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Considering health risks in decision-making in practice

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Bridging Science to Practice

Report

Considering health risks in decision-making in practice

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Managementsamenvatting

Nieuwe en toekomstige uitdagingen in drinkwaterkwaliteit en gezondheid vragen een geïntegreerde aanpak voor monitoring, risicobeoordeling en maatregelen.

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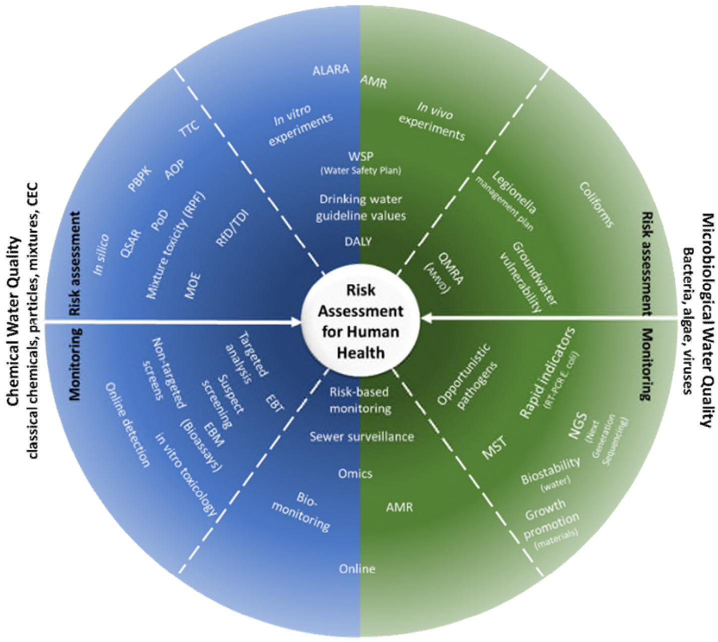
Dit rapport geeft een overzicht van nieuwe en opkomende bedreigingen, technologieën en methoden voor monitoring en risicobeoordeling van de waterkwaliteit. Daarmee biedt het een uitgangspunt voor een geïntegreerde strategie om de uitdagingen op het gebied van drinkwaterkwaliteit en gezondheid aan te pakken. Een omgeving die steeds complexer wordt als gevolg van menselijke activiteiten en klimaatverandering zorgt ervoor dat bij de productie van veilig en schoon drinkwater rekening moet worden gehouden met veel verschillende aspecten. Technologische ontwikkelingen leiden tot lagere detectiedrempels voor stoffen en brede screening benaderingen brengen nieuwe chemische en microbiologische verontreinigingen aan het licht. Hiervoor is een evaluatie van de potentiële gezondheidsrisico's en de noodzaak van aanvullende beheersmaatregelen, zoals extra zuivering, vereist. Zorgvuldige communicatie met het publiek, de belanghebbenden en de wetgevers is nodig om de samenleving bewust te maken van het belang van de waterkwaliteit voor de gezondheid en het milieu, waarbij het vertrouwen van het publiek in de drinkwaterkwaliteit behouden blijft.



Overzicht van terminologie met betrekking tot chemische en microbiologische waterkwaliteit en risicobeoordeling (niet uitputtend). Links staan chemische- en rechts microbiologische termen. De onderste helft betreft monitoringsmethoden en de bovenste risicobeoordeling. Termen dichter bij het centrum geven een meer kwantitatief resultaat.

Belang: veilig drinkwater in een veranderende wereld
Voor het ondersteunen van beheersmaatregelen in de praktijk neemt de behoefte van drinkwaterbedrijven aan risicobeoordeling en -karakterisering van de waterkwaliteit toe. Dit komt doordat de waterkwaliteit als gevolg van wereldwijde ontwikkelingen wordt bedreigd, zowel aan de bron als in het distributiesysteem. Jaarlijks komen er chemicaliën bij en deze komen vrij in het milieu.

Gelijktijdig leidt waterschaarste ertoe dat voor de productie van drinkwater minder beschermde bronnen moeten worden gebruikt. Met steeds betere analysemethoden kunnen meer bedreigingen op lagere niveaus worden gedetecteerd. Ook wordt de consument zich steeds bewuster van verontreinigingen in water en staat hier kritisch tegenover. Deze ontwikkelingen zullen zich verder uitbreiden en drinkwaterbedrijven zien in dat zij zich hierop moeten voorbereiden. Daarom is het belangrijk slimme keuzes te maken bij de inzet van beschikbare middelen en maatregelen met het meeste effect op de bescherming van gezondheid en milieu.

Aanpak: interviews met waterbedrijven en experts
Interviews met KWR-deskundigen zijn uitgevoerd om te komen tot een beknopt en systematisch overzicht van recente ontwikkelingen op het gebied van waterkwaliteit en gezondheid. Daarnaast zijn alle Nederlandse en Vlaamse drinkwaterbedrijven geïnterviewd over hun ervaringen, uitdagingen en opvattingen over dit vraagstuk. De resultaten zijn gebundeld in factsheets met een beschrijving van het onderwerp, belangrijke publicaties, uitdagingen in het onderzoek, huidige toepasbaarheid in de praktijk en onderzoeksperspectieven. Dit is aangevuld met een hoofdstuk over besluitvormingsmethodologieën.

Resultaten: adequate mechanismen zijn aanwezig, maar er is een goede toekomststrategie nodig
Drinkwaterbedrijven hebben mechanismen ontwikkeld om te weten welke bedreigingen er spelen voor de waterkwaliteit en hoe zij deze risico's kunnen beheersen. Binnen het BTO wordt gewerkt aan collectief onderzoek naar de chemische en microbiologische waterkwaliteit. Daarnaast wordt dit onderwerp onder de aandacht gebracht bij beleid (Vewin) en publiek (klanten en media). Toch blijven er uitdagingen bestaan naarmate het aantal (bekende) bedreigingen, methoden en technologieën toeneemt. Dit rapport illustreert de complexiteit van waterkwaliteits- en gezondheidsvraagstukken die in de nabije toekomst moeten worden aangepakt. De uitdaging is om slimme keuzes te maken om de urgente onderzoeksvragen efficiënt aan te pakken.

Toepassing: onderzoeksstrategie en uitwisseling in de praktijk
Het is onze aanbeveling dat de gezamenlijke aanpak voor het beheersen van de waterkwaliteit verder wordt doorontwikkeld. Elementen hiervan zijn:

- geïntegreerd kader voor risico- (impact) evaluatie en prioritering van gezondheidsrisico's voor de sector;
- onderzoeksstrategie voor aanpak van geprioriteerde onderwerpen en selectie van geschikte methoden en technologieën;
- uitvoeringsstrategie waarbij niet uitsluitend de technologische maar álle operationele eenheden binnen een waterbedrijf zijn betrokken;
- platform voor het uitwisselen van praktische benaderingen voor beheersing van de waterkwaliteit tussen waterbedrijven;
- gemeenschappelijke boodschap aan het publiek en de politiek; transparant, correct gericht en in begrijpelijke taal voor de doelgroepen.

Het Rapport
Dit onderzoek is beschreven in het rapport *Considering health risks in decision-making in practice (BTO 2022.014).*
Meer informatie:
- BTO 2019.023 Risicoperceptie.
- BTO 2018.030 Tools for human health risk assessment of emerging chemicals
- BTO 2014.008 Inventarisatie analyses microbiologische veiligheid drinkwater (AMVD)
- BTO 2010.042 Drinkwaterkwaliteit Q21: een horizon voor onderzoek en actie.

Contents

1 Introduction and aim

1.1 Introduction

The production of safe and clean drinking water requires consideration of many different aspects in an increasingly complex environment due to human activities and climate change (Escher et al. 2020). Pressures on drinking water sources are related to water availability (Van Vossen-Van den Berg et al. 2019) and water quality (Kools et al. 2019; Van Driezum 2019). Although many stakeholders and organisations are involved in the management of the water cycle and drinking water sources, here we focus on the measures that are taken by drinking water companies to safeguard the production of safe and clean drinking water, and tools and methods they apply to support the decision-making process on these measures. Technological developments resulting in lower detection thresholds and non-targeted screening approaches increasingly reveal new and more chemical micropollutants and (potential) pathogens, for which an evaluation of potential risks and of the need for management or removal is required. Insights in health risks, analysis methods, legislation and regulations are constantly changing, which complicates decision making on (the requirement of) treatment expansion and monitoring efforts.

The drinking water companies have a lot of experience addressing water quality challenges, and many different tools and methods have been developed to inform adequate measures in practice. For effective and efficient operation of water systems and risk management, drinking water companies integrate knowledge on the composition of water bodies, the influence of water treatment processes and the influence of transport and distribution on both the chemical and microbiological water quality. Where possible, knowledge is translated into 'PraktijkCodes Drinkwater'[1] to maintain efficient and high quality business operations (Meerkerk 2015). In the PraktijkCodes Drinkwater, guidelines are set to help drinking water companies in upholding water quality. For example, a closed water infrastructure and careful and hygienic work are advised, and only those chemicals and materials that are tested for their safety when in (contact with) drinking water are approved. In some cases, the Dutch drinking water regulation refers to the PraktijkCodes Drinkwater as a required standard.

In addition, research into the variety of potential risks is performed to determine whether the current systems and practices remain sufficient to provide safe drinking water now and in the future. Water quality researchers and managers apply various tools and methods to monitor potential chemical and microbiological hazards and assess their risks. Various methods for both monitoring and risk assessment are applied for this purpose. This can range from routine risk-based monitoring to extensive research projects on future emerging threats. New threats and insights continuously require the development of new methods for monitoring and risk assessment. This has led to a continuous development of new methods and tools. Whether a method or tool is considered applicable and effective to be applied in drinking water practice may also depend on its interpretability, complexity, accessibility and technological readiness level.

Compliance to legal requirements is the foundation for the production of safe and healthy drinking water by the drinking water companies. However, legal requirements are generally lagging behind the most recent insights. Therefore, risk based approaches are adopted to identify and manage emerging risks, for example through Risk Based Monitoring (RBM) or Water Safety Planning (WSP). These provide estimations of risks and the effect of mitigation measures as a basis for decision making by drinking water companies. However, since risk estimates differ in format, type and uncertainty, such decision making can be challenging, especially due to the number of various methods developed over time. Furthermore, the rate of technology development is increasing, and therefore the number of

[1] https://www.praktijkcodesdrinkwater.nl/

methods will also increase. This may lead to increased costs for the monitoring and risk assessment and more complexity in decision making.

Figure 1 provides an overview of relevant methods and terminology (not exhaustive) organised according to:

- Chemical or microbiological or both
- Monitoring of hazards or risk assessment / risk management
- Quantification of risk versus prioritization of risks
- Laboratory versus online monitoring
- Quantitative versus qualitative outcome

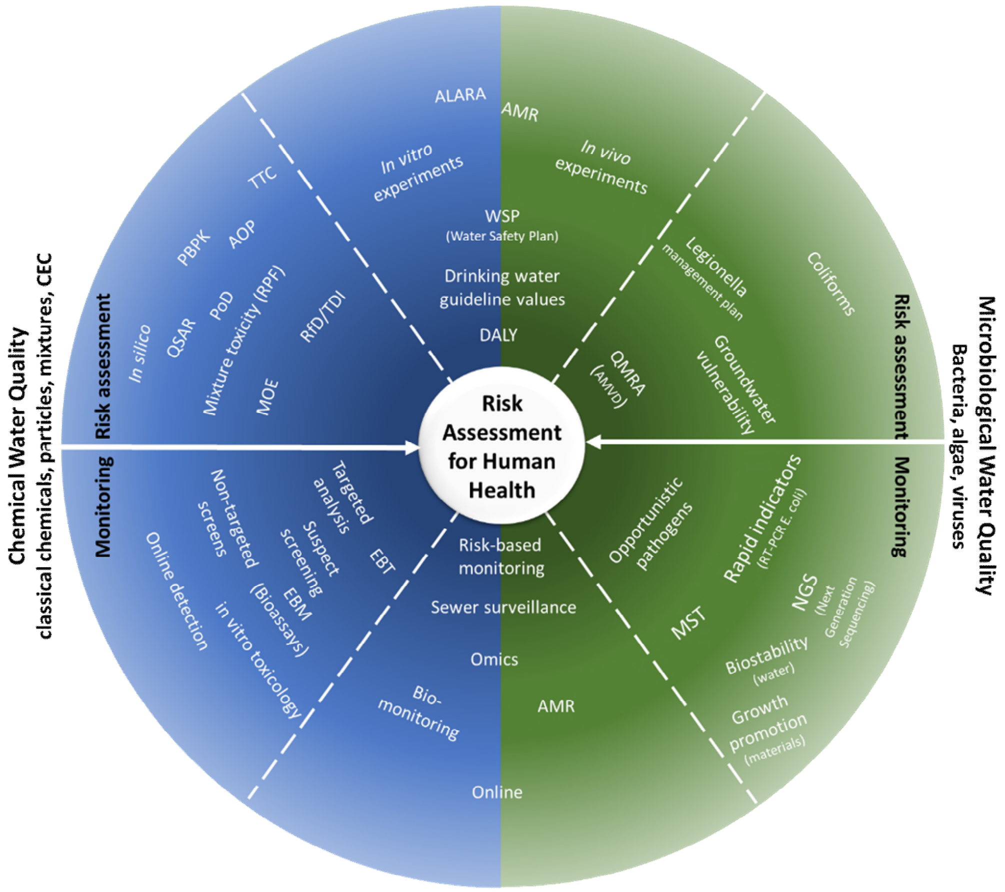


Figure 1 Overview of the chemical and microbiological water quality and risk terminology in drinking water (not exhaustive). The parameters are divided in monitoring parameters (bottom half) and risk assessment parameters (top half). Terms between the dashed lines refer to both chemical and microbiological aspects. Terms closer to the centre provide more quantitative information on human health risks.

1.2 Aim of the study

This study supports the development of an evidence-based approach to include health considerations into decision-making in the drinking water production practice. For this we interviewed water quality managers from all drinking water companies that participate in the joint research program (BTO) with respect to the water quality issues they are facing, which tools and methods they apply and how health risks are considered in their decision-making processes. These interviews with the BTO drinking water companies provide a starting point for sharing of experiences and approaches in risk management and decision making. We also interviewed KWR experts on the relevant topics of water safety. This report provides an overview of the available methods for the hazard monitoring and risk characterization regarding the microbial and chemical water quality. Each method is briefly described including references for further information. The current research challenges, practical applications and outlook for further research and development are discussed for each method. In addition, an overview is given of decision-making tools and how they link to various discussed methods, leading to recommendations for decision-making methods to include health risks.

Besides providing an overview, this report can support the drinking water sector in defining research to overcome current scientific or practical water quality challenges, while keeping the practical applicability of methods and suitability for decision support in mind.

1.3 Targeted readers

This report is primarily intended for water quality experts and decision makers at water companies. The fact sheets provide a quick overview of the current status and can be used as a starting point to learn more about a topic. Together with the examples of decision making processes, this provides a basis for developing management strategies for health and safety. The concise overview of all relevant topics can be used by researchers at water companies and KWR to support the discussion for prioritization in BTO and other research programs.

1.4 Organisation of the report

The report set out to provide concise information, relevant for this study, without repeating information elsewhere. The microbial and chemical methods are described in factsheets in Chapter 2 and 3 respectively. In each chapter a distinction is made between methods for monitoring and methods for risk assessment or characterisation. For the chemical methods, several distinct methods were combined into one factsheet since they are closely related. Combinations allowed for a more comprehensive description of approaches.

Each factsheet consists of the following elements:

- Description: A brief description of the issue that the method was developed for or needs to address and a description of how the method or methods work and how they can be applied to answer relevant water quality-related questions.

- Key publications: An overview of a limited number of key publications on the topic for further information, including the most relevant BTO reports

- Current challenges in research: Current challenges related to the discussed water quality and health issues are discussed, in particular if knowledge may be lacking to draw conclusions on the relevance for drinking water, or of the safety under current risk management. Discussed methods have pros and cons and it requires research and experience to overcome technical challenges and to correctly interpret results to support decisions. This section highlights these current challenges.

