THE Water Research FOUNDATION

PROJECT NO.
4951

Tools to Evaluate Quantitative Microbial Risk and Plant Performance/Reliability

CALIFORNIA Water Boards
STATE WATER RESOURCES CONTROL BOARD
REGIONAL WATER QUALITY CONTROL BOARDS

THE METROPOLITAN WATER DISTRICT OF SOUTHERN CALIFORNIA

Tools to Evaluate Quantitative Microbial Risk and Plant Performance/Reliability

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Co-sponsored by:

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Abstract and Benefits

Abstract:

The goal of project 4951 was to develop a sound technical framework for (1) the evaluation of direct potable reuse facility performance using a probabilistic assessment of treatment train performance (PATTP), and (2) the use of quantitative microbial risk assessment (QMRA) to assess the level of treatment required to achieve risk-based targets. This framework was built into a tool—called DPRisk—that allows the California State Water Resources Control Board's (State Water Board's) Division of Drinking Water to quantify and characterize pathogen risk in direct potable reuse applications. The Technical Work Group (TWG) overseeing the effort completed a literature review of previous PATTPs and QMRAs, and developed a framework for the consistent application of these approaches. The research team used the framework to develop the web-based DPRisk tool and an accompanying guidance document (Appendix B). Together the TWG and research team provided training to the State Water Board on the use of DPRisk. DPRisk and the guidance document will help the State Water Board identify or confirm the treatment requirements for direct potable reuse.

Benefits:

- Provides a tool and guidance for the California State Water Resources Control Board's development of direct potable reuse criteria.
- Provides a consistent approach for performing PATTP and QMRA.
- Provides a transparent tool with the flexibility to evaluate all of the inputs to QMRA.
- Allows for the evaluation of non-treatment or management barriers such as dilution, environmental die-off, and blending.
- Allows for evaluation of treatment failures and their impact on risk.

Keywords: Direct potable reuse, QMRA, PATTP.

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Figures

Acronyms and Abbreviations

ALCR	Air liquid conversion ratio
AOP	Advanced oxidation process
AWPF	Advanced water purification facility
BAC	Biological activated carbon
CCP	Critical control point
CT	Concentration × time (for disinfection)
ddPCR	Droplet digital polymerase chain reaction
DDW	Division of Drinking Water
DPR	Direct potable reuse
DPR-1	First of the direct potable reuse research topics
DPR-2	Second of the direct potable reuse research topics
DWTP	Drinking water treatment plant
EC	Electrical conductivity
EPA	Environmental Protection Agency
FI	Fluorescence intensity
GC	Gene copy (or genome copy)
GC:IU	Ratio of genome copies (GC) to infectious units (IU)
HRT	Hydraulic retention time
ICC-PCR	Integrated cell culture polymerase chain reaction
ICC-qPCR	Integrated cell culture quantitative polymerase chain reaction
IPR	Indirect potable reuse
IU	Infectious unit
KM	Kaplan-Meier
LRV	Log reduction value
LT2	Long Term 2 Enhanced Surface Water Treatment Rule
MBR	Membrane bioreactor
MDL	Method detection limit
MF	Microfiltration
MI	Multiple imputation
MLE	Maximum likelihood estimation
NF	Nanofiltration
PATTP	Probabilistic assessment of treatment train performance
PDT	Pressure decay test
QA/QC	Quality assurance / quality control
QAPP	Quality Assurance Project Plan
QMRA	Quantitative microbial risk assessment
qPCR	Quantitative polymerase chain reaction
RO	Reverse osmosis
RWA	Raw water augmentation
RWC	Recycled water contribution

SOP	Standard operating procedure
TOC	Total organic carbon
TWA	Treated water augmentation
TWG	Technical Work Group
UF	ultrafiltration
VCF	Volumetric concentration factor
WHO	World Health Organization
WRF	The Water Research Foundation

CHAPTER 1

Introduction

1.1 Purpose of Project

The California State Water Resources Control Board (State Water Board) recommended that research be conducted to support their development of criteria for direct potable reuse (DPR). Six research projects were identified to address the critical knowledge gaps. The first of the DPR research topics (DPR-1) focuses on developing tools for the State Water Board's Division of Drinking Water (DDW) to implement a probabilistic assessment of treatment train performance (PATTP) and quantitative microbial risk assessment (QMRA). The purpose of these tools is to quantify and characterize pathogen risk in DPR applications. These processes are critically important in identifying the log reduction values (LRVs) necessary for adequate protection of public health from waterborne pathogens. The tool—called DPRisk—may be used by anyone interested in characterizing the performance of a specific DPR system, but it was specifically envisioned for regulators and other stakeholders to use this tool to inform the development of risk-based criteria for the design and operation of DPR systems. An overview of the QMRA and PATTP processes are shown in Figure 1-1.

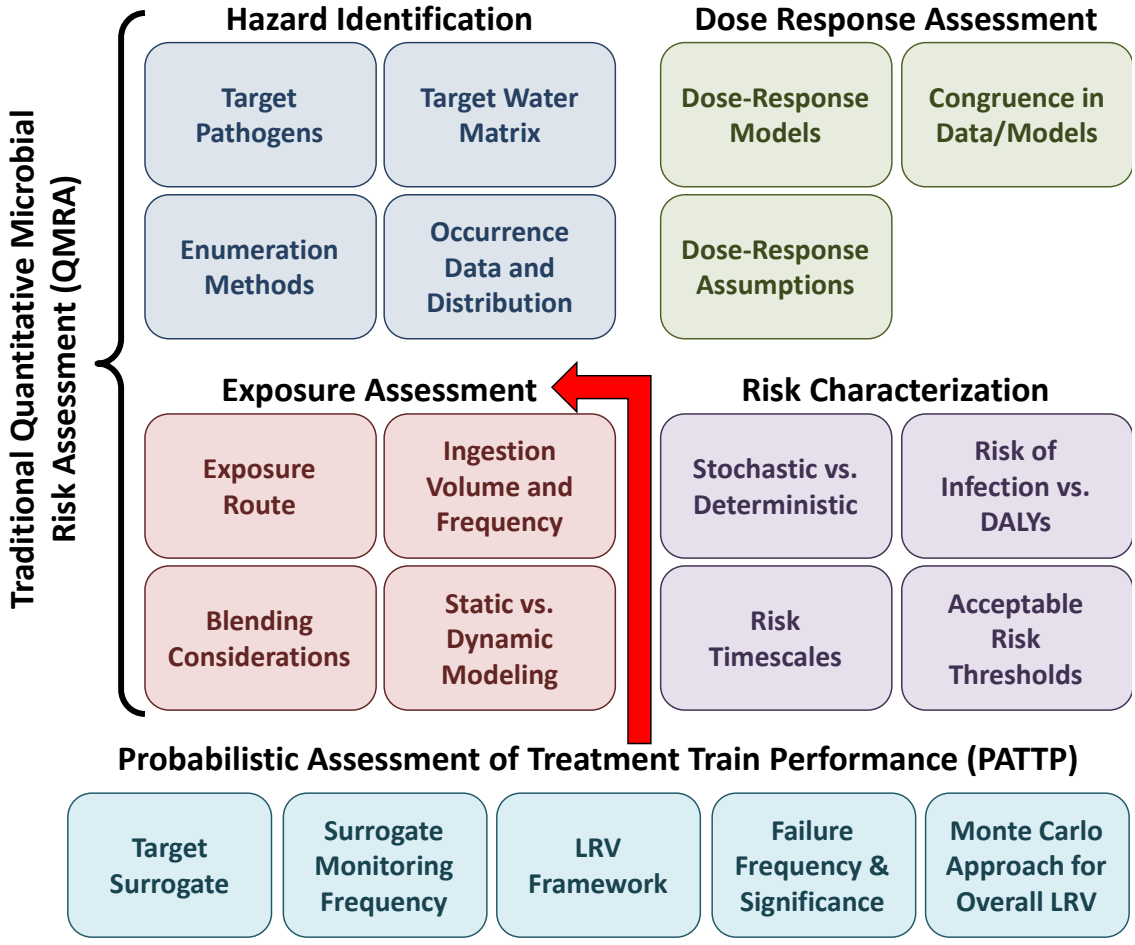

Figure 1-1. Overview of the Steps Involved in Quantitative Microbial Risk Assessment and Probabilistic Assessments of Treatment Train Performance.

1.2 Technical Work Group and Research Team

The State Water Board commissioned a Technical Work Group (TWG) and research team to conduct the DPR-1 research. The TWG provided technical support and review for all phases of the project including the literature review, the development of a framework for the PATTP and QMRA approach, specifications, and scope of work for the research team, and coordination with the research team on project deliverables. The research team was responsible for incorporating input from the TWG and developing tools and guidance for the use of PATTP and QMRA. The goal of the DPR-1 project was to develop sound technical opinions on two key topics: 1) development of guidelines for the evaluation of DPR facility performance (PATTP), and 2) the use of QMRA to assess the level of treatment required to achieve risk-based targets. The relationship between pathogen concentrations, treatment performance, and risk is shown in Figure 1-2.

