous calculation we derive the $80 million by simply multiplying the value of the benefit ($100m) by the probability (0.8) to derive expected value – this implicitly assumes risk neutrality on the part of the decision maker.

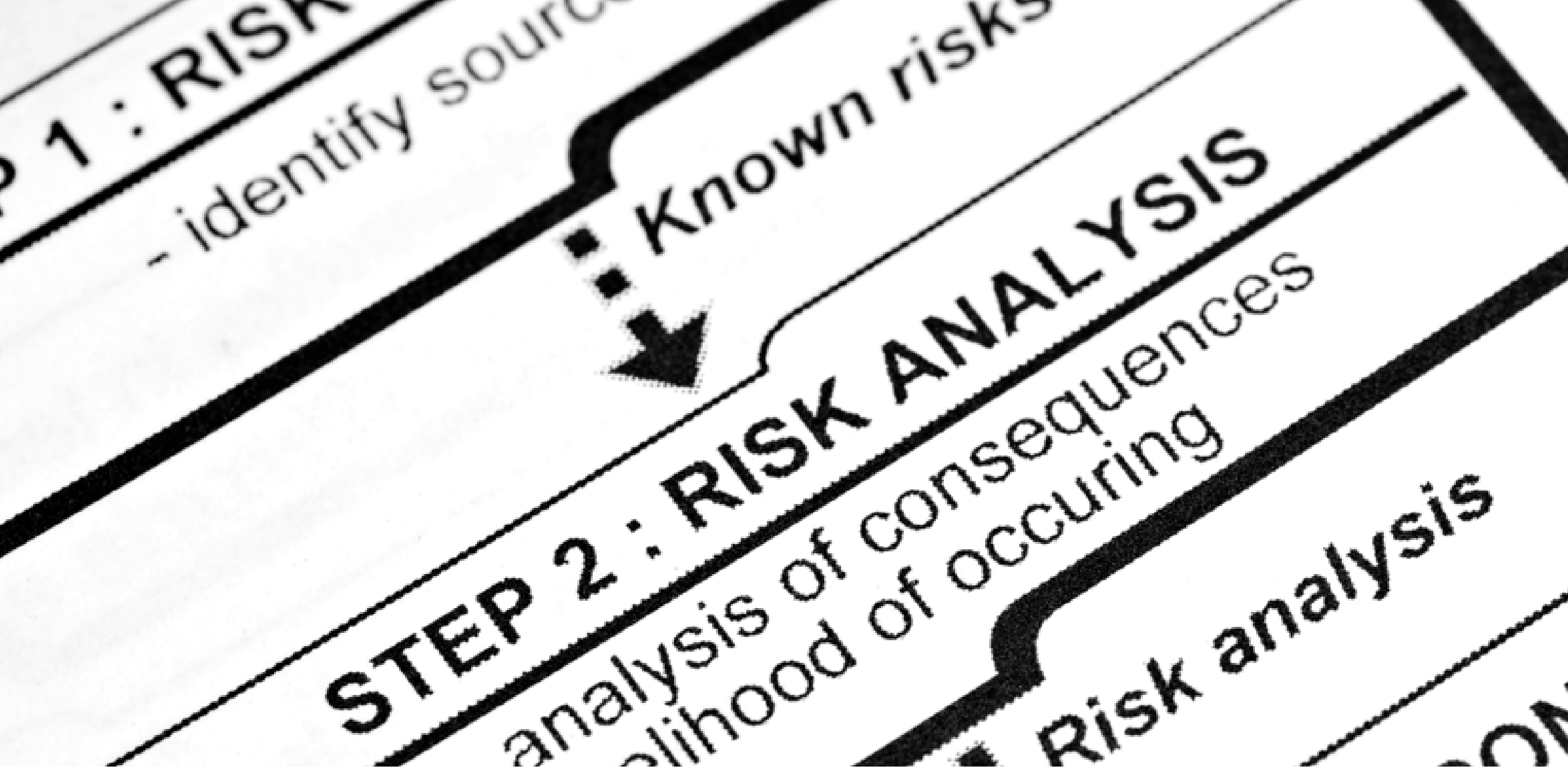
If the decision maker is **risk averse,** they will impose a subjective judgement that modifies the probability so the expected outcome will be less than $80 million.

Risk aversion has potentially important consequences for the way we approach decisions that relate to AMR. Given the potentially catastrophic consequences of AMR a decision maker might see value in applying some for of **insurance premium** (see case analysis on page 10). within the cost-benefit analysis.

In this case, a project might not satisfy the standard criteria of generating benefits in excess of costs, but the shortfall is less than the risk premium the decision maker would have paid to avoid the potentially bad outcomes. Clearly, the challenge with this approach is that an extremely risk averse decision maker accepts nearly all projects, even if the probability of a poor outcome is very low.

Where a choice is circumscribed by very little information, there may also be value in holding off making any choice, until more information becomes available. Economists use the notion of real options to explore these types of cases.

The idea behind **real options** theory is that a choice can sometimes be irreversible and if later proven wrong because additional information emerges, it is better to wait so that the unrecoverable investments are not wasted.