- Applicability from a practice view: The topics and methods are relevant for drinking water practice. However, there may be specific challenges in practice related to interpretation, setting water quality targets, costs, logistics, decision making etc. This section is largely based on the interviews with the water quality and risk managers of the drinking water companies.
    - Current application: How do drinking water companies currently address the issue or apply the methods in practice?
    - Decision making: How is the decision making process for this topic organised?
    - Applicability: How could the topic or method be applied in practice?
    - Challenges: What are the challenges for practical implication of topics or methods, e.g. interpretation, costs, logistics.
- Research outlook: given the above potentials and challenges, what research is suggested to develop the topic or method towards practical implementation, or to definitely appraise it as not relevant?

Chapter 4 provides an overview of decision making approaches that the drinking water companies currently apply when considering water quality and health challenges, as collected through the interviews. These are supplemented with a brief literature study on decision making tools and a discussion how they could apply to water quality and health issues. This section is particularly meant to inspire water companies and stimulate discussions and exchange of experiences.

In Chapter 5 we discuss the general issues that are relevant for all or several of the topics. It provides suggestions for developing future research and implementation efficiently, taking into account the limitations of resources, knowledge, legal frameworks and organisation.

1.5 Acknowledgements

We thank the representatives of the drinking water companies for their contributions to this research. Their commitment and open discussions during the interviews provided an overview of the water quality challenges they are facing, and how they are managing risks in practice. We also thank all experts for providing the current status of topics in the fact sheets.

2 Microbiological water quality

2.1 Monitoring

2.1.1 AMR Anti-Microbial Resistance

Description

The spread of antimicrobial resistance (AMR) provides a threat to public health. AMR spread leads to an increase of multidrug-resistant bacteria and increasing numbers of non-treatable cases in hospitals. Water is increasingly contaminated, due to the fact that it receives AMR from wastewater, industry, livestock and other animals. The water environment can form a breeding ground for development of AMR or exchange of AMR genes and a route for spreading AMR in the environment. The water sector has developed various tools to determine the AMR load (antibiotic components and resistance genes) in all types of waters. A novel potential application is high throughput PCR for microbial monitoring. With this method it is possible to process a large number of samples simultaneously and also to perform a large number of assays per sample. Regarding AMR genes, this method provides a rapid broad screening tool.

Key publications

1. Hornstra, L. (2017). *Antibioticaresistentiegenen in oppervlaktewater en in drinkwater zuiveringsprocessen*. BTO 2017.042, KWR, Nieuwegein.
2. Paulus, G.K., Hornstra, L.M., Medema, G. (2020). *International tempo-spatial study of antibiotic resistance genes across the Rhine River using newly developed multiplex qPCR assays*. Science of the Total Environment 706.
3. BTO project 'Verkennend onderzoek high throughput PCR' (project number 402045-187, unpublished).

Current challenges in research

- AMR has been demonstrated in drinking water sources, purification and the distribution network. It is considered unlikely, although yet not sufficiently clear whether drinking water is a relevant source for AMR distribution/spread compared to other sources such as food or healthcare facilities.
- There are worries for horizontal gene transfer (i.e. the non-sexual transfer of genetic materials between organisms), causing further spread of AMR genes in water relevant environments for which supporting data is needed.
- It is complex to assess the potential health impact of the presence of AMR in (drinking) water. Quantitative microbiological risk assessment (QMRA) is less suited for quantification of AMR related risks. AMR, however, poses a risk especially for vulnerable individuals. A risk assessment methodology is currently under development.
- Some water treatment processes are reported to increase the relative number of antibiotic resistance genes (ARGs).

Applicability from a practice view (including challenges)

- Current application: Drinking water companies are aware of the risks, and are, by the BTO program, involved in a project to determine levels of AMR genes in raw water sources, after treatment processes and in drinking water.
- Decision making: Current developments in knowledge may lead to adaptations in water purification technologies and/or policy making.
- Applicability: There are currently no water quality targets that can be used for decision making, because risk assessment is currently under development, however the WHO advice is to keep AMR levels as low as

reasonably achievable (ALARA). This reflects that a precautionary principle, in which precautionary measures are taken when insufficient research data is available, can be initially useful.
- Challenges: In current research the implementation costs of risk based AMR monitoring are under investigation.

Research outlook
- Current research focuses on investigating the sources (e.g. through sewage surveillance 2.1.12) and presence of AMR in raw water sources, after treatment processes, in the distribution system and in drinking water.
- Research is needed to quantify the relative risk of AMR via drinking water in relation to other routes.
- Depending on the need for implementing measures, the effectiveness of different potential measures needs to be determined. With this knowledge, the most promising measures can be selected.
- In consultation with the involved organizations the guide values need to be determined. This currently exists for a couple of antibiotics, but not yet for AMR genes.

2.1.2 Biostability (Biological Stability)

Description
Biological stability describes a drinking water system that leads to as little as possible changes in biology, so that health risks and/or consumers complaints, related to growth of (micro-)organisms, donot occur. Biological stability is, therefore, important for preventing issues including public health, discoloration, odour and taste in drinking water. Public health issues are mainly related to opportunistic pathogens (see 2.1.3 Growth Promotion and 2.1.8 Opportunistic Pathogens). There is a wide variety of methods to assess the biological stability of drinking water. Classic parameters include AOC-P17/NOx and biofilm formation rate (BFR). Novel methods include AOC-A3, biomass production potential (BPP) test for drinking water (BP7, BP7-BP0), continuous biofilm monitor (biomass accumulation rate (BAR) and FeAR (iron accumulation rate), Particulate and/or High Molecular Organic Carbon (PHMOC) and PFe (particulate-bound iron). All of these methods together provide information on the biological stability of drinking water.

Key publications

1. van der Kooij, D.; Martijn, B.; Schaap, P. G.; Hoogenboezem, W.; Veenendaal, H. R.; van der Wielen, P. W. (2015). *Improved biostability assessment of drinking water with a suite of test methods at a water supply treating eutrophic lake water*. Water Research 2015, 87, 347-55.
2. Hijnen, W., van der Wielen, P. (2017). *Biologische stabiliteit en nagroei: definities en positiebepaling van de bedrijfstak anno 2016*. BTO 2017.068, KWR, Nieuwegein.
3. van der Wielen, P. (2018). *Aandachtswaarden nieuwe methoden biologische stabiliteit*. BTO 2018.049, KWR, Nieuwegein.
4. Learbuch, K., van der Wielen, P. (2018). *Biologische stabiliteit ps Witharen nafiltraat, Archemberg reinwater en Hammerflier reinwater*. BTO 2018.073, KWR, Nieuwegein.

Current challenges in research
- A better understanding of the mechanisms of biofilm formation on the pipe wall and sediment.
- Identifying the role of different organic matter fractions in the biological stability of drinking water.
- The influence of the different treatment steps on the biological stability of drinking water.
- The development of additional treatment step(s) that effectively improve biological stability of drinking water.
- Identifying compounds in water, sediment and pipe materials that are associated with microbial growth in drinking water systems.

Applicability from a practice view (including challenges)

- Current application: There is a lot of attention towards reducing the organic matter load (including the biodegradable organic carbon) of drinking water. Controlling the biological stability of drinking water is widely incorporated.
- Decision making: Necessary on both strategic level (investments for better water quality) and operational level (e.g. frequency of flushing). Currently, one drinking water company uses pilot scale applications as guidance for decision making.
- Applicability: Better understanding the processes of biological stability can result in more effective and efficient control measures.
- Challenges: There are challenges regarding opportunistic pathogens, due to unclear regulations. Strategic choices between investments for prevention versus corrective strategies/actions need to be made.

Research outlook

- Climate change and anthropogenic changes in the subsurface lead to increased temperatures and likely enhanced growth of nuisance organisms. This is also highlighted as an issue by some drinking water companies.
- A better understanding of the processes and factors regarding biological stability of drinking water is still needed.
- A better understanding of processing and factors resulting in taste and odour complaints is still needed.
- Drinking water companies stress the need to maintain the biological stability of drinking water in the future, especially in order to distribute the water without a disinfectant residual.

2.1.3 Growth Promotion (Growth Promoting Potential Materials)

Description

There is a strong link between the biological stability and the materials that are used for drinking water. Materials that are for example used in the drinking water distribution network can release substances that promote growth of microorganisms in general and opportunistic pathogens like *L. pneumophila*. This therewith reduces the biological stability of the drinking water (also see the factsheet 'Biological Stability'). However, there can be a wide range in the growth promoting potential between materials and for some materials (e.g. polyethylene/PE) within the material batches. This provides challenges for suppliers, producers and drinking water companies. Furthermore, the use of various international standards further complicates the quantification of the biological stability of materials.

Key publications

1. van der Kooij, D., van Genderen, J., Heringa, M., Hogenboom, A., de Hoogh, C., Mons, M., Puijker, L., Slaats, N. Vreeburg, J., van Wezel, A. (2010). *Drinkwaterkwaliteit Q21 – Een horizon voor onderzoek en actie*. BTO 2010.042, KWR, Nieuwegein.
2. Learbuch, K. (2018). *Variatie in de biomassaproductiepotentie (BPP) van PE-materialen die door drinkwaterbedrijven worden gebruikt*. BTO 2018.007, KWR, Nieuwegein.
3. Learbuch, K. (2018). Invloed van leidingmateriaal op de uitwisseling van bacteriën tussen biofilm en water. BTO 2018.032, KWR, Nieuwegein.
4. van der Wielen, P. (2017). *Leidingmaterialen bevorderen microbiële groei*. TVVL Magazine.
5. Learbuch, K. L. G.; Lut, M. C.; Liu, G.; Smidt, H.; van der Wielen, P. W. J. J., *Legionella growth potential of drinking water produced by a reverse osmosis pilot plant*. Water Research 2019, 157, 55-63.

Current challenges in research

- There is a need for quality criteria to assess the biological stability of piping materials based on results of the BPP-test and that in addition relate to regrowth problems.
- There is a wide range in BPP-test results within certain materials. For example, different PE-materials show a large range in BPP-values, but the cause for these differences is not yet understood.

Applicability from a practice view (including challenges)

- Current application: The growth promoting potential is one of the criteria for the certification of materials that are used for drinking water.
- Decision making: It is challenging to find the optimum between growth promotion and handling properties, durability and costs.
- Applicability: Research outcomes should lead to testing protocols and criteria for applicability of materials.
- Challenges: Tuning and decision making between international suppliers, various international standards and control of the production chain.

Research outlook

- Depending on new insights from research on biological stability, better tests can be developed.
- Based on insights on growth promotion of different materials, more stable materials can be developed and applied for drinking water.
- Better quality criteria can support the collaboration between drinking water companies and material producers.

2.1.4 **Microbial Online Monitoring**

Description

There are several technologies available for inline, online and automated analysis of microbial water quality. These can be targeted on detecting faecal indicator bacteria (for e.g. *E. coli* and coliforms) or more generic patterns in changes of the microbiological water quality (e.g. total number of bacteria and ATP online monitoring). Several technologies that are investigated at KWR are the BactControl, the BugCount Online, the BactoSense, the continuous biofilm monitor (CBM) and the Biotrack. The use of these monitors can have several objectives, such as on site routine monitoring and the investigation of microbiological issues. Both the technology itself (sensitivity, specificity, robustness) and applications of the technologies are points of research. In addition, accurate frameworks have to be developed for the interpretation the outcomes of online monitoring methods.
Besides microbiological sensors there are several non-specific sensors (e.g. for online pH measurements) which may be used to also provide information about microbial issues. However, the interpretation of results obtained with these methods provides a challenge.

Key publications

1. Blokker, E.J.M., van Laarhoven, K. (2013). *De reductie van het infectierisico met behulp van online E. coli sensoren in het distributienet; op basis van het QMRA model*. BTO 2017.013, KWR, Nieuwegein.
2. Blokker, E.J.M., Smeets, P.W.M.H. (2017). *Toegevoegde waarde online E. coli sensor in het distributienet*. BTO 2017.014, KWR, Nieuwegein.
3. van Bel, N. (2017). *Prestatiekenmerken van de E. coli bepaling met het online monitoringssysteem BactControl.* BTO 2017.029, KWR, Nieuwegein.
4. Blokker, E.J.M., Mesman, G.A.M. (2017). *Responsstrategie na meting E. coli door sensoren*. BTO 2017.080, KWR, Nieuwegein.
5. Blokker, E.J.M., Smeets, P.W.M.H., Hessels, L. (2018). *Implementatie automatische snelle detectie van fecale verontreiniging in het distributienet*. BTO 2018.018, KWR, Nieuwegein.

Current challenges in research

- There are issues with low concentrations (sensitivity / detection limits) for faecal indicator organisms in drinking water. The online sensors do generally not achieve the same sensitivity as the conventional laboratory methods, which are the basis for current legislation.
- Threshold values ('alarmwaarden') need to be defined for each individual sensor. In addition, the performances need to be compared to the conventional laboratory methods.

- A standard framework for validation and data processing is necessary. This is complicated due to differences in measuring principles and units between the available methods.
- For evaluation of practical applications, the actual number of detections is often too low to validate the accuracy.

Applicability from a practice view (including challenges)

- Current application: The methods are used incidentally by water companies to evaluate the technology and to test it in the production plant or distribution system. At the moment only very few utilities standardly apply online microbiological sensors.
- Decision making: Rapid sensors for detection can be used to reduce the impact of a contamination event in combination with the right response (if a response plan is present).
- Applicability: May be used in distribution to supplement or replace conventional sampling. Monitoring of raw/surface water can detect unusual peak contamination that would require operational response.
- Challenges: Especially for faecal indicator sensors current sensitivity is insufficient for regulatory monitoring, costs are higher, practical placement on optimal locations can be difficult and the organizational change needed requires a supported company strategy.

Research outlook

- There is a need for further research on online methods, so that these methods can be applied in the future at drinking water companies. Several drinking water companies also indicate that the implementation could improve business operations. For this, the change in organization and working procedures needs to be taken into account.
- For many factors in drinking water there are yet no good sensors available or the current sensors are not yet fit to be used as a proxy for water quality.
- Collaboration with technology suppliers is needed to further improve the methods.

2.1.5 Microbial Source Tracking

Description

Microbial source tracking (MST) is widely applied in recreational surface waters. When occasional clues of faecal contamination are found in waterbodies, the source of contamination is not always clear. Thus, targeted actions to manage faecal contamination issues in surface water is hampered. The MST methods are based on specific detection of DNA markers related to group- or even species-specific faecal contaminants. These can be the detection of *Bacteroides* species, other gut bacteria or the direct detection of species-specific DNA. With this method the potential source of faecal contaminations can be identified. Several quantitative PCR (qPCR) methods have been developed over the years.MST can also be applied for drinking water. Further development of MST could provide better insights into contamination sources and thus make it possible to take targeted measures.

Key publications

1. Heijnen, L. (2015). *Eigenschappen van DNA-merkers voor fecale verontreiniging*. BTO 2015.023, KWR, Nieuwegein.
2. Heijnen, L., Learbuch, K. (2013). *Ontwikkeling en toepassing van kwantitatieve PCR methoden voor het identificeren van de bron van fecale besmettingen*. BTO 2013.014, KWR, Nieuwegein.
3. Kardinaal, E. (2017). *Bronopsporen fecale verontreinigingen in zwemwater 2017*. KWR 2017.077, KWR, Nieuwegein.

Current challenges in research

- There are challenges with the identification of selective faecal markers (often species belonging to the genus *Bacteroides*).
- The development of NGS methods with which entire microbial populations are mapped, provide novel tools for faecal source tracking (see also factsheet ‘NGS’).

- There are challenges regarding the specificity and the completeness (list of target animals) of the current method.
- There are challenges in the interpretation of possible correlations caused by the occurrence of natural populations of enterococci, which are generally not linked to faecal DNA markers.