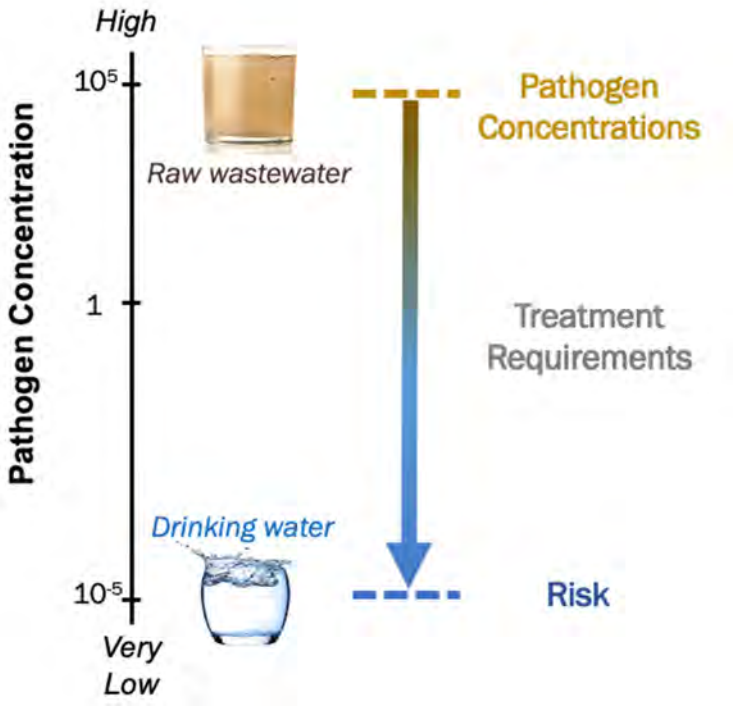

Figure 1-2. Relationship between Pathogen Concentrations, Treatment Performance, and Risk.

1.3 Key Deliverables

The project was divided into three phases that built off of each other. The major deliverables from the three phases are described below. Throughout the process, the TWG and research team had frequent communication and input from staff from the State Water Board, the Water Research Foundation, and the Research Coordinating Committee. All deliverables were reviewed by the relevant stakeholders.

1.3.1 Literature Review

The TWG developed the literature review to 1) review key assumptions associated with PATTP/QMRA, 2) develop a uniform method to evaluate PATTP/QMRA, 3) develop a set of relevant scenarios, and 4) develop guidance on how to review and evaluate findings. The literature reviewed served as the basis for the subsequent deliverables produced by the research team.

1.3.2 Specifications for PATTP and QMRA Tool

The TWG created specifications for the research team to help guide the development of the PATTP and QMRA tools. The document described the functionality, flexibility, and outputs of the tools.

1.3.3 Research Team Scope of Work

The TWG developed a scope of work for the research team describing the required tasks to develop the PATTP and QMRA tools, conduct quality assurance, engage with the TWG and the State Water Board, and provide recommendations for future work.

1.3.4 Quality Assurance Project Plan

The research team developed a quality assurance project plan (QAPP) to ensure the final web-based tool, guidance document, workshop materials, and other supporting information satisfied the requirements of the research team's scope of work and the technical specifications that were reviewed and approved by the State Water Board.

1.3.5 Guidance Document and DPRisk Tool

The research team developed a web-based tool called "DPRisk" and a guidance document (Appendix B) to facilitate the QMRA and PATTP processes so that users could easily evaluate various policy and treatment alternatives.

1.3.6 Training Workshops

Workshops were held on July 14 and August 4, 2020, to provide training to the State Water Board staff on PATTP and QMRA. Workshops were conducted by both the TWG and the research team.

1.4 Organization of Final Report

The three major deliverables from the project are the literature review, the DPRisk tool, and the guidance document. These documents are summarized in Chapter 2 and provided in their entirety as appendices. Chapter 3 concludes the Final Report with conclusions, recommendations, and proposed future efforts.

CHAPTER 2

Summary of Work Performed and Deliverables

2.1 Literature Review

The first phase of the project was a literature review with the following goals:

- Identify and compare key assumptions underlying published QMRAs, including the target pathogens evaluated (reference pathogens), the modeling of treatment performance, the metrics used for quantifying the presence and removal of pathogens, and assumptions regarding pathogen exposure and relevant dose-response functions.
- Develop a uniform method to review and evaluate PATTP and QMRA.
- Develop a set of most relevant and important scenarios (e.g., pathogen, treatment, and exposure route combinations) for consideration in the PATTP and QMRA.
- Develop guidance on how to review and evaluate the data and assumptions for PATTP and QMRA, including how to evaluate pathogen data from nonculture methods such as molecular methods, where viability and infectivity is a consideration.

The outcomes of the literature review were used to develop a scope of work including specifications and requirements for the PATTP and QMRA tools. The goal of the PATTP and QMRA tools is to provide DDW with a consistent approach that has been developed and vetted by the experts involved with the TWG and research team. The literature review was the first step to developing a consistent approach for PATTP and QMRA (Figure 2-1).

The literature review was submitted to DDW for review and comment. The final literature review can be found in Appendix A.

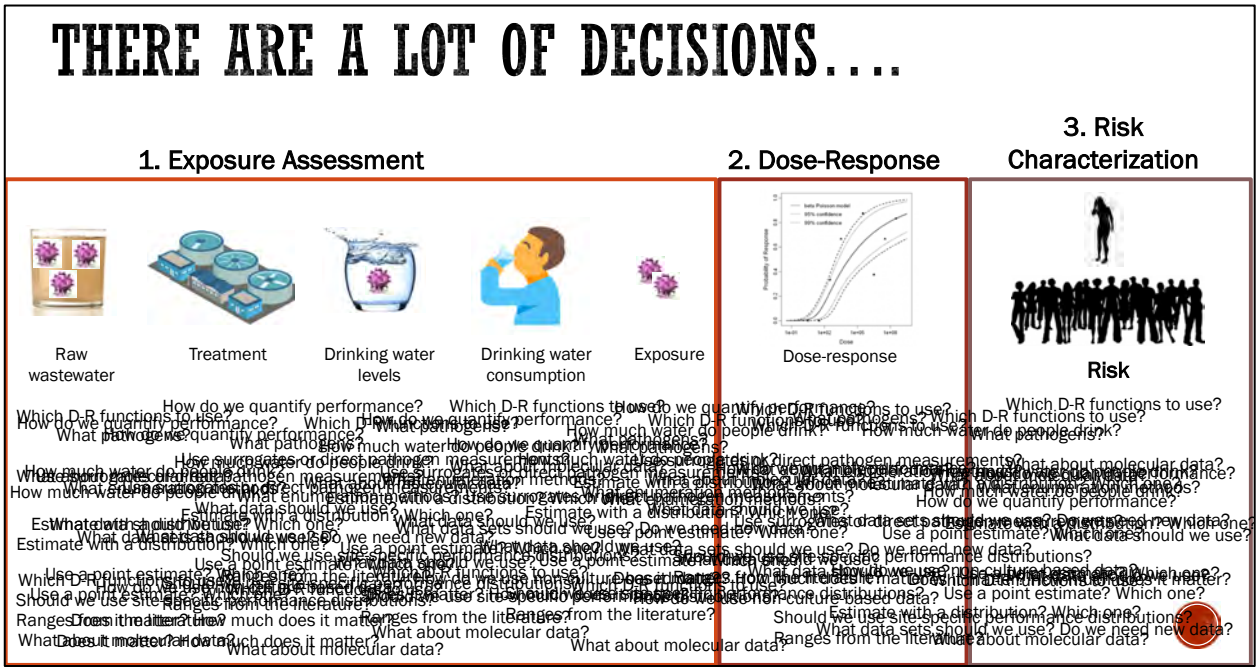

Figure 2-1. Literature Review Aimed to Develop Consistent Approach for PATTP and QMRA.

2.2 Specifications for PATTP and QMRA Tool

Upon completion of the literature review, the TWG put together specifications for the functionality of the PATTP and QMRA tool. The specifications acted as a blueprint for the research team's development of the PATTP and QMRA tools. The specifications included requirements for the defaults, functionality, flexibility, inputs, outputs, and limits for each step of the PATTP and QMRA process. The specifications provided the research team with a roadmap for how to develop a tool that would apply PATTP and QMRA with a consistent approach and would satisfy the desired end-uses for DDW.

Draft specifications were provided to DDW for review and comment. Comments were incorporated into the research team's scope of work.

2.3 Research Team Scope of Work

The TWG developed a scope of work for the research team. The scope of work described the expectations of the research team. The scope included the development of the PATTP and QMRA tools, development of a QAPP, communication and interaction with the TWG, development of workshop materials for the State Water Board, and development of a guidance document. The tool specifications were included as an attachment to the research team's scope of work.

2.4 Quality Assurance Project Plan

The research team developed a QAPP for the development of the PATTP and QMRA tools. The goals of the QAPP were to ensure the PATTP and QMRA tools would:

- Provide results that could be replicated/verified
- Be updated with new data appropriately
- Function as anticipated (no bugs/loop holes)
- Undergo appropriate quality assurance/quality control (QA/QC) prior to release.