In simple terms, the real option value acts against the insurance premium, described above, and requires benefits to exceed costs by a sufficient margin to offset any potential gains from waiting. The practical way this is often included in decision making, is to stage projects in smaller phases to assemble additional knowledge as the project rolls out, even if the staged approach is more expensive in standard cost terms.

Applying these concepts to the removal of antibiotic residues in wastewater streams yields some interesting results. First, the choice between upgrading centralised wastewater treatment or more decentralised improvements implies some form of binary choice.

Once we account for the different types of uncertainty this is unlikely to be the case; even a risk-neutral decision maker might reasonably opt to trial both, in order to better understand the effectiveness of each treatment. Second, a decentralised approach also carries with it the likelihood of some form of regulation of the decentralised entities. This has the attractive feature of being relatively reversible in an economic sense, thus avoiding large capital costs that might be ineffective in terms of AMR but nonrecoverable in centralised systems. Nonetheless, there are material costs related to **monitoring to bring compliance** (see case analysis on page 11) and these also need to be considered.

Conclusion and next steps

AMR is a serious risk that cannot be addressed with a single intervention: there is no silver bullet. The One Health approach helps conceptualise the challenges while highlighting the problem's wicked nature. There is a role for the water and wastewater sector and, the use of economics, offers a way of considering how the sector might best respond.

An opportunity exists now to engage on this issue. We welcome feedback on the ideas expressed in this thought-provoking piece and plan to release additional resources to support engagement.

Case analysis:
Wastewater upgrades and cost-benefit analysis

Contemplate a case where a wastewater utility is considering upgrading infrastructure to produce tertiary treated wastewater and subsequently on-selling this to irrigation customers. If the utility was operating solely in the private sector, the cost-benefit calculus would reduce to estimating the extra capital and operating costs of the plant and distribution infrastructure and forecasting whether the additional revenues would then adequately cover the costs of the project.

Here the scope of the project is defined by the commercial interests of the wastewater entity and the measurement of benefits is based on expected payments from customers, with some degree of probability to reflect the likelihood that future customers may pay less (or more). Construction cost estimates would be taken from similar engineering works as would operating costs. Importantly, because this private entity could invest in other projects, a cost of capital (e.g. interest foregone) would also need to be included in the cost calculation.

If the wastewater company expects the project to last for 20 years and collect revenues over that time, then future revenues would need to be discounted, since a dollar earned in the future is worth less than a dollar generated today. Finally, the company would make a decision by considering if the benefits (in this case the sum of discounted expected revenues) were sufficiently in excess of costs to warrant any risks related to the project.

While seemingly straightforward, even this relatively simple private sector example has a number of ‘unknowns’. Will construction costs change? If energy prices shift, how will the project fare? Will irrigators want the water at the prices on offer? Are there alternative water sources the irrigators might be offered? Will the cost of capital change? It is thus common practice to use expected values but to then test different assumptions and scenarios to establish how sensitive the results might be to specific assumptions.

In settings where external benefits and costs are major issues it makes sense for these types of wastewater projects to be government-owned. Managing wastewater has numerous health and environmental spill-over benefits and for that reason it is usually undertaken by an arm of government.

Government ownership has implications for how the steps in the cost-benefit analysis above transpire. First, the scope of the project would likely change, inasmuch as a wider set of benefits and costs, like environmental and social impacts, might legitimately be of concern to a publicly-owned utility. That is not to say that the commercial aspects are ignored; rather, the project would now be more likely to take account of improvements (or deterioration) in the natural environment.

For example, reverse osmosis might be required to treat AMR risks, but this produces wider environmental quality benefits that might now lay in scope. Government ownership also implies that additional consideration might be given to second-round employment impacts[1]. Second, this wider project scope means that measurement of benefits and costs will need to use other approaches, like stated-preference techniques or related-market techniques to determine values. Third, the discount rate chosen might not be the same for a government project.

For example, concerns about the possible downplay of impacts on future generations might see a lower discount rate included[2]. Finally, the decision rule will be similar, although in this case the cost-benefit analysis will form only one piece of information used by the decision maker.

Much of the information used in a cost-benefit analysis for a project like this would also be employed by any economic regulator. Centralised wastewater systems lend themselves to monopoly service provision and Australian jurisdictions attempt to control the behaviour of monopolies, including those owned by government.

The role of an economic regulator in this case would be to ensure that the charges applied to irrigation customers fairly reflect the costs of service provision. In effect, the regulator would need comfort that the revenue stream from the project is sufficient to cover all costs, including capital costs, to avoid the monopolist passing costs onto other customers. It would also need assurance that the revenues are not excessive and thus represent a transfer of rents to the service provider.

The Northern Adelaide Irrigation Scheme is a $156 million project that treats 12 Gigalitres of wastewater at the Bolivar wastewater treatment plant and distributes it to irrigation customers on the Northern Adelaide Plains. The business case for the project was based, in part, on the environmental benefits of reduced wastewater discharge to the Gulf of St Vincent and the economic and social benefits of intensified horticulture in the region. Expected water demand to support the project was assessed by a survey of potential users in 2015 (see, ARRIS 2015).