Applicability from a practice view (including challenges)

- Current application: In specific cases water authorities and drinking water companies consider microbial source tracking (MST) as a method to gain insights into contaminations. MST can be used to obtain an image of microbial threats.
- Decision making: Insights can support decision making for response or mitigation.
- Applicability: It can be used as an investigative tool in specific cases.
- Challenges: Faecal contaminations in drinking water are momentary. When MST is applied the contamination may be absent. Identifying the animal source does not necessarily improve the risk assessment when the relative contribution from several sources is not clarified.

Research outlook

- Adding more animal sources to the suite of MST methods increases the impact of the method.
- Increased knowledge on the significance of various animal faecal contamination sources is needed for risk assessment and risk estimation.
- A better discrimination between various groups of enterococci indicative for natural populations that are not indicative for faecal pollution will aid in our understanding of when enterococci do signify a health risk.

2.1.6 NGS – Next Generation Sequencing

Description

Next generation sequencing (NGS) and related molecular technologies provide the opportunity to analyse or detect the genetic material in (drinking) water samples. The method can be used for diverse applications including monitoring of treatment processes, microbial water quality assessment and to detect changes due to contamination. NGS is currently used in research for a variety of purposes. Current methodological developments and developments in data processing and interpretation will likely increase the value and power of the existing methods.

Key publications

1. Heijnen, L. (2016). *NGS voor detectie van fecale besmettingen. Korte verkenning van de mogelijkheden*. BTO 2016.026, KWR, Nieuwegein.
2. Wullings, B., Hijnen, W. (2017). *Analyse van de bacteriepopulatie met NGS in water, sediment en biofilm van het leidingnet in Kralingen en Braakman in 2014 en 2015 (EVIDES Waterbedrijf).* BTO 2017.033, KWR, Nieuwegein.
3. Heijnen, L. & Timmers P., (juni 2019); Suleiman, A. & Heijnen, L., (mei 2020); Heijnen, L., (januari 2021). Nieuwsbrieven “*Kansen van nieuwe microbiologische methoden voor toepassing in de drinkwatersector*”. BTO: themagroep biologische veiligheid, KWR, Nieuwegein.

Current challenges in research

- Turning the vast amount of data into useful information through data processing and databases.
- The majority of genetic data of drinking water samples is not included in existing databases.
- The concentration of genetic material in drinking water can be too low for NGS analysis.
- Species-level identification with current technologies is hampered.

Applicability from a practice view (including challenges)

- Current application: NGS is currently applied in research on various subjects, but not for operational water quality monitoring.
- Decision making: In the future NGS may provide alternative methods for decisions related to various microbial topics
- Applicability: NGS could supplement or replace several current methods. However, drinking water companies do not see NGS as a rapid future replacement for indicator organisms.
- Current challenges: High costs and the time required for data handling, analysis and interpretation. Compared to current culturing methods most NGS strategies cannot provide species-level identification.

Research outlook

- There are major external developments in NGS technologies, databases and software tools for implementation. For example, there are currently methods under development that make species-level identification possible. These newly developed methods need to be evaluated and can be potentially applied. A next step is to validate novel NGS methods for implementation in monitoring water quality.
- Methodological developments (as described above) are needed to make NGS suitable for the detection of indicator organisms. The application potential is seen by several drinking water companies.

2.1.7 Omics

Description

Novel omics-techniques provide promising tools for monitoring microbial diversity, potential and activity. Metagenomics can be applied to monitor the microbial potential and additionally for microbial identification up to species level. Metatranscriptomics can be applied to monitor microbial activity and it can additionally provide information on microbial diversity. Metaproteomics enables the monitoring on protein level of active processes at a specific time point. With metabolomics an overview is collected of the metabolites produced by a microbial population. For all of these omics techniques rapid developments are taking place, which makes application in monitoring processes likely more achievable in the near future. Note that omics-techniques can also be used to evaluate the impact of exposure to chemicals on human physiology or ecology.

Key publications

1. Heijnen, L. (2018). *Toepassingsmogelijkheden van metatranscriptomics, microbial profiling en MinION sequencing*. BTO 2018.044, KWR, Nieuwegein
2. Segrave, A., Medema, G. (2019). *Verkennend Onderzoek 2018-2023*. BTO 2019.202(s), KWR, Nieuwegein.
3. Learbuch, K., Timmers, P. (2020). *Microbiologische compositie en potentiele metabole processen tijdens drinkwaterdistributie*. BTO 2020.044, KWR, Nieuwegein.
4. Nieuwsbrieven BTO themagroep biologische veiligheid: *Kansen van nieuwe microbiologische methoden voor toepassing in de drinkwatersector*. Juni 2019, juli 2020, januari 2021, KWR, Nieuwegein.

Current challenges in research

- For drinking water, there is a limited reference frame in which only few relevant studies are available compared to other research fields.
- Technologies are currently under development and rapidly develop and improve over time. Also, novel methods are rapidly replacing older methods. It is challenging to select the most appropriate and promising method(s).
- There is a huge application potential for a wide variety of methods, so choosing the most promising research directions is challenging.
- Data handling and data interpretation requires in-depth bioinformatics knowledge and an advanced informatics infrastructure. This requires investment and education.
- Omics analyses are dependent on reference databases that have limitations for the field of water research.

Applicability from a practice view (including challenges)

- Current application: Metagenomics methods are used in research and to gain understanding of systems in practice, but not for operation and routine monitoring. Metatranscriptomics and metaproteomics are at the early stage of research application.
- Decision making: Omics techniques are not yet used in decision making.
- Applicability: Omics techniques can be used to gain understanding and to optimize systems and system operation.
- Challenges: Omics techniques are relatively expensive regarding data generation and data processing and require in-depth knowledge for analysis and data interpretation. There are no legal requirements for the use of omics techniques.

Research outlook

- Omics tools can be used to understand and optimize biological processes, biological stability and biological water treatment.
- Omics techniques have the potential to be used to better manage risks of opportunistic pathogens.
- Omics can be used to optimize the microbial breakdown and turnover of chemical compounds.

2.1.8 Opportunistic Pathogens

Description

Opportunistic pathogens in drinking water pose a risk to human health due to growth in distribution systems. *Legionella pneumophila* is the best-known opportunistic pathogen for which risk management is already implemented. However, other opportunistic pathogens (e.g. *Pseudomonas aeruginosa*, *Aspergillus fumigatus*, *Stenotrophomonas maltophilia*) have been detected in drinking water, but their interpretation to public health risk is still unclear. There is an interest from water companies to approach opportunistic pathogens in a similar way as the existing quantitative risk framework for faecal pathogens. This requires additional research.

Key publications

1. van der Wielen, P.W.; van der Kooij, D. (2013). *Nontuberculous mycobacteria, fungi, and opportunistic pathogens in unchlorinated drinking water in the Netherlands*. Applied and Environmental Microbiology 79 (3), 825-34.
2. van der Wielen, P. (2014). *Rol van drinkwater, biofilm en temperatuur op groei van opportunistische pathogenen*. BTO 2014.217(s), KWR, Nieuwegein.
3. van der Wielen, P. (2014). *Effect van waterkwaliteit, seizoen, drinkwaterinstallatie en verblijftijd/afstand op opportunistische pathogenen in drinkwater*. BTO 2014.015, KWR, Nieuwegein.
4. Van Bel, N. (2017). *Literatuuronderzoek naar de invloed van temperatuur op de groei van opportunistische pathogenen in drinkwater*. BTO 2017.024, KWR, Nieuwegein.
5. van der Wielen, P., Donocik, A., Dignum, M., El Majjaoui, J., Wubbels, G., Hijnen, W., Lut, M., Prest, E., Roosma, A. (2020). *Onderzoeksvisie opportunistische ziekteverwekkers in drinkwater*. BTO 2020.067, KWR, Nieuwegein.

Current challenges in research

- Quantification of the risk from opportunistic pathogens and other microorganisms of emerging concern (MECs) for public health.
- Quantification of the risk compared to faecal (indicator) organisms.
- Understanding why opportunistic pathogens grow in drinking water distribution systems.
- Quantification of the effect of temperature increases, linked to climate change and changes in the subsurface, on opportunistic pathogens.

Applicability from a practice view (including challenges)

- Current application: There are legal and operational guidelines regarding cultivable *Legionella* spp. In drinking water. For other opportunistic pathogens this is still lacking. Several water companies mention their concerns about opportunistic pathogens and on how to manage the risks.

- Decision making: Current decision making is based on management of general biological stability, but not specifically targeted to risk management of opportunistic pathogens (other than for *Legionella*).
- Applicability: Quantitative risk estimation would provide a basis for risk-based decision making, similar as for the current framework for faecal pathogens.
- Challenges: The risk factors regarding exposure and health effects differ between opportunistic pathogens and faecal pathogens. Developing a common science-based risk assessment framework that is accepted by health authorities and water companies can be challenging.

Research outlook

The drinking water companies have recently written a common research vision for research challenges regarding opportunistic pathogens mentioned above (BTO 2020.067 Onderzoeksvisie opportunistische ziekteverwekkers in drinkwater). This document is the framework for future research.

2.1.9 RT-PCR *E. coli* and intestinal enterococci– rapid methods for operational microbial monitoring

Description

Water companies have to sample distributed water to monitor for the presence of faecal indicator bacteria (*E. coli* and intestinal enterococci). Current methods take several days from sampling to the interpretation of the results. This limits the speed of action during maintenance and calamities. The RT-PCR method provides a rapid method with which results can be obtained within four to six hours. Currently, the method is legally accepted for *E. coli*, but not for other (faecal indicator) organisms for which monitoring is required (intestinal enterococci and faecal coliforms). Current research includes method development for enterococci and coliforms. Water companies have an interest in extending this method to other parameters.

Key publications

1. Heijnen, L., Timmers, P., Elsinga, G. (2019). *Ontwikkeling van een RT-PCR voor snelle detectie van enterococcen*. BTO 2019.209(s), KWR, Nieuwegein.
2. Smeets, P., Hootsmans, M., Heijnen, L., Vissers, L., Atsma, A., Rosenthal, L. (2019). *Evaluatie RT-PCR E. coli 2018 ten behoeve van ILT*. BTO 2019.203(s) and 2019.206(s), KWR, Nieuwegein.

Current challenges in research

- Legal acceptance of novel RT-PCR methods is based on comparability with current growth-based methods. The current definition of microbial parameters is based on growth on selective media and biochemical properties and not on genetic similarities.
- Comparison of methods around and on the detection limit is challenging due to the probability of discrete low numbers of detected organisms.
- Different microbial parameters may need other methods than the RT-PCR technique.
- Thinking about new methods also means rethinking the validity and application of conventional methods. This is also underlined by several water companies in relation to coliforms.

Applicability from a practice view

- Current application: The RT-PCR method is currently applied for the detection of *E. coli* during calamities or other urgent situations.
- Decision making: Detection of faecal organisms forms a direct basis for operational decision making.
- Applicability: Methods developed for other microbial parameters would allow a more rapid response during calamities and other urgent situations. Several water companies see a benefit of rapid RT-PCR-based methods.
- Challenges: Legal acceptance for novel RT-PCR methods is needed. However, there currently is no legal acceptance in Flanders. Rapid actions based on rapid methods require adaptations of drinking water company and laboratory organization and procedures. Current laboratories are optimized for classical methods. Switching to novel methods requires investments, resulting in temporarily higher costs. Legal acceptance is needed.

Research outlook

- Research is ongoing for the development of alternatives for existing parameters. There is a potential for methods that overcome the shortcomings of traditional methods.
- Interdisciplinary research including microbiology, process engineering, water infrastructure and client behaviour and perception can develop approaches to fully benefit from rapid methods in practice by adapting organization and procedures would add to the potential benefits of the ongoing research.

2.1.10 Aquatic Coliforms

Description

For over a century, coliform bacteria have been used as indicators for the biological safety of drinking water. Initially they were introduced as an indicator for faecal contamination, mainly due to the research focus on faecal species at the beginning of the 20th century. Currently *Escherichia coli* (*E. coli*) is considered a strictly faecal coliform species for which drinking water needs to comply with legal requirements. Several environmental studies have shown that many coliform bacteria occur in other sources, including plant material, soils and insects. Still there are also legal requirements for coliform bacteria as operational indicators. Coliforms can be further classified into species by using MALDI-TOF or sequencing tools. This raises questions how to interpret coliform findings in practice, both as a group and specific species.

Key publications:

1. Mark, E. van der; Smit, H. ; Kors, L. ; Asperen, R. van ; Schaaf, B. ; Sack, E. ; Dusseldorp, J. ; Penders, E. ; Smeets, P. CCC – Coli Coccen Combinatie. Waternet, Amsterdam 2016
2. Harwood, V., Shanks, O., Koraijkic, A., Verbyla, M., Ahmed, W. and Iriate, M. (2017). General and host-associated bacterial indicators of faecal pollution. In: J.B. Rose and B. Jiménez-Cisneros, (eds) Water and Sanitation for the 21st Century: Health and Microbiological Aspects of Excreta and Wastewater Management (Global Water Pathogen Project). (A. Farnleitner, and A. Blanch (eds), Part 2: Indicators and Microbial Source Tracking Markers), Michigan State University, E. Lansing, MI, UNESCO. https://doi.org/10.14321/waterpathogens.6

Current challenges in research

- Coliforms are defined based on specific culture conditions, however various cultivation methods are applied with different results.
- There are differences between the interpretations of the results, mainly due to differences in personal interpretation of the data, since this is based on expert opinions.
- The scientific definition of coliforms is currently adapted based on new (genetic) insights. Common (culture based) analysis methods may not necessarily reflect these genetic divisions in species and strains, leading to unclarity when interpretating the results.
- Coliforms are further classified into species by using MALDI-TOF or sequencing tools, however this provides limited information about their faecal relevance and interpretation of potential risk for most species. They may be faecal indicators, pathogens themselves, indicate ingress of water or grow in the water system itself.
- There is limited scientific information to determine the origin of specific species and for their risk interpretation.
- Appropriate risk-based targets for coliform species are context specific and is challenged by lack of scientific information on the various types of risks they may indicate or cause.

Applicability from a practice view (including challenges)

- Current application: Coliforms are a legal operational parameter for which exceedance has to be reported and which may require corrective actions by water companies. The regulator allows to distinguish between aquatic (non-risk) coliforms and possibly faecal (risk-indicating) coliforms. Water companies often consider them as precursor for *E. coli* detection.

- Decision making: Decisions on corrective action or further investigation are made based on context (known activities, repetitive detection). An estimation of the risk and its cause based on coliform species supports decisions for corrective actions to take.
- Potential applicability: The current list of coliform species knowledge still includes many uncertainties that need to be resolved for more accurate decision making. A similar approach to further specify the risk related to detection of other indicator-organisms and chemical parameters has been suggested by water companies and could be beneficial.
- Challenges: Coliforms may not be the preferred parameter to identify risks and to support decision making. However, the use of coliforms is dictated by legal requirements. Changing both legal requirements and the development of better alternatives are both challenging. Rapid methods for faecal indicator bacteria have been developed, however coliforms are still cultured, leading to long delays from sample to result.

Research outlook

- Further development of current database on coliform types and their characteristics.
- Development of rapid method for coliform detection
- Development of alternative indicator organisms to overcome shortcomings of coliforms
- Development of similar approaches for other micro-organisms and chemical risks.
- National and international collaboration on both research and governance to reach novel approaches that allow risk-based decision making rather than basing this on historical remnants of water quality monitoring techniques.

2.1.11 Treatment Performance – natural viruses

Description

Verification of virus removal performance by full-scale treatment in practice is key for the microbial safety of drinking water. The past experience with the legislative QMRA (AMVD in Dutch) showed this is challenging for many drinking water production procedures. In particular, membrane filtration processes require accurate membrane integrity verification, in order to prevent viruses passing the membrane. Recent research has demonstrated that the use of natural viruses provides an effective and efficient method to determine virus removal by water treatment steps, and to verify membrane integrity. There is a potential to extend this principle to other types of water treatments.