The QAPP was reviewed by the TWG and submitted to DDW for review. The QAPP provided the research team and TWG with a roadmap of items (directly related to the technical specifications) to address as the tool and guidance document were developed.

2.5 Guidance Document and DPRisk Tool

The research team developed the DPRisk Tool and the accompanying guidance document (Appendix B). The development of these deliverables included multiple workshops with the TWG as well as frequent conference calls with the TWG to ensure proper flexibility and functionality was included in the DPRisk Tool.

The tool was developed using RStudio's freely available, web-based Shiny platform. RStudio provides open source software that allows the user to leverage the R statistical language (https://www.r-project.org/), which is increasingly being used for QMRA and the analysis of complex microbiological data (e.g., metagenomics applications). The free Shiny add-on (https://shiny.rstudio.com/) allows for interactive web-based user interfaces. DPRisk was developed with significant flexibility to allow for adaptation to a wide variety of potential treatment scenarios. A screenshot of the home screen for DPRisk is provided in Figure 2-2.

DPRisk provides the user with the ability to specify the following:

- Raw Wastewater Pathogen Concentrations
  - Target pathogen

    - Concentration dataset (raw data or as a distribution)
- Treatment Train Performance
    - Log reduction for multiple unit processes described using raw data, a point estimate, or a probability distribution
- Treatment Failures
    - Magnitude, duration, and frequency of failures applied to unit processes or overall treatment train
- Management Barriers
    - Inclusion of blending, dilution, and pathogen die-off
- Exposure
    - Volume and frequency of consumption of water in a day either by point estimate, probability distribution, or a user-input file
- Dose-Response
    - Dose response model and parameters including the option for a user-input dose-response model

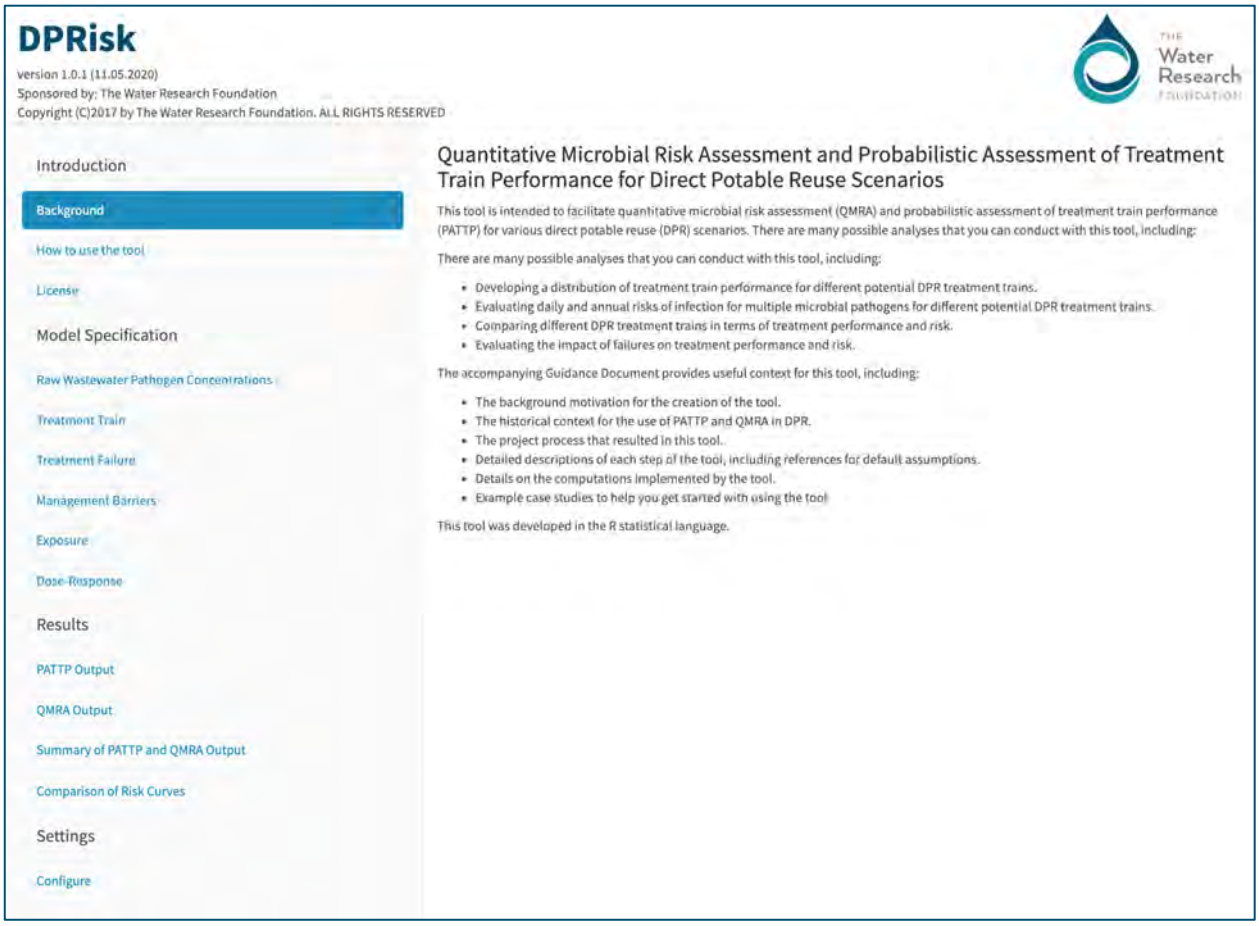

Figure 2-2. Home Page of the DPRisk Tool.

The primary outputs from DPRisk include the resulting distributions of treatment performance, daily risk, and annual risk. Figure 2-3 shows an example of a daily risk output. These results are available to the user to download.

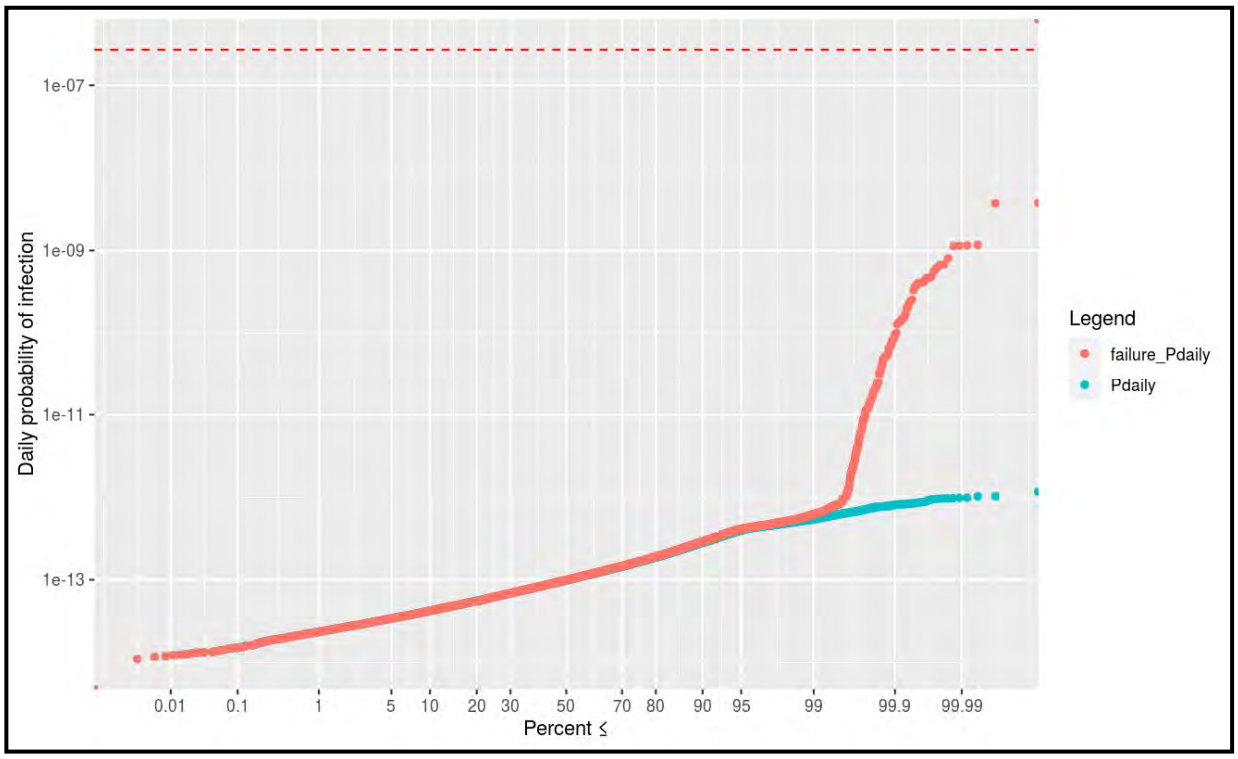

Figure 2-3. Example Output of Daily Risk Distribution.

The guidance document accompanies DPRisk and is the "user guide" for the tool. The guidance document describes the functionality of each step of the DPRisk tool and provides case studies from the literature as examples for the user to become familiar with the inputs and outputs of the tool. These case studies also acted as QA/QC on the tool to ensure DPRisk could accurately replicate studies from the literature (Figure 2-4). The guidance document provides insights into how changing certain parameters in the PATTP and QMRA will impact the resulting risk of infection.