Prices for recycled water in South Australia are regulated by ESCOSA, the economic regulator. This occurs because the provider of recycled water (SA Water) is a fully integrated monopoly in the state and holds market power. ESCOSA's approach to regulating prices for recycled water is 'light touch' and limited to ensuring the nine principles embodied in the National Water Initiative pertaining to pricing recycled and stormwater are adhered to. SA Water publishes its pricing schedule for NAIS and announced a review of pricing to enhance customer uptake in 2022.

1 There are complications from including employment impacts, especially if they are added to only one part of the cost-benefit analysis.

2 Hone *et al.* (2022) note that the routine choice of a 7% discount rate gives rise to a variety of concerns.

Case analysis:

The insurance premium for non-rainfall dependent water

In the midst of Australia's millennium drought many towns and cities were confronted with dwindling water supplies. Moreover, at that time, predictions about the impacts of climate change pointed to increased variability of rainfall, including the prospect of more severe and extended droughts. In mid-2007 Melbourne's freshwater storage fell below 30 per cent and the spectre of a city of almost four million people facing significant water shortages was real. The Age newspaper was publishing a daily clock predicting the point at which water supplies would be exhausted.

This provided the background to the state government announcing the construction of one of the world's largest desalination plants. The Victorian desalination plant had a capital cost of $3.5 billion (2009 dollars) and was developed as a public-private-partnership with AcquaSure.

The announcement about the construction of the desalination plant was accompanied by decisions to enhance the connection between Melbourne's water supplies to irrigation water held in catchments north of the city (the North-South pipeline) and to expand wastewater recycling.

Prior to these announcements, water shortages were being managed by restrictions being placed on water use along with a range of incentives for water users to adopt more water efficient appliances. Arguably, these earlier approaches could be justified on standard cost-benefit terms, inasmuch as they had the benefit of forestalled major capital expenditures and the demand management measures had gained broad acceptance by the community, at least initially, suggesting the costs were not too onerous.

In contrast, the desalination plant embodies distinct insurance characteristics, perhaps representing the risk aversion of decision makers at that time.

These insurance components are most overt in the contracting arrangements between the Victoria government and AcqaSure. The payment to AcaquaSure has two components: (1) a water security payment which covers the cost of design and construction along with operational and maintenance costs, regardless of any water supplied (2) a water usage payment that is tied to the volume of water ordered by the Minister of Water on 1 April of each year. Water orders can take the form of 0, 50, 75, 100, 125 and 150 Giglitres.

Since commissioning in 2012, orders of water from the desalination plant began in 2016-17 with 50 Giglitres and peaked at 125 Giglitres each year between 2019-20 and 2020-21. The cost to consumers of the water security payment where no water is ordered has been estimated at about $608 million per year (Australian Cost Engineering Society, n.d.).

Case analysis:

Trade waste management by wastewater utilities

Australian jurisdictions already have experience managing waste streams in sewage using a combination of centralised and decentralised institutions. This is commonly expressed in the form of trade waste agreements between customers who produce liquid wastes and the operator of the receiving wastewater treatment plant. The legislation that covers these types of agreements can vary across jurisdictions; for instance, in regional NSW liquid trade waste is defined under local government regulations, whereas in Victoria the Water (Trade Waste) Regulations sit within the state's Water Act.

The rationale for managing trade waste differently to household and 'general business' sewage is that the waste stream is of sufficient quantity and/or quality that it represents a risk to the management of the centralised treatment plant. It is also large enough to warrant individual metering. At a technical level, the local waste stream requires more treatment and, at an economic level, this entails additional cost that would otherwise be borne by the wastewater treatment plant. Most jurisdictions follow similar protocols but there can be marked variations around key elements, even between wastewater utilities in the same state.

In order for a customer to discharge trade waste to the sewer network they must first secure approval from the plant operator (i.e. Council, Water Utility). A risk assessment usually follows to ascertain the potential impacts of the wastewater stream on the sewer network and wastewater treatment plant and this is then built into an agreement with the customer.

Key parameters of interest include the volume of waste, the Biochemical Oxygen Demand, Suspended Solid, Total Kjeldahl Nitrogen and Total Phosphorous. For some trade waste customers, their agreement commits them to generating wastes that do not exceed specific biological and chemical thresholds.

A charge is levied on the volume of waste that lies below those thresholds with additional fees applied when non-compliance occurs. There may also be charges levied to cover inspection and monitoring activities. Repeated breaches can result in forcible disconnection from the sewer network and prosecution.

In simple terms, the impact of this regulatory approach is to shift the onus for choosing and managing a wastewater technology to the decentralised customer base. Obviously, this initially reduces costs for the centralised operator but it can be a sizeable undertaking – in SA, trade waste customers represent around 1.5% of all customers (approximately 10,000 customers).

In order to bring compliance across such a large number of customers requires a significant monitoring and enforcement investment. In some cases, this is complicated by the volume of technical information expected to be read and understood by customers. SA Water, for instance, provides almost 50 fact sheets on its website to help customers navigate this relationship. Accordingly, while it is feasible for these regulatory arrangements to offer some flexibility as new knowledge and technology emerges, significant resources are still required to manage any transition.

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