Key publications

1. Hornstra, L., da Silva, T.R., Blankert, B., Heijnen, L., Beerendonk, E., Cornelissen, E.R., Medema, G. (2019*). Monitoring the integrity of reverse osmosis membranes using novel indigenous freshwater viruses and bacteriophages*. Environmental Science: Water Research & Technology 5:1535-1544.
2. Hornstra, L. (2020). *Natuurlijke virussen om de verwijdering van virussen door zuiveringsprocessen te bepalen*. KWR 2020.009, KWR, Nieuwegein.
3. Hornstra, L. (2020). *Inzetten van natuurlijke virussen om de verwijdering van virussen door bodempassage te bepalen*. KWR 2020.071, KWR, Nieuwegein.

Current challenges in research

- Determining characteristics of the currently used virus markers to compare them with characteristics of pathogenic viruses.
- The current method is based on the enumeration of viruses. Determining the effect of water treatment processes based on inactivation of viruses while the genomic material remains intact, is not possible. The adapted procedure that is capable of detecting damage to distinguish between active and inactive viruses needs further optimization.
- Some water matrices with typical characteristics contain insufficient quantities of the current virus markers. For these matrices, new virus markers need to be identified.

Applicability from a practice view (including challenges)

- Current application: The method is currently explored for verification of treatment performance in the framework of the legislative QMRA.
- Decision making: Operational detection of treatment failure to initiate needed actions and repairs. As a result of the QMRA more strategic decisions on the treatment design and operation can be taken.
- Applicability: If costs are reduced and knowledge and experience is increased this method can be used for operational membrane integrity monitoring and potentially for other treatments. This may be especially relevant for decentralized systems.
- Challenges: Acceptance of natural viruses as an alternative process indicator organism by the inspectorate is needed.

Research outlook

- The currently developed approach has a large potential for application in operation, verification and research.
- The developments in molecular methods can contribute to the extension of the principle to oxidizing water treatment processes. This can additionally provide a better link between natural viruses and pathogen removal.
- Additional efforts are needed for further knowledge development of natural virus characteristics in relation to relevant human viral pathogens.

2.1.12 Sewage Surveillance – Microbial

Description

By monitoring the occurrence of pathogens in the sewer, the circulation of infection in the population can be monitored. In the past decades, sewage surveillance has been sporadically applied to monitor infectious diseases such as polio. It's application drastically increased during the Covid-crisis, when the information was directly used to support decision making by the government. The knowledge and experience gained from this research has the potential to develop into an approach to investigate the impact of drinking water on public health. It can also provide insights into emerging pathogens in drinking water sources.

Key publications:

1. Medema, Gertjan, et al. "Presence of SARS-Coronavirus-2 RNA in sewage and correlation with reported COVID-19 prevalence in the early stage of the epidemic in the Netherlands." Environmental Science & Technology Letters 7.7 (2020): 511-516.
2. Lian Lundy, et al. Making Waves: Collaboration in the time of SARS-CoV-2 - rapid development of an international co-operation and wastewater surveillance database to support public health decision-making, Water Research, Volume 199, 2021.
3. Izquierdo-Lara, Ray, et al. "Monitoring SARS-CoV-2 circulation and diversity through community wastewater sequencing, the Netherlands and Belgium." Emerging infectious diseases 27.5 (2021): 1405.

Current challenges in research

- Current molecular methods allow rapid developments of methods to identify specific pathogens and their genetic variance.
- Detection in sewage water does not provide the source of infection in the population. Therefore, linking sewage surveillance to drinking water quality is challenging.
- Dilutions and dynamics lead to variations in the monitored concentrations not related to the level of infection of the population. Methods to correct for the actual amount of faecal input in the sewage have been developed.

Applicability from a practice view (including challenges)

- Current application: This method is now widely applied and gains a lot of attention for SARS-CoV-2-monitoring. Currently there is no direct link to drinking water.
- Decision making: An increase in waterborne pathogens could be used to investigate drinking water as a potential source.
- Applicability: Monitoring emerging pathogens in sewage provides information on their potential as a waterborne pathogen and thus their relevance for drinking water production. Methods may be developed to link infection levels to water quality.
- Challenges: Drinking water companies are not directly linked to sewage monitoring and there are many other influences from person to sewage and from sewage to drinking water. Links between sewage and drinking water are therefore complicated.

Research outlook

In relation to drinking water the potential of sewage monitoring for identification of emerging waterborne pathogens and AMR (2.1.1) that could impact drinking water safety could be of interest. In addition, the effect of drinking water quality on public health could be investigated.

2.2 Risk assessment

2.2.1 Risks of Antimicrobial Resistance (AMR) spread

Description

Water is an important reservoir of antimicrobial resistance (AMR). Water recreation, water in the urban environment, the use of water for food production and water reuse all provide exposure pathways with AMR. Globally, increased antibiotic use leads to increased resistance in man and livestock and associated increased AMR discharges to water bodies.
The assessment of the risks includes the quantification of the sources of AMR in water, AMR fate in the environment and AMR removal by water treatment. Also, by ranking exposure pathways the risks can be assessed. Surface waters are of increased concern due to the presence of environmental bacteria that can obtain resistance and therewith contribute to the further spread of AMR.

Key publications:

1. Hornstra, L. (2017). *Antibioticaresistentiegenen in oppervlaktewater en in drinkwater zuiveringsprocessen*. BTO 2017.042, KWR, Nieuwegein.
2. Medema, G. (2019). *Risk assessment of AMR in the environment*. European perspectives – presentation.
3. WHO, FAO, OIE (2020). *Technical brief on water, sanitation, hygiene and wastewater management to prevent infections and reduce the spread of antimicrobial resistance*. ISBN (WHO): 978-92-4-000641-6 (electronic version).
4. Timmers, P., Steenbeek, R., Hornstra, L., Been, F. (2020). *Wastewater based epidemiology (WBE) werkt als spiegel van humaan antibioticagebruik door monitoring antibioticumresistentiegenen*. KWR 2020.054, KWR, Nieuwegein.
5. Paulus, G.K. (2021). *Dissemination of antibiotic resistance via wastewater and surface water*. PhD Thesis.

Current challenges in research

- Knowledge on AMR in the water cycle is limited. Specifically, knowledge about potential gene transfer in the environment is lacking.
- The quantification of the risks of AMR compared to other risks is difficult, because the risk factors regarding exposure and health effects differ between AMR and faecal or opportunistic pathogens.
- Quantification of the risk of AMR through drinking water compared to other routes of exposure.
- The development of a general consensus about how to determine AMR-related risks.

Applicability from a practice view (including challenges)

- Current application: AMR is currently mainly considered in research and less in legislation or routine monitoring.
- Decision making: Findings could lead to strategic decisions e.g. on adapting water treatment, or prevention of contamination in sources for drinking water production.
- Applicability: AMR risk assessment could be implemented along the same lines as the QMRA (AMVD in Dutch) when a framework is present.
- Challenges: There are currently no health-based or legal target values and guidelines for AMR in drinking water. There are a few guidelines for antibiotics, but not for genes.

Research outlook

- Research is done to develop a framework for quantification of AMR so that it can be compared to other risks. Guidelines for water quality could be based on the AMR risk assessment approach/framework that is being developed in the field of food safety research.
- Genetic information of the transfer risk of specific gene regions (like mobile elements representing high transfer risks) may be included in the risk assessment.
- Information about the potential of water treatment methods to remove AMR-related pollution will facilitate the implementation of these methods on AMR pollution hot spots, (like hospitals), therewith contributing to a reduction of AMR in the environment.

2.2.2 Legionella Management Plans

Description

Legionella, particularly *L. pneumophila* are opportunistic pathogens that grow in water systems and can cause life-threatening pneumonia. Therefore, there is a legal obligation to develop Legionella management plans to control risks in plumbing systems of priority building. This is not the responsibility of drinking water companies, however, the risk is related to drinking water and therefore relevant. In addition, the drinking water sector has developed much of the knowledge that contributed to this approach. Attention should go out to potential changes in water quality or other aspects of supply that could impact the effectiveness of the Legionella management plan.

Key publications

1. van der Wielen, P. (2013). *Klimaatscenarios en risico's op nagroei van micro-organismen in drinkwater*. BTO 2013.240(s), KWR, Nieuwegein.
2. Oesterholt, F., van der Wielen, P. (2013). *Naar Legionella pneumophila veilig drinkwater*. KWR 2013.007, KWR, Nieuwegein.
3. Van den Berg, H.H.J.L., Friederichs, L., Versteegh, J.F.M., Smeets, P.W.M.H., de Roda Husman, A.M. (2019). *How current risk assessment and risk management methods for drinking water in The Netherlands cover the WHO water safety plan approach*. International Journal of Hygiene and Environmental Health 222(7); 1030-1037.
4. National Academies of Sciences, Engineering and Medicine. (2019). *Management of Legionella in Water Systems*. The National Academies Press: Washington, DC; p 304.

Current challenges in research

- The role of drinking water versus other routes for exposure of *Legionella*.
- The focus on *Legionella* spp. versus *L. pneumophila* in the management plans.
- The role of climate change (warming) and changes in the subsurface that lead to increased temperature of drinking water at the point of house connections. Temperature management is the most important factor to control *Legionella*.
- The links between risk factors such as water quality, biofilm ecology, materials and physical conditions in relation to *Legionella* occurrence and growth are not yet fully understood.
- A quantitative risk assessment has not been sufficiently developed to support decision making.

Applicability from a practice view (including challenges)

- Current application: The *Legionella* management plans are legally enforced for priority buildings (e.g. hospitals, nursery homes, hotels).
- Decision making: Compliance and corrective measures taken at the building level. Drinking water companies are not directly involved.
- Potential applicability: Insights in *Legionella* risk factors may lead to adaptations in the water supply systems to better prevent risks from water supply and plumbing systems. This can also result in changes in (the effectivity of) Legionella risk management plans.
- Challenges: Translating new insights to legislation is challenging due to different expert opinions, for instance whether legislation should focus on *L. pneumophila* or *Legionella* spp. Feasibility of controlling risk factors also depends on external factors and developments, such as climate change and anthropogenic activity in the underground leading to increased temperatures of drinking water. This is also a general concern of water companies.

Research outlook

- Developing quantitative risk assessment tools for *Legionella.*
- Insights into the *Legionella* risk factors.
- Development and assessment of novel concepts and innovative technologies for risk control of *Legionella.*
- Development of novel monitoring tools to gain insights into biological processes that lead to *Legionella* risk.
- Assessment of the impact of external factors and developments on *Legionella* risk.
- Assessment of the role of drinking water in developing Legionnaires' disease compared to other sources.

2.2.3 QMRA

Description

According to legislation, Dutch drinking water companies are required to perform a risk analysis on all drinking water production facilities based on microbiological parameters. For surface water systems the infection risk needs to be determined through 'Quantitative Microbial Risk Assessment' (QMRA), which is the core part of the Dutch 'Analyse Microbiologische Veiligheid Drinkwater' (AMVD). For this, the quality of the source and the effectiveness of the subsequent purification steps needs to be quantified. This is performed by analysing for pathogens in raw water, monitoring indicator organisms before and after treatment steps. Through Monte Carlo simulation the concentration of pathogens in the drinking water and the subsequent risk for consumers is assessed. For groundwater the safety of water extraction is assessed for vulnerable hydrogeological systems. The vulnerability is assessed for a theoretical contamination scenario.

Key publications

1. BTO 2014.008 Inventarisatie Analyse Microbiologische Veiligheid Drinkwater (AMVD)
2. PCD 8-2020 (november 2020): Protocol referentiedocument AMVD
3. Richtsnoer Analyse Microbiologische Veiligheid Drinkwater (AMVD) – Inspectie Leefomgeving en Transport (2020)

Current challenges in research

- Reliable quantification of pathogens in water sources due to limitations of analysis methods and variability of contamination in time.
- Reliable quantification of treatment efficacy due to limited presence of process indicator organisms at later stages of treatment.
- Limited scientific knowledge on treatment efficacy in literature and limitations in applicability of this knowledge for practical conditions.
- Challenges in mathematical risk modelling due to data limitations and differences between approaches that are currently applied.

Applicability from a practice view (including challenges)

- Current application: Drinking water companies are legally required to demonstrate compliance to health-based targets with QMRA. QMRA is also used to support decisions in treatment design and operation.
- Decision making: Choices on how to perform the QMRA can impact the outcome with regard to compliance. Therefore, QMRA is not an objective alternative for expert knowledge. A better link is desired between the operational and theoretical (QMRA) part and improved accessibility for process engineers. A QMRA-light version could support the uptake of QMRA in practical decision making processes.
- Potential applicability: The research can lead to more practical methods and approaches and reduced ambiguity in QMRA.
- Challenges: Currently QMRA has to be performed for a set of index pathogens and 'other pathogens that may be relevant'. However, there currently is no framework for when other pathogens have to be considered. Assessment of groundwater vulnerability, monitoring of groundwater quality and their interpretation towards quantitative risk is challenging due to uncertainties about the source of contamination, the local geohydrological conditions and the infrequent detection of indicators. The current QMRA framework focuses on the main water flow and does not address issues of recontamination. Water companies have concerns about risks of opportunistic pathogens for which a similar legally required QMRA is currently lacking.

Research outlook

- Improving the reliability and efficiency of water quality monitoring methods for pathogens in source waters.
- Identification of alternative process performance indicators and development of methods to determine them.
- Development of methods for QMRA of opportunistic pathogens for comparison to faecal pathogen risk.
- Expanding the knowledge-base on water quality treatment performance.
- Improving mathematical methods for QMRA.
- Improving accessibility of QMRA methods and outcomes for practical decision making.

2.2.4 Groundwater vulnerability – Microbiology

Description

Protected groundwater is considered a microbial safe drinking water source. In line with the *Richtsnoer AMVD*, both the vulnerability and the presence of hazards is assessed to evaluate the safety of the groundwater supply. Vulnerability is assessed through hydrogeological modelling of a defined leaking sewer scenario to determine the minimal protection area. Then the absence of hazards within that zone needs to be demonstrated. The scenario includes pathogen transport modelling. Vulnerable supplies are required to monitor bacterial and viral indicator organisms in the abstracted water. Determining the vulnerability of groundwater sources is complicated due to the lack of detailed knowledge of the local underground and hydrogeological situation. Monitoring is hindered by limitations in sample concentration and analysis techniques, especially in iron rich groundwater.

Key publications:

1. Van Heerde – KWR in het nieuws – hoe kwetsbaar is onze drinkwatervoorziening
2. BTO 2019.049 AMVD model duinfiltratie en freatische winningen, update 2019
3. PCD-8 2020 (november 2020) Bijlage webtool toelichting bodempassage
4. Richtsnoer Analyse Microbiologische Veiligheid Drinkwater (AMVD) – Inspectie Leefomgeving en Transport (2020)

Current challenges in research

- Hydraulic modelling and pathogen transport at relevant scale
- Sensitive monitoring of indicators for abstracted groundwater
- Methods to identify these or new indicators that are affordable, sensitive, reliable and specific.
- Approaches that take spatial and temporal variability of contaminations into account.

- Adequate quantitative risk assessment based on the above information.

Applicability from a practice view (including challenges)

- Current application: Hydraulic modelling of a contamination scenario has been implemented in the 2020 revision of the QMRA guidelines. Monitoring of somatic coliphages has not yet led to conclusive decisions on the microbial safety of the abstracted water.
- Decision making: Non-compliance will legally require adaptations for better protection or additional treatment of the water.
- Potential applicability: A more consistent and convincing conclusion about groundwater vulnerability will support decisions for investments.
- Challenges: Characterizing the spatial variation of conditions in the underground that are relevant for pathogen transport is challenging. The knowledge base for predicting pathogen transport is limited to a number of studies with specific conditions at specific locations. Current monitoring findings are generally inconsistent and therefore do not form a solid basis for investment decisions. The identification of contamination sources is challenging in practice.

Research outlook

- Better linking hydraulic models with pathogen transport in the underground. This may require improved hydraulic modelling for shorter timeframes and distances.
- Increasing the knowledge base for pathogen and indicator transport through the underground.
- Developing novel indicators for pathogen transport through the underground.
- Developing an approach for quantitative microbial risk assessment (QMRA) for vulnerable groundwater systems, taking spatial and temporal variability and uncertainty into account.