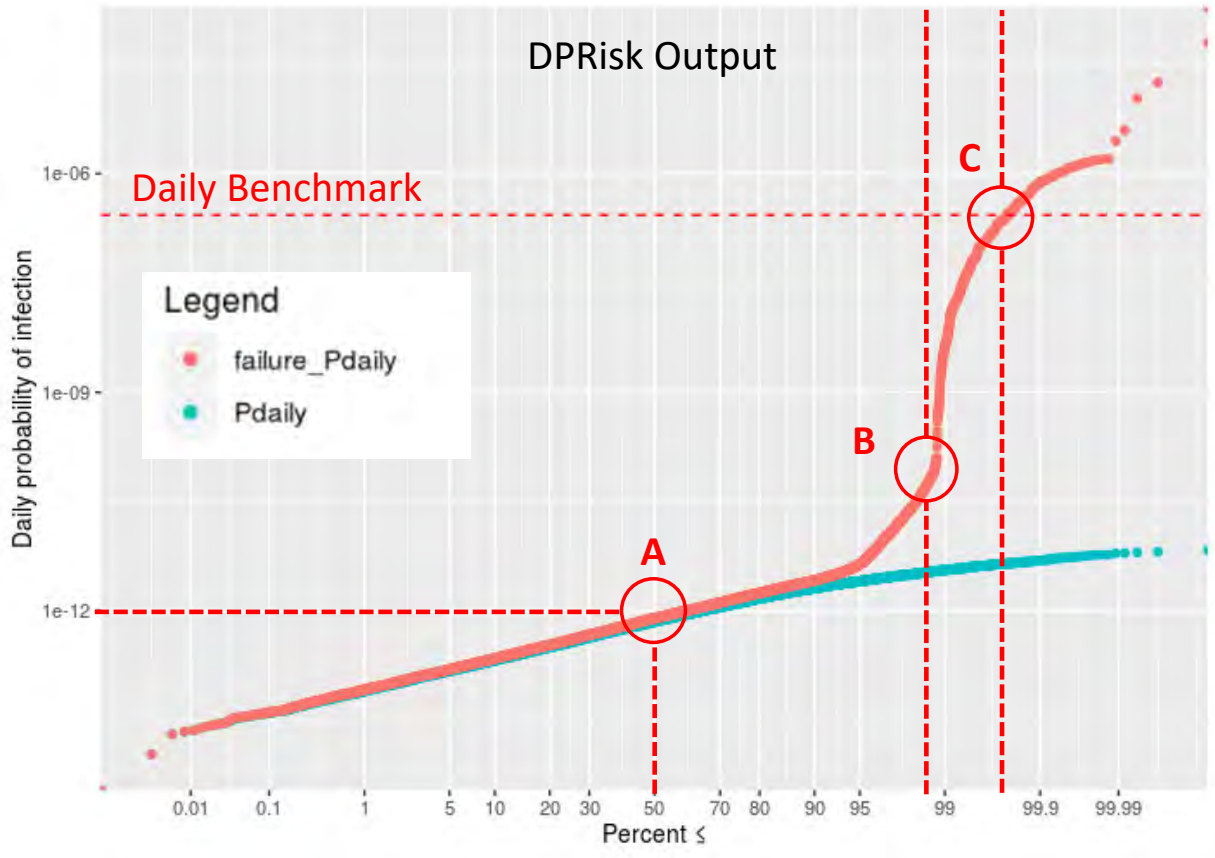

Figure 2-4. Case Studies Acted as QA/QC for DPRisk.

Both DPRisk and the guidance document went through multiple rounds of review with the TWG. The research team held a workshop with the TWG to introduce the first version of DPRisk and the guidance document. The TWG provided comments and provided QA/QC on DPRisk to ensure there were no bugs or loop holes in the tool's functionality. DDW was also provided with a period to provide QA/QC on the tool.

The guidance document and DPRisk were provided to DDW for review and comment. Comments were incorporated into final versions. The final guidance document is provided in Appendix B.

2.6 Training Workshops

In addition to the guidance document, the research team and TWG held two virtual training workshops with DDW.

The first workshop was held on July 14, 2020, and included the following agenda:

- Introduction and Background on PATTP & QMRA (Figure 2-5)
- Live Demonstration of DPRisk Tool
- Case Study – Live Demonstration

The goal of the first workshop was to provide DDW with background on the PATTP and QMRA processes and introduce the functionality of DPRisk. Following the first workshop, DPRisk and the guidance document were provided to DDW so they could become more familiar with DPRisk and develop questions or comments for the second workshop.

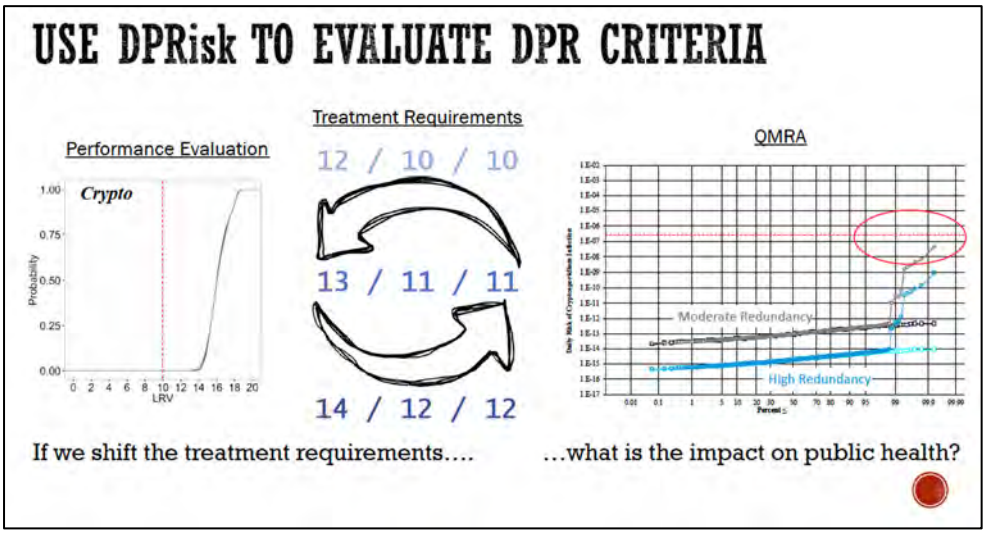

Figure 2-5. Slide from the First Virtual Workshop with DDW.

A second virtual workshop was held with DDW on August 4, 2020. The agenda for the second workshop included:

- Review Case Studies (Figure 2-6)
- Impact of Raw Wastewater Pathogen Concentration Assumptions
- Impact of Treatment Redundancy
- Impact of Treatment Variability
- Impact of Failure Assumptions
- Sensitivity Analysis

The goal of the second workshop was to dive deeper into the functionality of the DPRisk and provide insights on how different assumptions impact risk. The training and case studies were meant to introduce the various features of the tool to the State Water Board and demonstrate its capabilities and limitations. The TWG and research team did not provide guidance on how the tool *should* be used to develop regulations nor was this part of either group's charge.

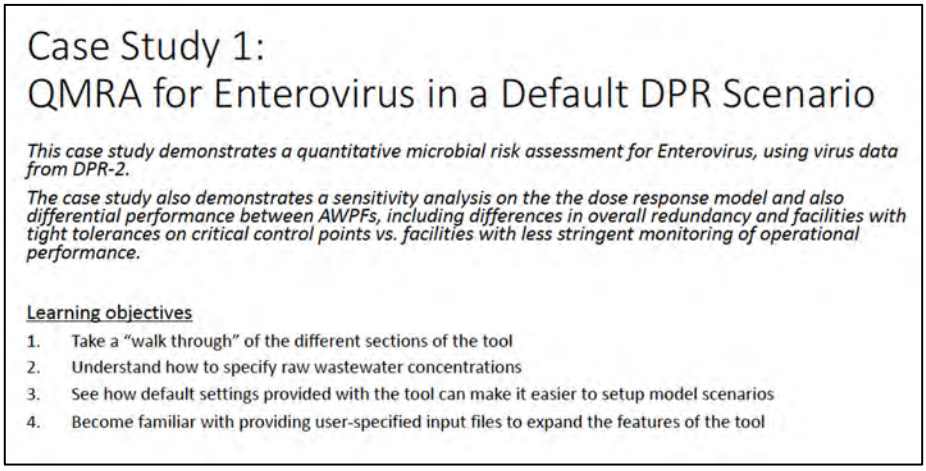

Figure 2-6. Slide from the Second Virtual Workshop with DDW.

The complete workshop materials are provided in Appendix C.