2.2.5 Water Safety Planning – Microbial and chemical

Description

Water Safety Planning (WSP) is a framework to manage water safety that includes qualitative to semi-quantitative risk assessment based on the probability and impact of risk events. In practice WSP is also called Risk Assessment / Risk Management (RA/RM). This assessment was originally used for microbiological risks but is also applicable for the chemical water quality. WSP is focused on practical aspects for risk management.
The WSP was developed and promoted by WHO and IWA and has been adopted in legal frameworks in many countries, including Belgium (Flanders). In the Netherlands the principles of WSP are embedded in various legislations, guidelines, regulations and operational procedures. Some utilities have developed or are developing WSPs for their water supply systems.

Key publications

1. Bartram, J. (2009). Water safety plan manual: step-by-step risk management for drinking-water suppliers. Geneva: World Health Organization.
2. Smeets, P., Medema G.J., and Dijk, J. (2009) The Dutch Secret: How to Provide Safe Drinking Water without Chlorine in the Netherlands. Drinking Water Engineering and Science 2, no. 1: 1-14.
3. BTO 2013.026 Water Safety Plans in Nederland, Ervaringen van Waterbedrijven. KWR.
4. Van den Berg, H., Friederichs, L., Versteegh, J., Smeets, P., de Roda Husman, A. (2019) How current risk assessment and risk management methods for drinking water in the Netherlands cover the WHO water safety plan approach. International Journal of Hygiene and Environmental Health 222:1030-1037.
5. Van den Berg, H. H. J. L., Friederichs, L., Versteegh, J. F. M., Smeets, P., & de Roda Husman, A. M. (2017). RIVM risicoanalyse en risicomanagement van drinkwaterproductie in Nederland. RIVM Rapport 2017-0036.

Current challenges in research

- Due to the qualitative nature of risk assessment in WSP it is challenging to determine when risks are sufficiently managed.
- Risk events are rare, therefore predicting their likelihood is highly uncertain.

- The nature of various risk events differs, which makes comparison between risks challenging.

Applicability from a practice view (including challenges)

- Current application: RA/RM is widely applied and embedded in the drinking water sector. Only a limited number of utilities explicitly applies the water safety plan framework. WSPs have led to screening groundwater quality before it reaches the abstraction to allow time for corrective measures. In Flanders the WSP is a legal requirement since 2013. Risk-based monitoring is an example of a practical result of the RA/RM approach. However, this is mostly applied to chemical monitoring (see 3.1).
- Decision making: The WSP framework provides a basis for decision making on prevention, response and mitigation of risk events in practice.
- Potential applicability: research could provide a more science-based and uniform basis and approach for risk assessment in the WSP.
- Challenges: RA/RM is deeply embedded in the current practice, but the way this is done varies between the water companies. This limits the development of a uniform science-based approach for determining the likelihood and impacts of risks.

Research outlook

- Improving the knowledge base on the likelihood and impact of events and the effect of prevention and mitigation measures.
- Exchange and cooperation between water companies on RA/RM can lead to a more uniform approach and evaluation of risks to support decision making.
- Currently a global water research coalition (GWRC) project on incorporation of effect based methods (EBM) in WSP is ongoing, with the aim to develop manuals and methods to support implementation and interpretation. This could feed directly into risk based monitoring strategies.

2.2.6 DALY Microbial and chemical

Description

The Disability Adjusted Life Years (DALY) approach quantifies risks by estimating the years of life lost or quality of life lost due to exposure to a hazard. The DALY method can be applied to compare the actual health impact from various hazards, including that of both microbial and chemical exposures. This allows for a direct comparison of different types of risks, thus supporting decisions across various risk sources (e.g. Havelaar et al. 2000). There is no legal DALY-based target in the Netherlands or Flanders. Nevertheless, DALY analysis can be used to support decision making on risk management by estimating the contribution of the drinking water exposure route to numbers of disease cases and the resulting total number of years of life lost in a population. This has been applied for arsenic (Ahmad et al. 2020).

Key publications:

1. [chemistry] C. de Jongh, Human health impact of chemical contaminants in drinking water. BTO 2011.044, KWR, Nieuwegein.
2. [chemistry] Jongh, C. de, Wezel, A.P. van – Toepassing DALY-concept voor chemische verontreinigingen in drinkwater beperkt – H2O 45(2012)8, p.48-49.
3. [chemistry] Ahmad, A., van der Wens, P., Baken, K., de Waal, L., Bhattacharya, P., & Stuyfzand, P. (2020). Arsenic reduction to <1 µg/L in Dutch drinking water. Environment International, 134,
4. [microbiology] Smeets, P., Schriks, M. and de Jongh, C. (2013) Health based investments for drinking water I, Overview of risks and methodology, BTO 2013.034, KWR, Nieuwegein.
5. [microbiology and chemistry] Havelaar, A.H., Hollander, A.E.M. de, Teunis, P.F.M., Evers, E.G., Kranen H.J. van, Versteegh, F.M., Koten J.E.M. van, en Slob, W. (2000): ‘Balancing the risks and benefits of drinking-water disinfection: disability-adjusted life years on the scale’, Environmental Health Perspectives 108: 315 – 21.

Current challenges in research

- Choices on how to perform the DALY analysis either for chemicals or microbial risks has impact on the conclusions. Clear methods on how to apply DALY analyses for water quality can improve the accessibility of DALY methods and outcomes for practical decision making.
- Calculation of the DALY requires knowledge on risk of illness, likelihood of disease outcomes and severity weighing which are also region-specific. This information is not available for all pathogens or chemicals in the region of the Netherlands.
- DALY can be used as the outcome of a QMRA. Therefore, challenges in QMRA are also relevant for DALY.
- Chemicals are in most cases considered not a direct hazard to develop a disease but a risk factor as often many uncertainties need to be accounted for when estimating risks of chemical exposures (such as the extrapolation of long term exposures to low concentrations of chemical hazards from shorter high exposures in toxicological studies).
- Exposures to mixtures of chemicals and other exposures may influence the health outcome. This is however not yet widely studied, and quantification of risks is difficult. This is however increasingly addressed in the Exposome and mixture toxicology research fields.
- Health outcome for a limited group of vulnerable persons (e.g. immunocompromised, pregnant women or babies) may be more severe than for the general population. Depending on hazard, specific risk groups can be considered, or incorporated in a population risk, which then also depends on self-protection and behaviour of these vulnerable groups or their care givers.

Applicability from a practice view (including challenges)

- Application: The DALY-concept is currently only used in a research setting, but not for practical decision making. WHO uses a target of 10^{-6} DALY in examples of risk-based approaches.
- Decision making: scarcely applied for decision making in the Netherlands.
- Potential applicability: the application of DALY can support decisions across various types of risks. Both microbial and chemical hazards can thus be compared, providing a framework for integrated evaluation in the complexities of drinking water safety.
- Challenges: there is no legal standard for DALY and application in practice can be challenging due to a lack of data.

Research outlook

- The DALY concept can be used to compare hazards with different health outcomes, for example enteric pathogens versus opportunistic pathogens or chemicals. As an example, the risk level associated with the current legionella risk management can be compared to the infection risk target in the AMVD.
- The DALY concept can be used to compare and balance risks of microbial and chemical exposures, like disinfection by-products (Meerkerk et al. 2022).
- Research can identify where the DALY concept provides an added value in comparing risks within the domain of water, but also outside this domain to evaluate relative impact of water related exposure to other foms of chemical or microbial exposure. This supports more integrated decision making at strategic levels.
- The development of a knowledge base and methodologies to facilitate DALY, especially focused on application in the Dutch and Flemish situation.

3 Chemical water quality

3.1 Monitoring

3.1.1 Environmental Fate including Sewage Surveillance - Chemical

Description

Chemicals are continuously released in the aquatic environmental from anthropogenic and natural sources and may reach drinking water sources. Therefore, it is critical to follow and predict the environmental fate of chemicals . Information on the source of an emission can be used for source protection.

Wastewater-based epidemiology (WBE) is an emerging field that uses wastewater as a source of information on population health and lifestyle and could be used as an early warning system ('sewage surveillance') for determining the sources and emission of chemicals into the water system (including CECs). The term WBE is most applicable when the effluent water quality data is used for the evaluation of health and disease state of populations, for example by measuring human health biomarkers. It has emerged as a cost-effective and time-efficient monitoring tool that uses measurements of CECs in wastewater to provide qualitative and quantitative information on the use of chemicals in a population (Gracia-Lor et al. 2018; Lai et al., 2018; Lorenzo and Pico, 2019). A major challenge however is the spatial and temporal variability in the occurrence of CECs in wastewater (Petrie et al., 2015). Nevertheless, variability may also be due to other factors such as, dilution by industrial inputs, degradation in upstream sewers, rainfall, analytical accuracy, and sampling uncertainty (Petrie et al., 2015; Huizer et al., 2021). Nevertheless, this is a complementary tool to monitor the occurrence of CECs in the water cycle. It is crucial to identify spatial and temporal variations in their discharge and/or use, emission sources/pathways and the relative contribution of different sources. This will help to take measures to contain CECs in their earlier stages of emergence. It is critical to measure water quality parameters in the untreated or the treated effluent, depending on the research question. Besides CECs originating from anthropogenic sources, also disinfection by-products such as bromate can be found in treated effluent.

Key publications

1. Baken, K.A. (2018). European regulatory framework in relation to chemicals of emerging concern. BTO 2018.079.
2. Emke, E., Vughs, D., Kolkman, A., de Voogt, P. (2018). Wastewater-based epidemiology generated forensic information: Amphetamine synthesis waste and its impact on a small sewage treatment plant. Forensic Science International. 286, Pages e1-e7.
3. Huizer, M., ter Laak, T.L., de Voogt, P., van Wezel, A.P. (2021). Wastewater-based epidemiology for illicit drugs: A critical review on global data. Water Research. 207, 117789.
4. Rousis et al. (2017). Wastewater-based epidemiology to assess pan-European pesticide exposure. Water Res. 121:270-279.
5. Meerkerk et al. (2022) Feitenoverzicht ten behoeve van bromaat normstelling. BTO 2022.009. KWR, Nieuwegein.

Current challenges in Environmental fate research for CECs

- Obtaining data about the occurrence, concentration, and persistence of CECs in the environment.
- Most CECs remain undetected, as many known and especially new or unknown substances are not part of current monitoring routines, although analytical methods exist to detect such substances. Therefore, target chemical analyses are complemented with screening tools (NTS and bioassays).
- Uncertainties related to sampling, methodology, analytical procedures, consumption and emissions.

- Differences in the physical/chemical properties of CECs such as organic, inorganic, more polar substances and particulate contaminants such as nano and microplastics complicate human and environmental exposure assessment.
- Methods for sampling and analysis of contaminants are not harmonized and tend to focus on specific emerging contaminant classes.
- Sewage treatment plants are implementing new treatment technologies that can lead to formation of CECs, which means that effluent needs to be examined in addition to the sewage to assess their release into environment.

Applicability and challenges of sewage surveillance for monitoring CECs

- Currently applied: Sewage surveillance can connect environmental surveillance (ES) of wastewater and the health information of the society (WBE). To date, it has been used extensively to determine exposure of a population to chemicals or to monitor the patterns and trends of contaminants for example illicit drug use. WBE is emerging as a convenient new method to complement more complex and lengthy surveillance approaches.
- Relation to decision making: The data obtained via the biomarkers of exposure and toxicity biomarkers can provide insights into the occurrence and sources of CECs, as well as the contribution of different sources. Sewage surveillance provides an overview of the threats of CECs to the general population, which can be used by authorities to take action where needed to reduce exposure. WBE needs to be further strengthened to help epidemiologists and health authorities properly assess the fingerprints of human activities in wastewater.
- Potential applicability: Sewage surveillance studies can provide information on potential exposure levels of contaminants, which could help target measures to identify the sources and reduce exposure. Elevated levels could highlight areas of possible excessive exposure and trigger an investigation into the causes. The research data can be used to establish a detailed protocol that provides a robust and harmonised approach to monitoring contaminants such as illicit drugs, pharmaceuticals or pesticides.
- Challenges: Currently there are significant hurdles to implement sewage surveillance and WBE in policy and practice. One of the major challenges is the high degree of uncertainty in many target indicators due to unknown disposal sources, variability in excretion rates, usage patterns, fluctuation in contributing population, environmental factors, or deterioration of the signal in the sewer network. There have been also many analytical challenges associated with sampling methods, wastewater analysis, selection of appropriate biomarkers (i.e., biomarkers that are specific to humans, stable in wastewater, and excreted in measurable amounts in wastewater), and normalisation of results to population size. The uncertainties associated with all of these factors are being characterised and best practice protocols are being developed to minimise them (Huizer et al., 2021).

Research outlook

- Wastewater can provide a wealth of data on the consumption of common drugs, the use of pesticides and other chemicals by the population. However, one of the uncertainties and challenge of this approach is the estimation of population and their activities in a given catchment. Because a change in population size or having to use data that are not very recent (census data may not always be recently updated) or the use of design capacity of wastewater treatment plants (which does not usually reflect real-time loading on the system) may radically increase or decrease the estimate of daily per capita consumption. Instead, dynamic estimates of the actual population in the catchment, for example, based on biomarkers of human metabolism in the wastewater can be used. Population normalisation using dynamic population estimates can be used for WBE to determine the size of the population that actually contributes to the sampled wastewater per capita and to improve the comparability of data from different locations.

- Environmental fate methods can be used to characterise trends and dynamics (temporal trends, seasonal patterns) in wastewater analysis and will help detect new threats, estimate exposure, improve risk assessment and predict effective mitigatory measures to improve surface water quality (including drinking water sources) and reduce risks to the environment and human health.

3.1.2 Non-Target Screening (NTS) in water quality monitoring

Description

The widespread production and use of synthetic chemicals leads to their presence in drinking water sources and, at trace levels, in drinking water itself (Brunner et al., 2019; Hinnenkamp et al., 2021). There are limits to the chemicals that require regular monitoring so contamination of drinking water by unknown substances may go unnoticed. Therefore, sensitive screening analytical methods are needed to continuously monitor the quality of raw and drinking water (Hinnenkamp et al., 2021). Targeted chemical analyses are thus complemented with advanced approaches such as non-target screening (NTS), which allows for the simultaneous detection and characterisation of a variety of chemicals including the chemicals of emerging concern (CECs) (Hollender et al., 2019; Pourchet, 2020). NTS, including suspect screening, can improve the identification of problematic substances at local, regional and EU-wide scales and support regulatory processes in environmental and chemical legislation, for example the Water Framework Directive, the Marine Strategy Framework Directive and the REACH Regulation (Hollender et al., 2019). Currently, hybrid high-resolution mass spectrometry (HRMS) systems are becoming more common in non-target analysis (Sobus et al, 2017; Hollender et al., 2019). HRMS instruments generate data on thousands of molecular features representing unknown compounds which makes data processing challenging. These are generally described in terms of their monoisotopic masses, retention times, and peak area or intensity. In some cases, these data are accompanied by fragmentation spectra (via MS/MS analysis) and predicted molecular formulae. Therefore, data processing techniques are needed to reduce the large number of features and prioritisation techniques that select the most hazardous and persistent chemicals (e.g. using QSARs) are important to find the features of interest for identification (Hinnenkamp et al., 2021). Another non-targeted approach is the use of effect-based monitoring using bioassays (see paragraph 3.2.2).

Key publications

1. Brunner et al. (2019). Integration of target analyses, non-target screening and effect-based monitoring to assess OMP related water quality changes in drinking water treatment. Science of The Total Environment. 705. 135779. 10.1016/j.scitotenv.2019.135779.
2. Béen et al. (2021). Risk-based prioritization of suspects detected in riverine water using complementary chromatographic techniques. Water Res. 2021 Oct 1;204:117612. doi: 10.1016/j.watres.2021.117612. Epub 2021 Aug 30. PMID: 34536689.
3. Albergamo, et al. (2020). Evaluation of reverse osmosis drinking water treatment of riverbank filtrate using bioanalytical tools and non-target screening. Environ.Sci.Water Res. 6,103-116.