CHAPTER 3

Conclusions and Future Efforts

3.1 Conclusions

Maintaining consistent control of pathogens is the most critical goal for public health protection in DPR. The DPR-1 research project provides the State Water Board with a framework for understanding how to characterize the risk from waterborne pathogens in DPR settings and how that risk can be controlled through treatment. The DPR-1 TWG and research team purposefully did not offer recommendations for specific treatment requirements in DPR. Nevertheless, the DPRisk tool can be used to evaluate how the selection of different log reduction targets—such as 12/10/10 for enteric virus/*Giardia*/*Cryptosporidium*—impacts the ability of a system to meet different performance or risk targets, such as the daily risk target of 2.7×10^{-7} infections per person. Given the stochastic approach recommended by DPR-1, the State Water Board will need to define the level of compliance that is sufficient to meet their requirements for both risk and treatment. Should compliance with the daily risk goal be achieved 90% of the time? 99%? These risk management decisions were not addressed by the DPR-1 project, but will be important decisions for regulatory development. The impact of treatment on compliance with the risk goal was illustrated during the August 4, 2020, workshop (Figure 3-1).

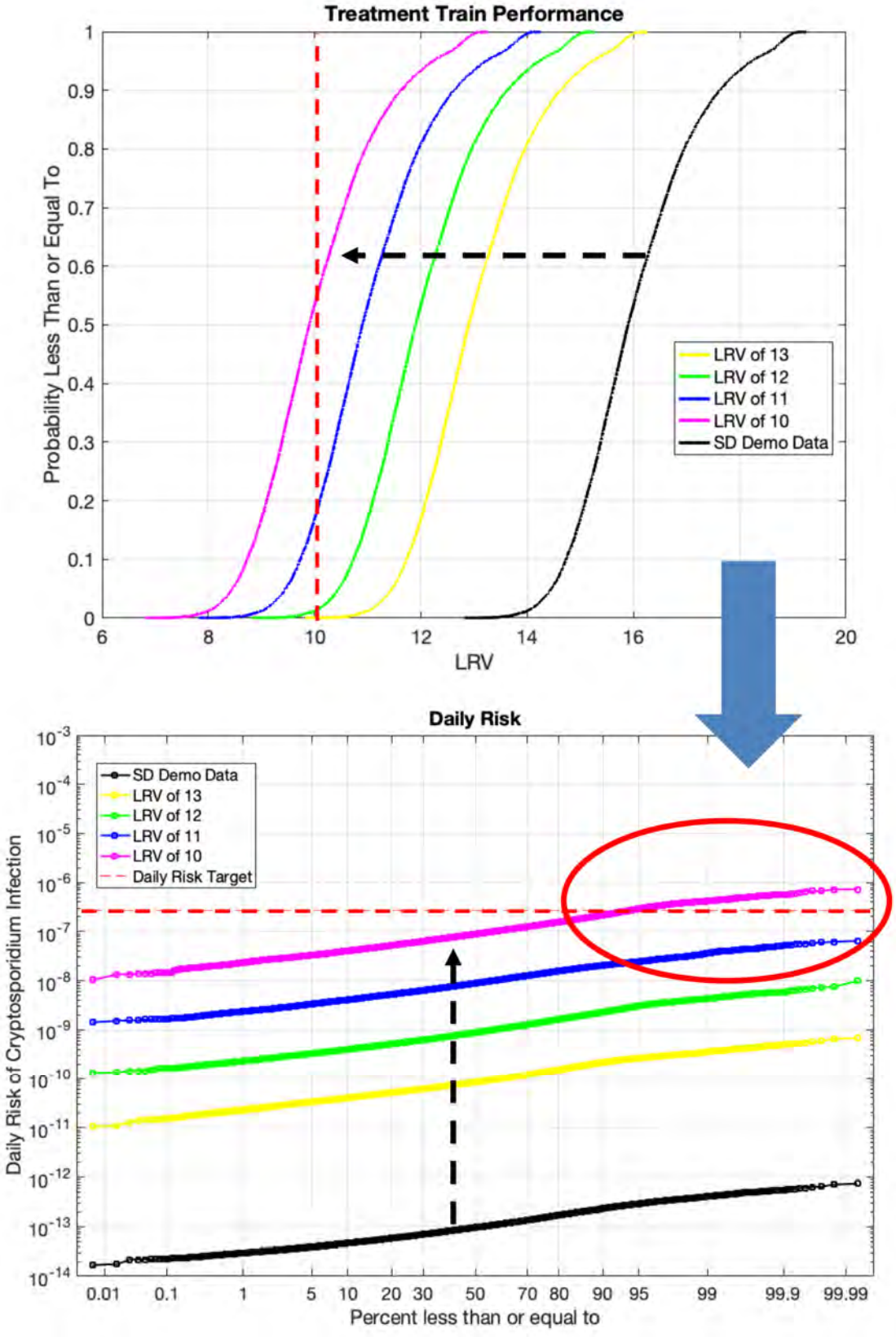

Figure 3-1. Impact of Treatment Redundancy on Compliance with the Daily Risk Goal.

While the DPR-1 project focused on the interaction between *treatment* and risk, it is important to keep in mind that multiple other elements of a potable reuse system factor into public health protection, including source control, monitoring, operations, diversions, secondary disinfection in the distribution system, blending, and storage. Because these elements work in tandem, a reduction in one element can often be compensated by augmenting another. For example, shorter storage times could be offset by elements such as a) more rapid monitoring that allows operators to identify water quality issues and divert before the water is distributed to consumers, or b) downstream treatment at a surface water treatment plant.

The key differentiator between DPR and indirect potable reuse (IPR) is the absence of a "significant" environmental buffer, i.e., one that complies with the requirements of the groundwater recharge or surface water augmentation regulations. The absence of the environmental buffer means that its benefits—including retention time and contaminant control (i.e., dilution and/or die-off)—need to be accounted for by other elements in the system. A recent series of papers provides additional discussion on the benefits of these buffers for public health protection (Pecson et al. 2018a, 2018b). One intermediate option that is open to raw water augmentation (RWA) DPR projects, however, is the use of a small reservoir (or groundwater basin) that cannot meet the requirements of the IPR regulations. The State Water Board acknowledged that such projects have a different (ostensibly lower) risk profile than either a hard-piped RWA project or a treated water augmentation (TWA) project (SWRCB 2016). In addition, the DPR Expert Panel encouraged the State Water Board to consider the potential benefits of environmental buffers, irrespective of size, as a means of taking advantage of temperature equalization, storage, and peak attenuation (Olivieri et al. 2016). The DPRisk tool includes the ability to evaluate the benefits of "management barriers" such as small reservoirs, engineered storage buffers, and blending, and to quantify their benefits in terms of pathogen control.

To fully understand the protection offered by DPR systems, the TWG recommends that the State Water Board continue to develop frameworks for incorporating the benefits of these management barriers into their analyses. Systems that use an environmental buffer might then be allowed to rebalance the level of protection provided by other barriers. For example, if a small reservoir provides weeks of retention time for a DPR project, then the requirements for automated diversions linked to real-time monitoring could be relaxed. The longer system response times would be the justification for rebalancing the monitoring and diversions. Similarly, if the reservoir provides significant attenuation of contaminant peaks, additional requirements for treatment could also be rebalanced to account for this protection. Rebalancing the requirements for systems that take advantage of an environmental buffer may drive more project sponsors to include these elements in their projects.

One of the key benefits of the environmental buffer that cannot be replaced by other DPR elements is response time. IPR systems have developed a balance between failure prevention and failure response that takes into account the significant response time provided by the environment. For example, the stringency of treatment can be relaxed if there is ample time to respond to treatment issues that occur. As failure response time drops from months (IPR) to hours or minutes (DPR), however, this approach will become increasingly less feasible. Consequently, DPR will require greater reliance on automated responses (e.g., diversions) that are linked to real-time monitoring. Improvements in monitoring and control systems will decrease the time needed to respond to a treatment excursion or failure. Such modifications will be critical to adapt to the shorter retention times provided in many DPR systems. The Water Research Foundation's project 4954 is currently developing a practical blueprint for an enhanced monitoring and control system that protects public health by providing real-time integration and response to performance data. The outcomes of this study will provide important information as the State Water Board determines monitoring and control requirements for DPR systems.

3.1.1 Flexibility of the DPRisk Tools

The DPRisk tool has been built with a high degree of flexibility to allow the State Water Board to easily incorporate new information into their future analyses. The TWG recommends that the State Water Board continue to identify and incorporate new research related to relevant PATTP/QMRA topics including new pathogen monitoring data, studies on pathogen inactivation and removal, the development of new dose-response functions for relevant pathogens, and the adoption of new frameworks for crediting unit processes. The most obvious future addition for DPRisk evaluations is the use of the new pathogen monitoring data from the second DPR research project (DPR-2). Once complete, these results will be added into DPRisk by the research team and TWG as a default dataset. Other examples include the findings from WRF project 4997, which recently developed an updated framework for pathogen crediting through membrane bioreactors including new log reduction values. These new point estimates can be added into the PATTP application of DPRisk to account for the modifications to the virus and protozoa removal credits. The US EPA is also currently seeking applicants to develop new or improved frameworks for monitoring and crediting virus removal through water recycling plants. Future findings from these studies could also be incorporated into a DPRisk evaluation.

Beyond crediting frameworks, researchers are also continuing to better understand the fate of pathogens through treatment. For example, recent advancements have provided additional insight into the fate of norovirus through disinfection processes. Rockey et al. (2020) recently published a study indicating that norovirus has greater sensitivity to ultraviolet light inactivation than other commonly used surrogates including MS2 bacteriophage. This finding, which was based on polymerase chain reaction analyses, was also recently confirmed through the use of the new norovirus culture method by the same group (unpublished data). Similar data for other pathogens of interest can be incorporated into DPRisk through the use of updated LRVs in the PATTP side; the impacts of these data can then be observed for both treatment and risk.

3.1.2 Impact of SARS-CoV-2

The COVID-19 pandemic demonstrated the importance of emerging pathogens on all aspects of life, including the water sector. One immediate concern with any new pathogen, in addition to factors such as environmental persistence, transmission route, dose-response, etc., is to know whether the pathogen can be controlled by existing safeguards, or whether it requires additional levels of control. For example, do the IPR requirements of 12/10/10 log reduction for virus/*Giardia*/*Cryptosporidium* sufficiently control SARS-CoV-2? As described in the DPR-1 project, multiple inputs are needed to make this assessment including 1) knowledge of its concentrations in raw wastewater, 2) an understanding of its removal and inactivation through treatment, and 3) knowledge of its dose-response characteristics. Many of these items were knowledge gaps at the beginning of the pandemic, though rapid progress has been made to understand each of these topics. For example, DPR-2 included monitoring for SARS-CoV-2 in all of its samples at five different wastewater treatment facilities since March 2020. A number of additional researchers across the country and globe have also been actively compiling these data. Studies on SARS-CoV-2 and similar coronaviruses provide insight into its fate through treatment processes and progress has also been made to model the dose-response characteristics of the virus. With these data in hand, the DPRisk tool can be used to confirm whether or not the existing requirements—based on enteric viruses—will need to be reset based on SARS-CoV-2.

3.1.3 Using Molecular Data in DPRisk

One of the limitations of quantifying pathogen concentrations with molecular methods is the uncertainty regarding the ratio of genome copies to infectious units (GC:IU). In line with Van Abel et al. (2017), the TWG recommended in the Literature Review that a range of assumptions from 1:1 to

>10,000:1 be evaluated as part of the sensitivity analysis. While the DPRisk tool does not include the ability to specify different GC:IU ratios, the impact can be evaluated by simply adjusting the raw wastewater concentration inputs across multiple scenarios (i.e., a sensitivity analysis on GC:IU ratio).

Eftim et al. (2017) developed statistical distributions to describe raw wastewater norovirus concentrations as a base 10 lognormal distribution with a mean of 4.0 $\log_{10}$ gc/L and a standard deviation of 1.1 $\log_{10}$ gc/L. Converting this to the base *e* lognormal distribution results in a μ of 4.0×2.303 = 9.2 and σ of 1.1×2.303 = 2.5 (Figure 3-2). Using these parameters as a baseline scenario would essentially represent a GC:IU ratio of 1:1.

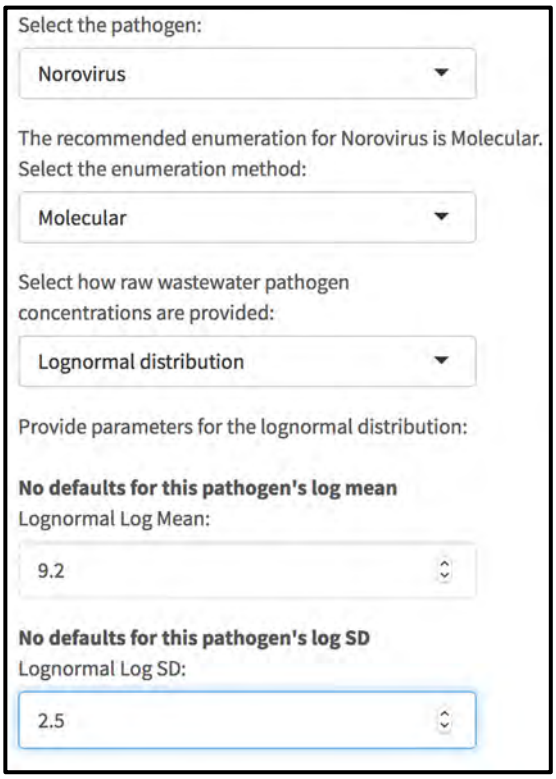

Figure 3-2. DPRisk Input of Norovirus Concentrations Using a Base *e* Lognormal Distribution.

After setting up a scenario with this raw wastewater concentration input, the bottom of the QMRA Output screen includes a link to download the underlying parameter set. The raw wastewater pathogen concentrations in units of gc/L are listed in the second column of that file (i.e., the "input" column). One way to implement the sensitivity analysis is to simply divide those concentrations by the desired GC:IU ratio. For example, a GC:IU of 100 means that for every 100 genomes detected by molecular methods, only 1 represents an infectious virus. After dividing each concentration by 100, the 10,000 data points could be transferred to a new .csv file, which could then be used as an input file for a subsequent modeling scenario. This process could then be repeated, each time dividing the original concentrations by a new GC:IU ratio, until the full range from 1:1 to 10,000:1 had been captured.

This same approach can be used when starting with a user-defined input file for the baseline scenario. For example, Soller et al. (2018a) used a $\log_{10}$ uniform distribution to describe secondary effluent norovirus concentrations with a minimum-to-maximum range of 3.9-6.2 $\log_{10}$ gc/L. Similar to the adenovirus example in Case Study 3 in the guidance document (Appendix B), $\log_{10}$ uniform distributions require a user-defined input file. Different GC:IU ratios could then be evaluated by modifying the concentrations as described above. A GC:IU ratio of 10:1 would shift the $\log_{10}$ uniform distribution so

that the new minimum-to-maximum range would be 2.9-5.2 $\log_{10}$ gc/L. Corresponding shifts to 1.9-4.2 and 0.9-3.2 $\log_{10}$ gc/L would account for 100:1 and 1000:1 ratios, respectively.

Figure 3-3 illustrates the examples from Eftim et al. (2017) and Soller et al. (2018a) for GC:IU ratios ranging from 1:1 to 10,000:1. One important note is that the concentrations in the input file should not be log-transformed; the data should be actual concentrations in gc/L. The graphs show $\log_{10}$-transformed data for clarity.

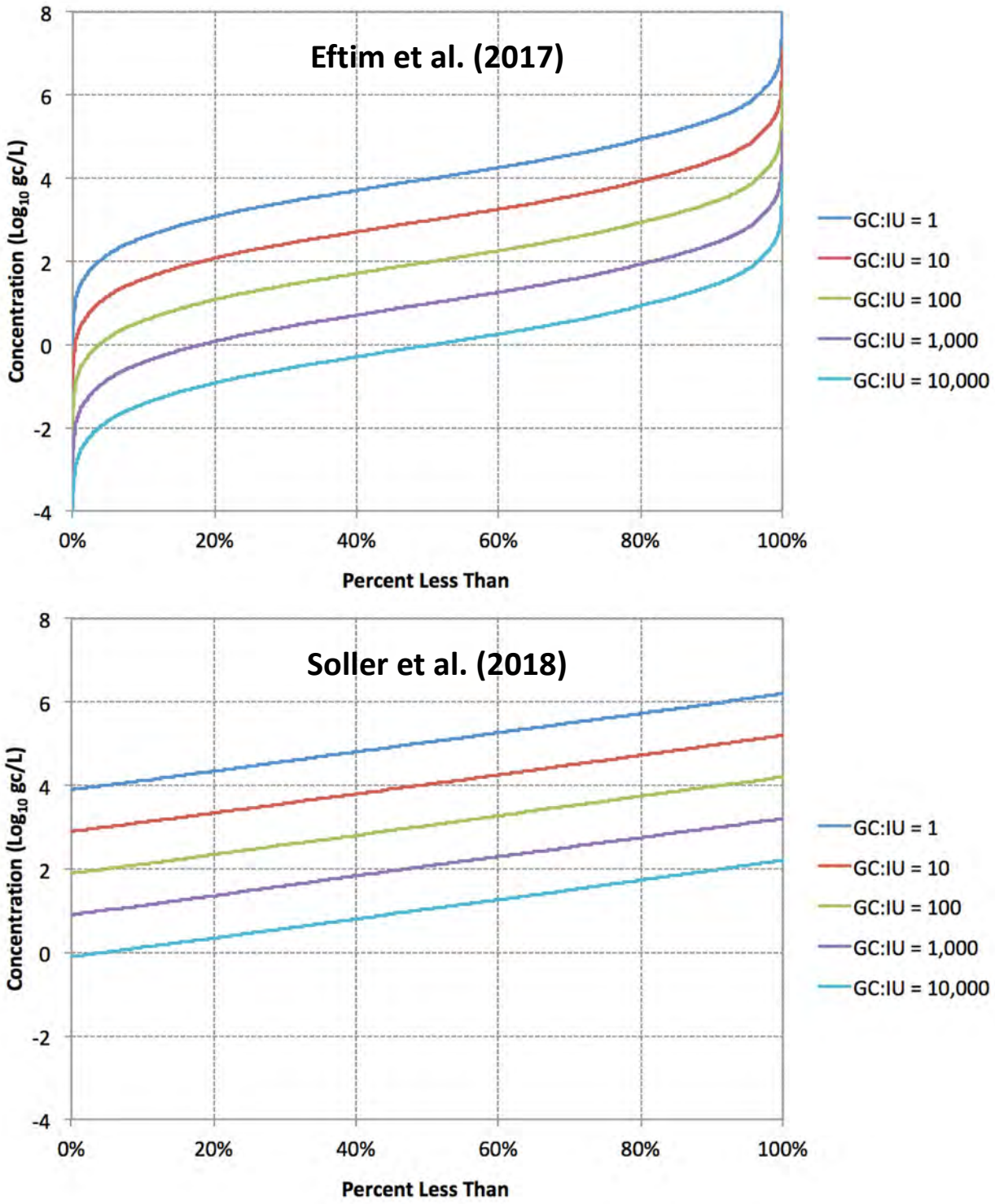

Figure 3-3. Illustration of a Sensitivity Analysis Evaluating Different Assumptions about Genome Copies to Infectious Units (GC:IU).