Current challenges in research

- Identification of unknowns. A high number of compounds still remain unidentified with the current NTS approaches that rely on matching of the MS/MS spectra of a given unknown feature with those of chemical and spectral database entries such as MassBank, MoNA and mzCloud.
- Identification is particularly challenging for compounds with generic elemental formulas, for which many thousands of candidate substances are present, and compounds with poor fragmentation spectra or a lack thereof.

Applicability and challenges of NTS

- Currently applied: Developments in the field of NTS, particularly in identification tools, software and online databases, are currently proceeding at a rapid pace. Drinking water companies apply NTS as part of Risk-

Based Monitoring (RBM) for early detection of possible threats to water quality. Drinking water laboratories are working on implementation of NTS which can reduce costs and make application more feasible.

- Relation to Decision making: Implementation of NTS continues to pose challenges for water quality managers (drinking water companies) and regulators, particularly with respect to interpretation of data resulting from high-throughput data analysis, a lack of signalling values and identification following features prioritisation. There are issues related to standardisation and reproducibility, as there is currently no uniform approach for identifying compounds with NTS. Efforts have been made in this regard recently. For example, the Dutch Technical Appointment (NTA) has recently published a standardization for NTS analysis (NEN-NTA). In addition, there is an EU initiative to do the same within ISO and more harmonisation will occur in the near future.
- Potential applicability: The application of NTS is a promising strategy to advance our knowledge of the human chemical exposome (total of exposures via all possible routes). Moreover, it will enable better prediction of potential future health threats and related risk assessments and regulatory actions. Drinking water companies use NTS as a method to signal and identify compounds to include into their risk-based monitoring programs. Retrospective evaluation of digitally stored analytical data of representative environmental samples can promote the selection of chemicals to be included in the Water Framework Directive (WFD) Watch List, the chemicals that are to be re-evaluated in the Pesticides or REACH Regulation, and the mitigation measures to be taken (e.g. upstream measures or upgrading of wastewater treatment plants).
- Challenges: It is expected that the collection of large amounts of water quality data on large number of substances, for which the degree of certainty on their identity may vary, holds a particular challenge in communication to consumers. Different regulatory and quantitative issues related to monitoring, chemical management, and prioritization will require different strategies and analytical NTS approaches. Formal guidance is needed to include NTS data in formal risk assessments, taking uncertainty of the chemicals' identity into account.

Research outlook on NTS

- Adding onto the Dutch Technical Appointment (NTA) that is published as standardization for NTS analysis (NEN-NTA), additional steps are needed to support the practical implementation of NTS (normalization, uniformity of data presentation, interpretation, cost efficiency).
- Increased efforts are needed to integrate suspect and non-target screening approaches into the prioritization process for risk-based monitoring and to establish open-access databases and multivariate analysis of chemical patterns and toxicity profiles detected in the environment.
- Prioritization results based on concentrations observed in the environment can be further improved through modelling and verification (and *vice versa*).
- The integrated prioritization process will support the identification of commonly occurring chemicals and (e.g., source-related) mixtures to be considered.
- Efforts could focus on the compounds that are currently of greatest concern in terms of human and environmental impacts and identify measures to effectively reduce the net impact of chemicals.

3.2 Risk Assessment

3.2.1 Toxicological risk assessment of contaminants of emerging concern (CECs)

Description

To ensure a high level of protection for human health and the environment, chemicals are authorised for use by ECHA and other competent authorities. In Dutch laws and regulations, REACH criteria are used to determine which emissions of chemical substances can be expected to have harmful effects. Substances that meet these criteria (Substances of Very High Concern, SVHC) are of particular concern to humans and environment. Such substances are subject to strict rules, including the obligation to minimise emissions. In the Netherlands, companies (e.g. metal processing, waste management and chemical industries) are required to apply for an environmental permit from the municipal or provincial government. Efforts are ongoing to optimize the criteria and knowledge base for authorities on which basis permits are given.

Permitted and unpermitted point and diffuse pollution from human populations (e.g., pharmaceuticals), agriculture (e.g., pesticides), domestic use, and industry (e.g., perfluorinated compounds) have brought new challenges to assessment of exposures and risks in the drinking water and wastewater sectors in recent decades (Stein et al., 2018). Some of these contaminants were previously unknown or unrecognized and have only recently emerged as contaminants of concern (CECs) with unknown environmental and human health risks due to their inherent toxicity and persistence (Cantoni et al., 2021; Rasheed et al., 2019). CECs are continuously released into the environment from various sources, albeit at low concentrations and many go undetected (micropollutants) (Stein et al., 2018). For many CECs, concentrations and effects on the environment or drinking water sources are often not yet sufficiently known, and no regulations have been established for them within the EU Water Framework Directive or national legislation. An added concern is that chemicals, including those that are classified as CECs, can undergo various transformations, particularly in the aquatic environment, and the resulting transformation products (TPs) can be more persistent and/or toxic than their parent compounds (Yang et al., 2021). These TPs could also be considered as a category of CECs.

CECs are often not (completely) removed from wastewater, because the treatment technology for their removal in the wastewater system is generally not optimised for this task (Valbonesi et al, 2021). Even industries that have their own treatment processes often do not remove all of these chemicals (Hofman-Caris et al., 2015). However, there are ongoing efforts to improve current water treatment methods to remove CECs (Hofman-Caris, 2015).

Different methods and approaches can be included in the risk assessment of CECs, such as, exposure assessment, review of existing standards and risk threshold, review of existing risk assessment by competent authorities, toxicological studies (including *in vitro* mechanistic studies), epidemiological evidence and *in silico* modelling. This requires an integrated and systematic approach and close collaboration between different scientific fields, in particular toxicology, epidemiology, exposure science, risk assessment and statistics, in order to adequately integrate the data from all these disciplines which is currently not done comprehensively.

Risk is a function of exposure and toxicity, and importantly, risks can also be caused by non-SVHC chemicals. Based on knowledge on toxicity, (provisional) drinking water guideline values can be derived, describing at which lifetime exposure via drinking water does not lead to (unacceptable) risks. To derive such a drinking water value, sufficient toxicological data is needed to define an exposure level that did not lead to adverse effects in the studies ['point-of-departure' (PoD)], from which an exposure level which does not lead to (unacceptable) risks for humans can be derived [e.g. a 'reference dose' (RfD), 'tolerable daily intake' (TDI) or a similar descriptor]. The margin of exposure (MOE) explains the difference between the safe dose and actual exposure via all possible exposure routes. The effectivity of reducing concentrations of CECs in drinking water to limit exposure depends on the proportion of exposure via drinking water in comparison to other exposure routes (e.g. food, inhalation).

Many efforts are ongoing to develop high-throughput and high-content technologies for toxicological hazard and risk assessment. These systems have the potential for the rapid testing of CECs, and water samples (mixtures), for example in *in-vitro* and alternative animal models, such as human organotypic cultures and zebrafish. In addition, quantitative modelling using molecular (omics) approaches can identify exposure-related cellular and molecular changes that cannot be detected by standard toxicology tests.

The Dutch drinking water sector applies the risk-based monitoring approach based on the assessment of microbial, chemical and physical risks as described in the Directive 2015/1787/EC (EU, 2015) (implementation of the revised EU drinking water directive is currently ongoing). Research findings about potential risks and prevalence of CECs, can be used to define risk management measures in the drinking water practice. Ongoing research focuses on decreasing and considering uncertainties in toxicology, health effects and exposures. Moreover, knowledge on potential risks can be used to identify and prioritize CECs that are candidates for regulation (Stein et al., 2018) which leads to adaptations in water treatment practice and/or policy-making.

Key publications

1. Baken, K.A., Sjerps, R.M.A., Schriks, M., van Wezel, A.P (2018). Toxicological risk assessment and prioritization of drinking water relevant contaminants of emerging concern. *Environment International.* 118, 293-303.
2. BTO (2018). European regulatory framework in relation to chemicals of emerging concern. BTO 2018.079.
3. BTO (2018). Tools for human health risk assessment of emerging chemicals. BTO 2018.030.
4. Cantoni, B., Penserini, L., Vries, D., Dingemans, M.M.L., Boekkers, B.G.H., Turolla, A., Smeets, P.W.M.L., Antonelli, M (2021). Development of a quantitative chemical risk assessment (QCRA) procedure for contaminants of emerging concern in drinking water supply. *Water Research. 194, 116911*.
5. Van Wezel, A.P., Ter Laak, T.L., Fischer, A., Bauerlein, P.S., Munthe, J., Posthuma, L (2017). Mitigation options for chemicals of emerging concern in surface waters; operationalising solutions-focused risk assessment. *RSC Environ. Water Res.Technol.* 3,403-414.

Current challenges in research on risks of CECs

- Insufficient data on human health relevance (toxicological effects and relative exposure) of many CECs appearing in the water cycle as well as their transformation products.
- Insufficient knowledge concerning the mechanisms of toxicity for on several water-relevant endpoints (in particular reproductive and developmental toxicity and immunotoxicity).
- Differences in the physical/chemical properties of CECs such as organic, inorganic, more polar substances and particulate contaminants such as nano and microplastics complicate human and environmental exposure assessment.
- Lack of robust risk assessment methods for low-level mixtures of CECs.
- Lack of robust risk assessment method for shorter exposure periods (*less-than-lifetime* exposure).

Applicability and challenges in toxicological risk assessment of CECs

- Currently applied: Drinking water companies are aware of the risks associated with CECs and have been engaged through the BTO programs to address risk assessment of drinking water CECs. Drinking water companies also apply the precautionary principle through generic signal values and the Threshold for Toxicological Concern (TTC) for data-poor substances.
- Relation to Decision making: In-depth research on the health risks and concentrations of CECs in drinking water sources can support decision-making regarding adaptations in risk management measures such as source protection, water treatment technologies and/or water quality policies. If large investments are required to manage potential risks, the risk assessment is generally developed further (with increased data requirements) to result in a substantiated (less conservative) threshold value. Another route is through policy actions to reduce release of compounds in the environment (such as a reduction of permitted volumes emitted in the environment, or EU member states petitioning for a general prohibition of PFAS).
- Potential applicability: A more accurate and reliable risk assessment that includes all relevant CECs in a water system can support decisions on large investments or stricter regulations. It will directly benefit both drinking water companies in prioritizing monitoring process as well as regulators in decision making. It would allow the drinking water companies to base decisions on health targets as well as the precautionary principle to achieve efficient safe water supply.
- Challenges: Development of knowledge on toxicology of different CECs requires time and effort and may exceed the available resources in the water sector. This can be solved by close collaborations with academic research, and the definition of clear knowledge needs by the water sector. A specific challenge relates to the fact that water treatment processes may not only lead to the formation of desinfection-byproducts (Vughs et al. 2018), but may also result in the formation of unknown transformation products

(transformed CECs), which needs more in-depth studies on the behaviour of substances and characteristics of TPs in different treatments and treatment conditions.

Research outlook on CECs

- The development of (high-throughput and high-content) testing methods can support in-depth research on yet unknown toxicity mechanisms of CECs. The role of the water sector is to define which toxicological endpoints for water relevant chemicals this research should focus on (e.g. the zebrafish (*Danio rerio*) neurotoxicity bioassay to study the effects of chemical mixtures on neurodevelopment).
- Non-Target Screening (NTS) and Effect Based Monitoring (EBM) using bioassays can be used to detect a wide range of CECs in different environmental matrices and human tissues, including markers of human chemical exposure in biomonitoring (measuring chemicals in human tissues), and can support epidemiology (health) studies, risk assessment and policy with early warnings.
- Research into the link between effects in cell-based systems for *in vitro* toxicology and adverse human health effects will aid in risk interpretation (as studied in the project Virtual Human Platform). *In silico* methods, such as use of QSAR Toolbox can be used for predicting the toxicity of chemicals for which no or limited toxicity data is available by read across with structurally similar substances. In addition, *in silico* methods can be used for prioritization of follow-up research based on identification of structural alerts and corresponding potential health effects.
- Use Environmental ate and Sewage Surveillance to evaluate exposures and risks of CECs in water, with information on local differences in time and spatial concentrations (see 3.1.1).
- An integrated approach of *in vivo*, *in vitro* and *in silico* methods, together with meta-analysis of high quality toxicological and human epidemiological data can help in robust risk assessment of CECs and chemical mixtures (see 3.2.2).
- The use of molecular (omics-based) methods to detect early biological molecular effects that may lead to functional adverse effects that are measured in traditional test systems for human and environmental toxicology. These methods can also be used for biodiversity studies.

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3.2.2 Toxicology and risk assessment of chemical mixtures

Description

Mixture toxicology is of increasing interest for both scientists and regulators, as it is increasingly recognized that a large number of chemical substances are released into environment in varying concentrations, resulting in complex low-level mixtures in environmental matrices including the aquatic environment. Currently, general chemical policies and risk management worldwide focus primarily on the safety of individual chemicals (Drakvik et al., 2020). People are protected by ensuring that, as much as possible, chemical contaminants do not exceed levels that are associated with known adverse effects. However, there is growing understanding that chemicals may produce joint toxicity potentially resulting in harmful effects to human health and environment even when present at low concentration, due to the potential additivity of the individual components. Moreover, some interactions can modify toxic effects if concentrations are high enough for this interaction to occur (Hernández et al., 2013). Generally, the conservatism in current approaches for the derivation of safe levels is expected to be sufficient to allow for potential mixture effects at the low concentrations generally occurring in the water system. Nevertheless, the Water Framework Directive (WFD) has been criticized for not being sufficient to protect against or manage the effects of accidental mixtures of water pollutants (Kortenkamp et al., 2019). The Dutch National Institute for Public Health and the Environment has recently advised to address risks of (unintentional) mixtures in the evaluation of chemical emission permits (Bodar et al. 2022).

Requirements for assessing risks from chemical mixtures (from simple to complex and intentional to unknown environmental mixtures) have recently been included in several regulatory frameworks in the EU, the US and some other countries (Rotter et al., 2018). Several organisations, including the Organisation for Economic Cooperation and Development (OECD), the European Food Safety Authority (EFSA), and the World Health Organisation (WHO), have recently published guidance and considerations for risk assessment of mixtures, providing an updated description of approaches, methods, and specific challenges and research needs (WHO, 2017; OECD, 2018; EFSA, 2019). Specific challenges for risk assessment and management of chemical mixtures have recently been summarised in a publication by the EU Commission's Joint Research Centre (JRC) (Bopp et al., 2019). Proposals for new methodologies are also made in this report.

Simultaneous exposure to different chemicals in drinking water at low levels is common, but the low-level mixture of chemicals can vary in composition and concentrations over time which is a particular challenge for risk assessment (WHO, 2017). In a water quality context, the effect of low-level mixtures in water can be studied in effect-based monitoring using small organisms and cell-based systems. It is most often not feasible to decide on (the absence of) a risk based on this type of data. Nevertheless, effect-based trigger (EBT) values define those effect sizes at which a risk for human health or the environment cannot be excluded. For risk interpretation based on the responses in cell-based systems, a defined bioassay battery is required that includes the test systems that can jointly detect the specific mechanism that needs to be studied to predict a particular health impact. Moreover, more toxicological information on individual substances and mixtures is needed to develop more informative effect-based trigger values.

There has been extensive research on chemical mixtures in past years but there is still a lack of experimental data on the effects of different low-level mixtures that can occur in drinking water. Whole mixture effect data are only available for a limited number of mixtures, and information on single chemical hazard, dose-response, and mode of action (MoA) needed for component-based approaches (individual components of the mixture) is often lacking for many chemical classes. To prevent under- or overestimation of the risks of mixtures, additional research is needed on the toxicity of chemical mixtures for a better understanding of their potential consequences. Tiered assessments, in which data requirements increase stepwise, and that may also apply effect-based methods (EBM) in combination with chemical analysis methods such as non-target screening, have been proposed to address this need. These methods can be adapted on a case-by-case basis for both whole mixture and component-based assessments, and a tiered approach for low-level mixtures in drinking water could be developed.

Key publications

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Current challenges in research on chemical mixtures

- A lack of toxicology data. Only for a rather limited number of individual chemicals (individual components in low-level mixtures) there is sufficient information on their mode of action.
- Identifying relevant chemical mixtures in (drinking) water for water quality, hazard and risk assessment, monitoring and control.
- Developing more comprehensive methods for assessing the hazards and risks of chemical mixtures.
- Uncertainty analyses in hazard and risk-assessment of mixture toxicity.

Applicability and challenges in toxicological risk assessment of chemical mixtures

- Currently applied: There are sum parameters in water quality legislation to monitor total concentrations of mixtures specific types of chemicals (cyanides, PAHs, PCBs, pesticides, trihalomethanes, PFAS). Water companies also use bioassays to include mixture toxicity in risk screening and in detecting trends. There are currently no regulations on chemical mixtures for decision making.

- Relation to Decision making: Health risk reference values for mixtures and effect-based trigger values (EBT) for bioassay responses are needed to make decisions on priorities in source protection measures or adaptations in water treatment technologies. Inclusion of such values in water quality policies and standards would support the use of EBM in RBM.

- Potential applicability: Target values for individual chemicals under the Water Framework Directive are not considered a feasible approach because of the vast number of chemicals and the reality of mixture toxicity. Health risk reference values for mixtures and EBT for bioassay responses that take into account potency differences (relative potency factors; RPF) between to different individual constituents in a mixture can provide a solution that addresses both issues.

- Challenges: For the risk assessment of mixtures, it is necessary to establish minimum data and quality requirements that can be accepted as a basis for risk assessment and (decisions on) risk management. As with risk assessments for individual chemicals under the Water Framework Directive, risk assessment for mixtures should allow for the protection and assessment of effects on multiple receptors, including all relevant biological quality elements (not limited to a few taxa) and humans. This requires the integration of human and ecotoxicological risk assessment into a coherent framework.

Research outlook on chemical mixtures

- Prioritization of relevant mixtures and their individual constituents for further research and the extrapolation to low doses for the assessment of possible health risks from exposure to chemical mixtures such as in drinking water.
- Defining endpoint-specific EBM test batteries of cell-based systems that are developed in the context of innovative risk assessment and have the potential to address health risks of exposures to mixtures in water (which is not yet feasible with current EBM approaches).
- The development of relative potency factors (RPFs) for water relevant chemicals that can be used to define health risk reference values and water quality guidelines for mixtures. RPFs are also needed to relate the corrected sum of measured concentrations of individual mixtures constituents to such a mixtures water quality guideline.
- Adverse Outcome Pathways (AOP) can be particularly useful for risk assessment of mixtures to support the grouping of substances into assessment groups related to modes of action and to identify joint upstream key events. The AOP model can be used for identifying the sequence of events causing a particular adverse health effect (outcome).

4 Health considerations in decision-making

4.1 Risk management and decision making

Risk management and decision making are interconnected processes. Risk management involves identification of a problem (like a health hazard) and actions to reduce the risk of the problem to an acceptable level. Risk management involves several steps but generically it begins with identification and diagnosis of the scope and purpose of risk management. This includes hazards, estimation of risk, relative contributions of exposure routes (including and in comparison to drinking water), an inventory of possible risk reduction measures and an analysis of their efficacy (Miller et al., 2009).

Decision making can be broadly classified into three levels; strategic, tactical and operational (Figure 2). The strategic level concerns processes for defining an organizations strategy, direction and allocating resources to pursue the strategy. Strategic decisions are made for the long term (>1 year). Tactical decision-making concerns planning in the short term (<1 year), with an emphasis on current operations. Finally, operational processes define what portion of the strategic plan will be put into operation (implementation), defines milestones for success in a specific period and concerns day to day operations. Strategic planning is the most complex and health risks may therefore be overlooked in terms of decision making, however it can also be the most impactful in the long run (Beuken et al., 2020).

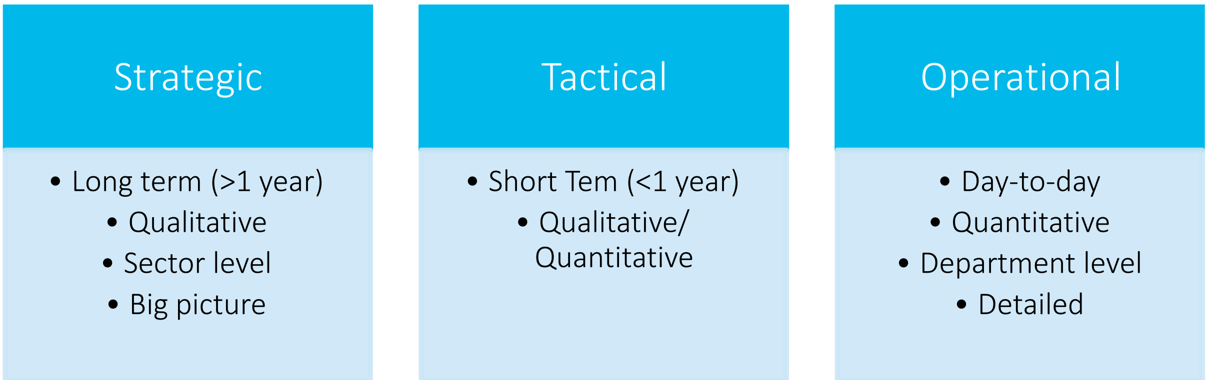

Figure 2 Levels of decision making in organizations and associated characteristics for each level

To include health risk considerations in decision making, two aspects are generally required. On the one hand, processes or frameworks in order to come to a decision at each of the strategic, tactical and operational level need to be established. On the other hand, suitable and reliable data on which to base decisions is needed. Methods and tools to collect suitable and reliable chemical and microbial data to include health considerations in decision-making are covered in sections 2 and 3. Decision making at the strategic, tactical and operation level however require different handling. Strategic level planning requires consideration of many different stakeholders (sometimes within an organization) and integration of different needs and to achieve a good balance. As a result, more qualitative methods are used more often at the strategic level. Decision making at the tactical and operational level tends to be more based on quantitative methods. It can be a challenge to connect the detailed water quality knowledge available at the tactical and operational level to the long-term goals and strategies of the strategic level (Beuken et al., 2020). Therefore, effective communication within and between organizations is key.

Decision making tools which incorporate detailed or quantitative health-related data, for example on the chemical and microbial water quality, can help to link strategic, tactical and operational decision making. For example, decision making tools can quantify the uncertainty of assumptions or lack of data while also helping to develop an understanding of the possible consequences of different decisions and future scenarios (Carpitella et al., 2020). Tools also help to shift reliance for decision making away from individual 'expert' knowledge and qualitative methods to more evidence-based approaches.

4.2 Tools for Tactical and Strategic Planning

Risk based decision making within asset management (AM) has been researched at KWR and parallels can be drawn between decision making for asset management and health-based decision making (Smeets et al. 2013). Within AM two common methods for integrating knowledge and decision making between the tactical and strategic level are Key Performance Indicators (KPIs) and the risk matrix.

KPIs

KPIs are used to monitor the effect of decision-making in quantitative terms, preferably in €/year for example for water quality, customer satisfaction, sustainability, cost (Beuken et al., 2020). The drinking water companies use the KPI *Substandard Delivery Minutes* (in Dutch *Ondermaatse LeveringsMinuten*, OLM) as a way to quantify the length of time a customer received drinking water which does not meet the required quality standard (Beuken et al., 2020). Other KPIs in use include pipe failures, complaints, inspection frequency (Beuken et al., 2020). Possible KPI's for water quality include the percent of sample exceeding a standard value for e.g. *E. coli*, turbidity, nutrients, micropollutants etc., see Vieira et al., 2008 for more water quality related KPI's. A DALY KPI could be developed to include all health-related water quality aspects, microbial and chemical, in a single value. The DALY can be interpreted as a threshold, or as a trend for improving or deteriorating quality. Quantifying the health effect of pollutants can be challenging, however the focus could be on the most relevant ones (Smeets et al. 2013).

Risk Matrix

A common way to assess risk is to identify hazardous events which may cause harm and categorize the likelihood of the event and the consequence based on discrete scales (Lindhe, 2010). This categorization of risks results in a risk matrix, with the probability and consequence of hazardous events on each axis (Figure 3). Risks are then grouped according to the cumulative risk score as acceptable, unacceptable and uncertain. These groups are further prioritized with specific actions associated with each risk group. For example, risks which are catastrophic but very unlikely can be handled with insurance (Transfer); catastrophic and highly likely risks should have preventative and emergency measures in place (Reduce likelihood); while low consequence, low impact risks may be accepted (Accept risk) (Beuken et al., 2020; Wijnia, 2012). Guidelines for how to define risks for water quality, that ultimately could lead to health risks, are available, for example Fewtrell et al., 2001; Bartram et al., 2009.

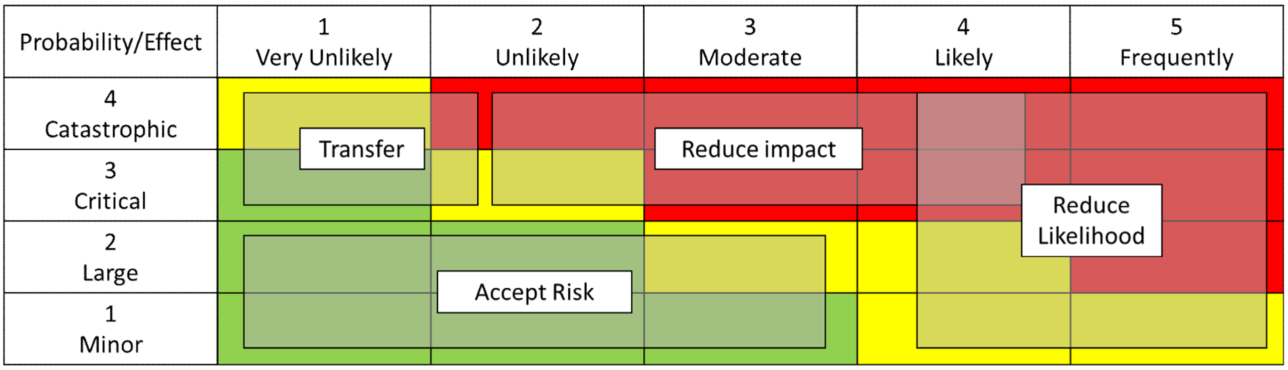

Figure 3 The risk matrix categorizes hazards according to the probability (horizontal axis) and effect (vertical axis). The colouring indicates the risk grouping: green: acceptable, yellow: medium, red: unacceptable. The risk matrix is overlaid with the groupings

Risk matrices are simple and strong communication tools however there are several limitations. For example, hazards are limited to one event and the matrix cannot incorporate combinations of risks and/or multiple or compounding effects. For example, health effects due to mixtures of chemicals. Risk matrices also tend to underestimate small risks with long-lasting impacts and large (catastrophic) risks with low probability. For example, chronic exposure to low levels of micropollutants or low probability events such as natural disasters, bioterrorism or global pandemics.

There is also a preference for quantitative categories over less easily quantifiable/qualitative categories, which may be considered a benefit or a drawback. The benefit of quantitative categories is the ability to make evidence-based decision making, while a drawback is the lack of inclusion of categories where data is lacking but a risk still exists. For example, consider a pipe burst. The cost of a pipe burst is relatively easily quantifiable whereas the loss of public trust and/or changes to public perception of the drinking water companies is much less quantifiable (Brouwer et al. 2019). Both may be of equal importance to the client. Finally, risk matrices do not account for the cost and feasibility of mitigating actions, while in practice the acceptable level of risk for water quality is weighed against the cost and ability to implement any preventive measures. Large investments in risk management measures may be more supported when a health-based standard, when exceeded, is univocal and generally accepted, while this is less the case when the exceeded health-based limits are tentative or indicative. For example, costs of increased inspections, frequency of measurements, target vs. non-target screening etc.

4.3 Tools for Operational Decision Making

Several tools have been developed for decision making at different steps along the drinking water chain. These include legally required tools, general decision-making tools and ‘Nexus’, serious games and governance capacity tools. Legally required tools are defined by the Drinking Water Act (DWA) (I & W, 2009) which all drinking water companies in the Netherlands must comply with. Generic decision making tools can be applied to any decision making topic, including water quality and health (Alvarado et al., 2016). Finally, other tools available include tools which assess water issues within the wider context of climate, land, energy and food (‘Nexus’); tools which use a ‘learn-by-doing’ approach (serious games) (Savic et al., 2016); and finally tools which assess how well organizations and governments are able to collaborate and make decisions (Koop et al., 2015).

Legally required tools

The DWA contains a number of technical provisions which link between the strategic and tactical level. The DWA incorporates the requirements for drinking water companies to comply for water quality requirements, security of supply and continuity and efficiency. Within the DWA, six legally required risk assessment and risk management approaches are defined that cover water quality and health aspects (Van den Berg et al., 2019);

1. Quantitative Microbial Risk Analysis (QMRA): Dutch drinking water companies must conduct a QMRA at least every four years to demonstrate that the drinking water they produce is safe. QMRA consists of a system description; identification of possible microbial hazards and hazardous events; and monitoring requirement from source to treatment (Van den Berg et al., 2019).

2. Drinking water protection files: Drinking water protection files consist of information about the quality of the source water, possible sources of pollution and risks for contamination, and the vulnerability of the source. These files are created with different parties and also serve as a communication and collaboration tool for different stakeholders (Van den Berg et al., 2019).

3. Disturbance Risk Analysis (DRA) as part of the Drinking Water Supply Plans: Assess long-term threats and hazards which could affect the quality and/or quantity of drinking water supply, and possible control measures to minimize risks (I & W, 2011).

4. Legionella Prevention Control in drinking water installations: Legionella prevention is mandatory in the Netherlands for drinking water supplies in buildings with high-risk populations (e.g. hospitals, retirement homes, hotels, swimming pools) (I & W, 2011). Building owners are responsible for assessing the risks and the drinking water companies inspect the buildings where they supply water (Van den Berg et al., 2019).

5. Code of hygienic practice for drinking water supply: Code made by the drinking water companies as a system to ensure the quality and risk management to ensure the microbiological safety of drinking water during storage and distribution (I & W, 2011; Meerkerk, 2015).

6. Risk-based monitoring program drinking water quality: Drinking water companies are required to set up an annual monitoring program from source to tap, as prescribed by (I & W, 2011). The monitoring program is based on the assessment of the microbial, chemical and physical risks as described in the Directive 020/2184 (EU, 2020). Legal parameters are complemented with company-specific monitoring parameters. This risk-based approaches gives the opportunity to 'measure what matters' and omit parameters that can be considered obsolete (in discussion with and when confirmed by the inspectorate).

A review of the Dutch drinking water risk assessment and risk management policies found that the legally required approaches cover all the steps of the WHO Water Safety Planning (WSP) (Van den Berg et al., 2019). WSP is a framework from the WHO which sets out requirements for risk assessment and risk management in all steps of the water supply, from source to consumer (Bartram et al., 2009).

Other tools exist for decision making at different levels of drinking water treatment and distribution. These include, for example, Reliability Centered maintenance (RCM), Failure Mode Effects and Criticality Analysis (FMECA), HAZard and OPerability (HAZOP) and the Bow-Tie methods, for more information see (Agudelo-Vera et al., 2016; Wols et al., 2017).

Specific tools which explicitly address chemical water quality, and are therefore relevant for health, include the TAPES emerging substances and the Freshwater decision support systems, previously known as ABATES (Fischer et al., 2010, 2017). Tapes is a decision support system for the management of contaminants of emerging concern within the urban water cycle, from wastewater, surface water and groundwater to drinking water. TAPES contains background information (chemical, physical characteristics, toxicity) on contaminants of emerging concern, sources in the water cycle and a database of possible mitigation methods (Fischer et al., 2010, 2017). In 2017 KWR developed the Aquapriori tool that predicts the removal of micropollutants by various treatment processes (De Vries et al. 2017). In 2020, KWR developed the Water Wise tool, a concept that estimates the microbial and chemical quality of water, compares this quality against relevant national and international guidelines, and offers users a basic risk assessment process to support decisions concerning their water cycles, in order to identify solutions for optimal water use and water reuse (Hockin et al. 2020). Table 1 summarizes decision support systems which include fresh water and emerging contaminants. As can be seen, many tools have been developed, which each try to fit a niche set of requirements and no universally adopted system exists or is likely to have the level of detail required and universal applicability necessary. As a result, some level of reliance on expert opinion and more specific tools such as the risk monetizing approach as used by one of the Dutch drinking water company may be necessary.