Source: Data from Eftim et al. 2017 and Soller et al. 2018.

When working with a lognormal distribution, such as the Eftim et al. (2017) example, there is also a much simpler approach to conduct the sensitivity analysis. For each GC:IU ratio, the μ, or lognormal mean, should be reduced by ln(GC:IU). So, for a μ of 9.2, a GC:IU ratio of 10 would require the input to

be reduced by ln(10) or 2.3, resulting in a revised μ of 9.2 – 2.3 = 6.9. A GC:IU ratio of 100 would require the input to be reduced by ln(100) or 4.6, resulting in a revised μ of 9.2- 4.6 = 4.6, and so on. No change is required for the standard deviation so the σ parameter should remain at 2.5 for all GC:IU scenarios.

In DPRisk, there is also a way to confirm that these modifications to the lognormal modification are accurate. As shown earlier, the original lognormal distribution from Eftim et al. (2017) (i.e., μ = 9.2 and σ = 2.5) can be input into DPRisk to generate a parameter set file containing raw wastewater concentrations. These baseline concentrations can be divided by 10 (i.e., GC:IU = 10) to generate a new .csv input file, and this new input file can be used in a subsequent modeling scenario, with DPRisk instructed to assume a lognormal fit for the data (Figure 3-4). Then in the QMRA output, the parameters of the fitted lognormal distribution will be displayed (i.e., μ = 6.9 and σ = 2.5).

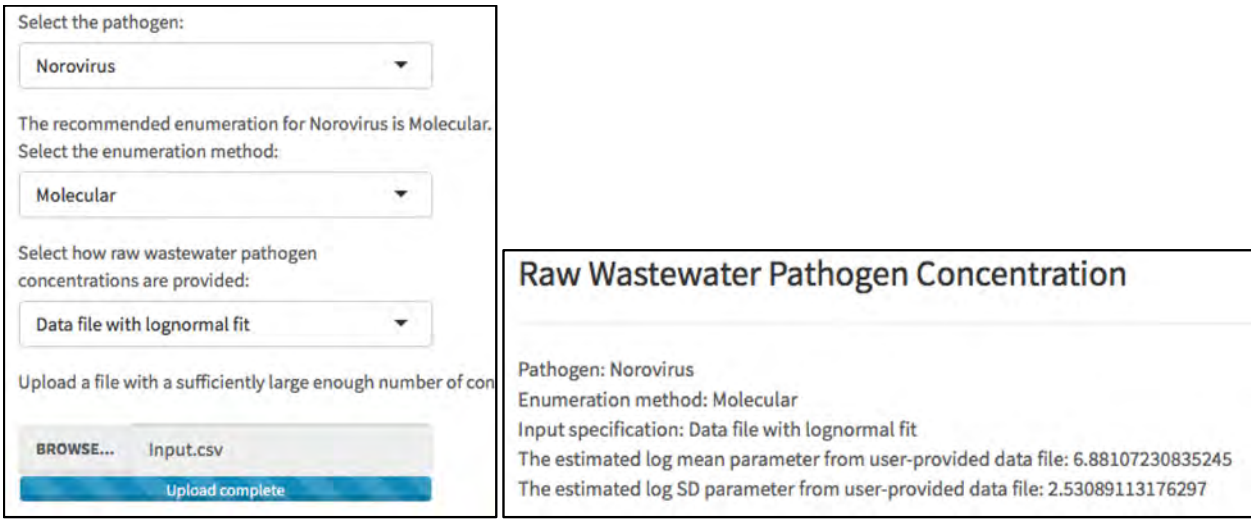

Figure 3-4. DPRisk Input Window for Raw Wastewater Pathogen Concentrations (Left) and Confirmation of the Settings in the Output Window (Right).

3.2 Future Efforts

Throughout the DPR-1 project, a number of knowledge gaps were identified. In each case, adequate assumptions or workarounds were identified and incorporated. The TWG has identified a few relevant topics that should be considered for future research efforts.

3.2.1 Pathogen Monitoring Studies

Based on the preliminary results, the DPR-2 project appears to have made significant advancements in the monitoring of pathogens in raw wastewater. The low rate of non-detects across all of the pathogen groups suggests that the new QAPP and standard operating procedures (SOPs) may offer increased method sensitivity compared to previous studies. Furthermore, the QA/QC requirements—including the use of matrix spikes—allows for the quantification of recovery efficiency and better insight into sources of variability between samples and locations. Consequently, the DPR-2 data set provides an important new baseline for understanding pathogen concentrations in raw wastewater and should be included in the default data for DPRisk.

While DPR-2 provides 120 data points to characterize these concentrations (i.e., five facilities collecting 24 samples each), additional pathogen monitoring data from these and other facilities would continue to offer advantages. On the drinking water side, surface water treatment plants are required to perform a watershed sanitary survey every five years that includes—among other requirements—a summary of

source water quality monitoring data and a description of activities and sources of contamination (CCR Section 64665). The Long Term 2 Enhanced Surface Water Treatment Rule (LT2) supplemented existing regulations to address *Cryptosporidium* in systems with higher risk. LT2 requires two rounds of source water monitoring to characterize the risk from *Cryptosporidium* (categorized into four risk "bins") and to determine the appropriate level of treatment to control that risk. These 24-month campaigns require monthly monitoring of *Cryptosporidium*, *E. coli*, and turbidity for most treatment plants (40 CFR § 141.701). The logic of characterizing source waters and confirming treatment requirements would seem to apply to all potable applications regardless of the source water. This "source to tap" view of protection is a part of the Safe Drinking Water Act and was recommended as an appropriate strategy for potable reuse as well (Tchobanoglous et al. 2015). Given the relative lack of pathogen information in wastewater compared to surface waters, requiring periodic monitoring campaigns would provide additional data with which to understand the risks from pathogens in DPR. Unlike conventional sources where the presence of pathogens is a possibility, it is an expectation that they be present in wastewater systems. If the State Water Board includes requirements for monitoring, the TWG recommends that agencies utilize the QAPP and SOPs developed by the DPR-2 project (Pecson et al. 2020).

3.2.2 Failure Analysis

One of the key recommendations from the DPR-1 project is for the State Water Board to consider the impact of treatment failures on risk. The literature review, guidance document, and training workshops emphasized that even short-term or rare failures can have important consequences on risk. Unfortunately, there are only a limited number of studies that have characterized the frequency, magnitude, and duration of failures that occur at wastewater and advanced water treatment facilities. While additional studies are recommended, such information may be particularly difficult to obtain since it requires operations staff to document the errors and failures that occur at their plant. This tension may help explain why there are so few published papers on this topic. As a starting place, it may be beneficial to convene a group of regulators who have knowledge of known treatment plant failures (including at the wastewater, advanced water, and drinking water treatment plants) and use their experience to help develop reasonable failure scenarios for the modeling. Through such discussions, the State Water Board may develop a rationale to assign the type and frequency of the production of off-spec water and/or overt failures to different unit processes on a process-by-process basis. In the meantime, the global failure approach described in the guidance document (Appendix B) is the recommended strategy for incorporating failures.

It should also be noted that many of the failures that were modeled would likely have been identified by the surrogate monitoring framework (or some other fail-safe practice). This fact highlights again that multiple elements are included to protect public health with treatment being only one of them. Even though high risks were reported during failure events, the inclusion of other elements—such as monitoring, storage, and diversions—could be employed to prevent that water from being distributed to a consumer. It is important to understand failures and the implications for risk, but it is also important to understand whether those risks would actually be realized by the community or if the system has other features to respond and mitigate those risks.

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APPENDIX A

PATTP & QMRA Literature Review

A.1 Introduction

The California State Water Resources Control Board (State Board) has recommended research be conducted to address knowledge gaps that are necessary for developing criteria for Direct Potable Reuse (DPR). Six research projects have been identified to address these gaps. The first of the DPR research topics (DPR-1) focuses on developing tools for the State Board's Division of Drinking Water (DDW) to implement a probabilistic analysis of treatment train performance (PATTP) and quantitative microbial risk assessment (QMRA). These tools can ultimately be used to help DDW confirm the necessary log removal requirements to protect public health from enteric viruses, parasitic protozoa (*Cryptosporidium*, *Giardia*) and other relevant bacterial pathogens[1].