Table 1 Summary of decision support tools which include emerging contaminants, from (Fischer et al., 2017).

Name	Organisation/ Project	Type	Applicable for	Description	Year	References
MULINO	The MULINO consortium/ EU FP5	Computer system CD-ROM	Competent water authorities	Enables sustainable use of water resources at a catchment scale.	2004	(Giupponi, 2007)
HACCP	EPA (USA)	Guidance document	Drinking water suppliers	Enables identification and control of microbiological contamination in the distribution system.	2007	(EPA, 2007)
SOCOPSE	The SOCOPSE consortium/ EU FP6	Guidance document	Water authorities	Enables management of EU priority substances at European, national or river basin level.	2009	(Baartmans et al., 2009)
Water Safety Plan Manual	WHO/IWA	Guidance document	Drinking water suppliers	Enables development and implementation of Water Safety Plans to systematically assess and manage risks.	2009	(WHO/IWA, 2009)
ARTEM-WQ	LERES (France)	Computer system	Small water supply systems	Calculates a health assessment based on water quality (with regards to micro pollutants), catchment type, treatment in place and DOC removal.	2013	(Delpla et al., 2014)
WFDE	Deltares	Computer system	Water management authorities	Calculates effect of restoration and mitigation on ecological and chemical quality of surface waters.	2013	(Junier and Mostert, 2014)
RiBaTox (under development)	SOLUTIONS consortium/ EU FP7	Web based system	Water authorities	Enables prioritisation, risk assessment and abatement of emerging pollutants and their mixtures.	2015	(Brack et al., 2015)

General Decision-Making Tools

In addition to tools which address decision making by incorporating specific chemical and microbial data for drinking water, generic decision-making tools also exist that could be used to include health considerations in operational decision making. Popular decision-making tools include multi-criteria decision analysis (MCDA), SWOT (strength weakness opportunities threats) analysis and cost-benefit analysis – all of which can be adapted to use at different levels of risk assessment and risk management. For example, in MCDA, a set of criteria are defined to evaluate a specific matter. For example, in the case of safe and healthy drinking water, criteria may include security of supply, microbial quality, chemical quality, cost of treatment etc. For each criteria a common unit is to be defined and a user can give each criterion a weight based on the importance to the overall decision. MCDA is useful to simplify complex, multidisciplinary problems and used frequently in the water sector (Alvarado et al., 2016).

Nexus, serious games and governance capacity tools

Water issues are often considered within the wider context of climate, land, energy and food, and the interconnectedness of the system ('Nexus') is complex with consequences and feedback of one sector on the other. Considering health aspects as a part of the Nexus allows a systematic and integrated approach which can make the interaction between sectors more visible and increase the likelihood of implementing resilient and sustainable solutions to water quality and health related issues. Nexus approaches are increasingly popular among policy makers to better prepare for changes with unknown effects, such as climate change or the use of new technologies (Beuken et al., 2020). The main advantages of the Nexus approach are the insight into the sensitivities, interconnectedness and consequences of the systems involved, and the decisions therein. However, as the systems involved in the nexus are highly complex, the number of possible choices is virtually infinite, with many different solutions solving one or more parts of the problem, while there is also the possibility of creating new problems or unforeseen consequences. For this reason, simplifications must be made which inherently means the systems considered no longer fully reflect reality (Beuken et al., 2020).

Serious games are one approach to tackling integrated decision making in complex systems (Savic et al., 2016). The goal of serious games is to lead participants through a realistic situation, thereby developing competencies and experience of the participant through a 'learning by doing' approach. A serious games approach is simpler than a system simulation and requires less detailed data, in comparison to system models which require large datasets to adequately model the systems in question. Serious games are often supported with specific models (for example the QMRA model for microbial water quality) or decision support tools, such as cost-benefit analysis or systems modeling (SIM4NEXUS project). For more information about serious games in the water sector see Beuken et al., 2020; Savic et al., 2016. Serious games could be used to evaluate how well processes already in place consider health related aspects in decision-making.

There are also other tools that analyze how well organizations, multi-level governments and stakeholders collaborate in solving water related issues. For example the City Blueprint approach (Koop et al., 2015) is used to quickly scan how well cities are managing their water cycle and demonstrates how cities can improve their governance capacity. The tool is used to aid in long-term strategic planning and give insight into management performance and where resources can be most effectively allocated.

Other important factors in decision making

Other important factors when including health considerations in decision making include human behavior influencing tactics, often known as nudges or choice architecture. Nudge theory influences people's decision making through positive reinforcement. For example, having the default option be the safest option when developing guidelines for operational processes is an example of 'nudging' decision making to achieve a good outcome, as the default option is often the most chosen.

Other behavioral impacts may be an unwillingness to deviate from long-established processes. Legal requirements were set within the limitations of knowledge and (analysis) technologies at the time. Over time they have come to be considered as the 'gold standard'. Newly developed technologies or methods may be more accurate from a scientific point of view for assessing or managing risks. However, it is common that is takes quite some time before regulators accept such new technologies and methods as they are used to the existing methods (including their flaws). Also, a lot of emphasis is put on flaws or imperfections of new methods, without evaluating the total balance of what improvement they could still bring. One example is the rapid method for *E. coli* analysis which took a long time to implement, even though it might be more protective and accurate than the traditional culture method in most cases.

Implementation of new methods may also encounter practical hurdles due to highly optimized practical routine procedures. For example, with the development of rapid/real time PCR tests the time to result has been reduced from two days to a few hours. This allows for much more rapid operational decision making and better protection of the population by earlier detection of water contamination. However, this has implications for logistics and planning, which people may be reluctant to adopt, and may increase costs at least at the start.

Besides these practical hurdles, a delay in the implementation can also be related to questions on the interpretation of the results of new research/techniques (e.g. for data derived collected with bioassays; non-target / suspect screening, coliform typing). This holds also for the increased application of non-targeted chemical screening (NTS) analysis to complement targeted chemical analysis (Brunner et al. 2020). While NTS is more comprehensive than targeted analyses, quantification of levels of detected substances is challenging. This hampers a comparison with safe levels, the current fundament of chemical safety assessment for water, and thus the evaluation whether risk mitigation measures are required or not. Each new type of parameter thus requires the development of an interpretation and prioritization framework, when applied by itself or in combination with other monitoring tools in a monitoring strategy. In such a strategy, bioassays and NTS can be used as signaling tools that inform the selection of new parameters after full identification of the chemical contaminant and possible adoption in targeted analyses. In general, strategic decision making on the implementation and integration of new methods/information on a tactical and operational level is needed.

4.4 Integrating specialized knowledge into decision making at drinking water companies

There are many but not a universally adopted tool to include health considerations in operational decision making in the drinking water sector. There is also no consensus within the Dutch drinking water companies on how to make health-based decisions or what tools to use (Smeets et al. 2013). None the less, integrating knowledge into decision making process is necessary, especially in organizations or fields where there is a high degree of fragmentation or specialization, as is the case in the drinking water sector. Good decision making depends on the availability and reliability of suitable data, an understanding of the relationships (cause and effect) with related systems (water, food, climate, energy), human behavior, the possible abatement options and the uncertainty in each of these previous steps.

For example, for the case of health assessments around emerging contaminants, practitioners must assess the exposure, hazard and abatement options often from limited data (Ter Laak et al., 2014) while large datasets and specialized knowledge from a several of disciplines and (academic) collaboration is needed. Many methods and tools are available, for example, the use of non-target screening (NTS) to provide a more complete picture of the presence of organic micro-pollutants in water (Brunner et al., 2020), for which interpretation and prioritization frameworks need to be developed in many cases to make them useful for decision-making (see also paragraph 4.3).

Exposure assessment requires information on the concentration of emerging substances in the water cycle. Where data is lacking, data can be supplemented with new information, e.g. monitoring or model calculations based on, for example production volumes and emission routes. Hazards assessment requires toxicological properties and knowledge on effects and at what concentrations substances pose a threat to human/environmental health. Where toxicological data is incomplete it can be supplement with new studies or model data, for example based on quantitative structure-activity relationships (QSAR). Based on the exposure and toxicological assessment, practitioners can make a risk assessment on abatement options, which may include supplemental water treatment techniques, policy and/or social interventions among others. For all these different aspects in risk assessment, new approaches can be and are being implemented based on a multitude of developments in related academic fields.

Risk ranking can be used to prioritize research topics and inform decisions on risk mitigation measures (if needed) (SNFA, 2018). Risks between different exposure conditions (different CECs, CEC mixtures, pathogens) can be based on concentrations in water (measured or predicted), their margin to safe levels and the severity of health effects these contaminants could contribute to. For decisions on risk mitigation measures that can be taken by the drinking water sector or others, it is helpful to quantify the relative contribution of exposure via (drinking) water, when compared to other sources of exposure (air, food, consumer products).

5 Discussion and recommendations

5.1 Discussion

The fact sheets in Chapters 2 and 3 addressed specific chemical and microbial topics, whereas Chapter 4 discussed the decision making processes. In this chapter we address cross-cutting issues that occurred in several topics and in the discussions with the water companies. The research outlooks on the specific topics in the previous chapters are not repeated here.

5.1.1 Legal requirements <-> precautionary principle

The main task of drinking water companies is to provide safe drinking water against reasonable costs. Compliance to the water quality targets in the drinking water guidelines is the basis for their practice and mode of operation. However, the companies are aware of potential new hazards and risks that are not yet regulated and take their responsibility of protecting public health. For instance, the Dutch water sector has decided to collectively aim for a more stringent level of arsenic in drinking water than legally required, based on an evaluation of health impact and costs for treatment (Ahmad et al. 2020). Through investments in research and monitoring they stay ahead of emerging risks and take measures where needed. This leads to a constant tension between costs and a precautionary approach, which needs constant consideration. This is a driver for clear and quantitative interpretation of risks to support decisions related to water quality in practice. This can also support discussions with other stakeholders that meet in the water system such as inspectorate, legislation, governance authorities (municipalities, provinces), water authorities and industry.

5.1.2 Expanding topics and methods <-> limited resources

With an increase of available methods and knowledge, more issues can be identified and addressed in various ways. However, resources for research are not unlimited and the drinking water sector thus needs to make smart decisions about which issues and methods to pursue in research projects to address the most relevant ones. This is reflected in the organisation of the joint research program (BTO). This includes screening for developments in society (via the *BTO-Horizon scanning*), screening of emerging methods in related fields of science (e.g. BTO-*Newsletter molecular microbial methods*), research on initial applications in drinking water context (BTO-Exploratory research), application of methods in collective research (*BTO-Thematic research*) and implementation in practice (nationally through laboratories, internationally in collaborations e.g. GWRC). This approach has proved its effectiveness in the past, for example molecular method developments such as next generation sequencing are rapidly developed for medical applications. Application for (drinking) water analysis requires limited further development. Still occasionally the sector is confronted with a new or re-emerging challenge (PFAS, bromate) for which adequate response strategies need to be developed.

Even though the water sector has developed a science based approach to make choices which signals for water quality issues to follow-up, it is critical at the same time to keep close contact with health authorities such as RIVM and EFSA to quickly adapt to new challenges, e.g. by developing preliminary water quality targets for new compounds. It can also happen that concerns in society for specific chemicals or pathogens can urge (exploratory) research on potential health risks, even if such substances can be expected to be of low or even negligible relevance from a health perspective, or the contribution to exposure via drinking water is negligible compared to other exposure routes (e.g. food, air or consumer products).

5.1.3 Overcoming hurdles for innovation

Technical innovations that have potential to be implemented in practice can provide economic benefit or safety improvement. The joint research program (BTO) generally results in the proof of concept and proof of value of an innovation. However, the drinking water companies need to actually implement these innovations in their practice to achieve impact and reach an improved future. This implementation often goes beyond technical implementation alone and can require change in procedures, logistics or organisation. In parts of an organisation that are completely optimised for the current situation to reduce costs, there may be resistance to implement a new method. On the one hand, it is inevitable that initially there will be bugs that need to be resolved. On the other hand, practical implementation can also be a driver for rapid improvement of methods and techniques, including interpretation of the data. People need to be adequately informed, get used to and gain trust in a new innovation, and gain experience to appreciate it as a new and improved standard approach. This will require investments of resources (money and time) whereas the financial benefits or improved safety may take some time to develop and cannot be predicted accurately beforehand. This means that a strong business case may not be feasible at the time that implementation is needed. Nevertheless, covid-19 wastewater surveillance was implemented as an early warning system within two years, fuelled by international projects and collaborations (Medema et al. 2020).

In short, several hurdles need to be taken before implementation of an innovation is successful. This requires visionary management that is focused on an improved future, not only supporting but really driving this process as it requires resources and affects the whole organisation. Collaboration and exchange of knowledge and experiences in the sector can further stimulate this implementation and increase the impact. The valorisation research within the BTO can develop pathways to further improve this implementation phase.

5.1.4 Drinking water <-> other exposures

Drinking water is only one of the exposure routes for the contaminants of concern discussed in this report. Other water exposures such as recreational water, public fountains, rain, cooling tower and wastewater aerosols can also result in relevant exposure. Similarly non-water exposures through air, food and materials in consumer products may contribute to exposures that potentially lead to adverse health effects. Some of the non-water exposure routes may nevertheless be transported via water, for instance by uptake of chemicals in water into fish and in food crops (in particular of relevance when irrigated with treated wastewater) . The exposure through drinking water thus needs to be put in perspective to the other routes to ensure that public resources are directed at the most effective and efficient measures to reduce any risks. Putting things in perspective is also effective to manage public perception on drinking water safety.

5.1.5 Health <-> perception, image, trust

Trust in the quality and safety of drinking water in the Netherlands and Flanders is very high. However, this can change with news about (trace) contaminants in our water sources that may end up in our drinking water. Studies have shown that ‘the public’ doesn’t exist and that people have diverse perceptions and information needs about their drinking water quality and safety (Van den Berg et al. 2019). This provides a challenge to the drinking water companies. On the one hand they send out warnings where needed and raise public awareness and political attention for the protection of our freshwater sources (Kools et al. 2019). On the other hand, they can ensure the public that their water is safe and healthy, and that everything is under control (ILT, 2020). The (collective) drinking water research provides a scientific basis for these statements and supports the safeguarding of water quality. Studies have shown that transparency is of great importance for trust in drinking water and that the way of communication on this needs to be adapted to the public. This aspect has also been included in the revised Drinking Water Directive (article 17 and Annex VI) of which the implementation in EU member states is ongoing. More elaborate support on risk perception is provided in the report BTO 2019.023 Risicoperceptie. (Brouwer et al. 2019).

5.2 Recommendations

Drinking water companies have organised research and developed mechanisms in place to know which water quality risks are eminent and to develop strategies to manage these risks. They collectively work on research for water quality and safety (BTO) and in efforts to influence politics and public (Vewin). Challenges remain as the number of hazards, methods and technologies increase. The overview of techniques and methods in this report illustrates the complexity of water quality and health issues that need to be addressed in the near future. Because of limits to resources, evidence-based choices on research priorities need to be made. We recommend to further develop a joint approach for water quality and risk management including:

- an integrated risk evaluation framework to evaluate and prioritize risks for the water sector
- a research strategy how to address the prioritized topics and select the appropriate methods and technologies
- an implementation strategy that goes beyond a business case and involves all operational units within a water company, not only technology
- a platform for sharing practical approaches for water quality and risk management between water companies
- a common message to the public and politics, correctly targeted and in understandable language for the target groups while being transparent.

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