DPR-1 is led by a Technical Work Group (TWG) that provides technical support and review for all phases of the project. The goal of the DPR-1 project is to develop sound technical opinions on two key topics: 1) development of guidelines for the evaluation of DPR facility performance (PATTP), and 2) the use of QMRA to assess the level of treatment required to achieve risk-based targets. The first phase of the project is a literature review to address the following topics:

- Identify and compare key assumptions underlying published QMRAs, including the target pathogens evaluated (reference pathogens), the modeling of treatment performance, the metrics used for quantifying the presence and removal of pathogens, and assumptions regarding pathogen exposure and relevant dose-response functions.
- Based on the literature review, develop a uniform method to review and evaluate PATTP and QMRA.
- Develop a set of most relevant and important scenarios (e.g., pathogen, treatment, and exposure route combinations) for consideration in the PATTP and QMRA.
- Develop guidance on how to review and evaluate the data and assumptions for PATTP and QMRA, including how to evaluate pathogen data from nonculture methods such as molecular methods, where viability and infectivity is a consideration.

The outcomes of the literature review will be used to develop a scope of work including specifications and requirements for the PATTP and QMRA tools that will be implemented by the Research Team in Phase 2 of the project. The tools will provide DDW with a consistent approach that has been developed and vetted by the experts involved with the TWG and Research Team. DDW will also be trained by the Research Team and TWG so that DDW can use the tools to assist them with DPR regulatory development. An overview of the QMRA and PATTP processes are shown in Figure A-1.

[1] The PATTP/QMRA tool—referred to as DPRisk—has the flexibility to model additional pathogens in these classes as well as other classes of pathogens. The information needed to evaluate additional pathogens includes: a) raw wastewater concentrations of the pathogens, b) knowledge of the reduction of the pathogen through treatment processes, and c) dose-response data.

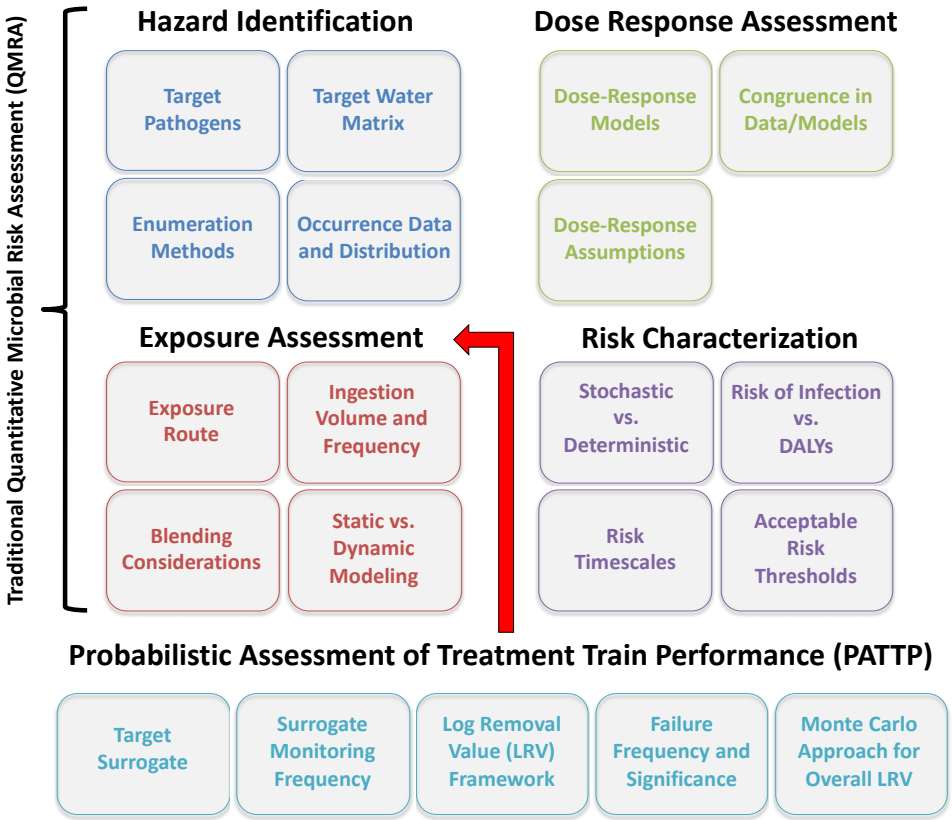

Figure A-1. Overview of the Steps Involved in Quantitative Microbial Risk Assessment (QMRA) and Probabilistic Assessments of Treatment Train Performance (PATTP).

A.2 Historical Context of QMRA and Risk-Based Targets

The primary goal of potable water applications is to provide drinking water that *reliably* protects public health. The two main groups of contaminants of public health concern are toxic chemicals and pathogenic microorganisms. At the concentrations found in municipal wastewaters, most toxic chemicals do not lead to a health impact after a single exposure, but rather require longer periods of chronic exposure to potentially exert a health effect. Brief periods of exposure to high or low concentrations of toxic chemicals are less relevant for understanding health impacts than the *average* lifetime concentrations. Pathogens, on the other hand, can initiate an infection after a single exposure and so represent an *acute* threat to public health[2]. As a result, treatment barriers must be consistently effective to reduce pathogen concentrations to acceptable levels.

One of the key moments in the history of public health was identifying the link between waterborne pathogens and human disease. Once understood, the water industry began using a bacterial standard to verify the microbial acceptability of drinking water: if the treated water was shown to have non-detectable levels of total coliform, it was deemed to be suitable for human consumption (NRC, 2004). With a treated water standard as the sole requirement, it was not necessary to quantify the *removal* of pathogens through treatment; it was sufficient to simply show that the treated water met the standard. Eventually, the scientific community realized that other pathogens—including enteric viruses and

[2] Many pathogens lead to acute infections that are characterized by a rapid onset of disease followed by a relatively short period of symptoms and then resolution. Certain pathogens, such as poliovirus and hepatitis C virus, however, may lead to chronic health outcomes.

protozoa—were more resistant to treatment than bacteria. Reliance on the coliform standard alone was deemed to be insufficiently protective. As a result, enteric viruses, *Giardia lamblia* cysts, and *Cryptosporidium* oocysts were added to drinking water regulations in the U.S. in the late 20th and early 21st centuries.

With the introduction of the new viral and protozoon pathogens, treated water monitoring was no longer capable of demonstrating adequate pathogen control: the acceptable levels of virus and protozoa were below those that could be detected with existing monitoring techniques (Regli et al. 1991; Macler and Regli 1993; Trussell et al. 2013). Instead, the new regulations required that a minimum degree of pathogen reduction through the treatment train be demonstrated, such that the treated water would achieve the low levels considered to be acceptable. One option for defining the microbial acceptability of potable water is to set limits on the risk of infection associated with its consumption. This risk target can then be used in QMRA in which experimental data are combined with mathematical models and statistical probabilities to estimate the required removal of a particular microbial hazard to be acceptable (Haas et al. 1999; World Health Organization, 2016).

Traditionally, QMRA has been used to estimate adverse outcomes and public health risks (Haas et al. 1999), and aid in risk management, risk communication, and decision making (Beaudequin et al. 2015; Petterson and Ashbolt 2016). One of the risk management strategies is to specify treatment requirements to ensure that source waters are adequately treated to reduce the concentrations of pathogens down to acceptable levels. Since the Surface Water Treatment Rule in 1989, risk-based treatment standards have been developed for drinking water and potable reuse (EPA, 1989; EPA, 1998; EPA, 2006; DDW, 2018). These standards include log-removal requirements for enteric virus, *Giardia*, and *Cryptosporidium* (V/G/C) of 4/3/2 for surface waters in the United States (U.S.) and 12/10/10 for potable reuse in California (and other states). While the specific pathogen treatment requirements needed to produce drinking water from surface water differ from those needed for potable reuse, both were developed with the same risk-based target in mind (i.e., 10^{-4} infections per year or an annual risk of 1 in 10,000 people). Given the link between treatment and risk, QMRA can help identify appropriate levels of treatment to achieve public health targets. Regulators use this information to establish treatment requirements that help to ensure that the risk-based targets are met.

Both processes include multiple steps that can be approached in different manners. The following sections a) describe the various inputs required for the evaluation of treatment train performance and QMRA, b) lay out the options for completing each of these steps, and c) provide guidance on how to consistently perform both PATTP and QMRA.

A.3 Influent Raw Wastewater Pathogen Concentrations

A.3.1 Pathogens to Include in QMRA and PATTP Evaluations

One of the key questions in undertaking PATTP/QMRA is, "What are the pathogens of greatest relevance?" One option is to focus on the pathogens whose reduction is mandated by existing regulations. Under EPA's Surface Water Treatment Rules, pathogens in drinking water are controlled by specifying log reduction requirements for three enteric pathogens[3]: enteric viruses, *Giardia* and *Cryptosporidium* spp. (EPA, 1989; EPA, 1998; EPA, 2006). These same three pathogen groups are regulated under California's potable reuse regulations for groundwater recharge and surface water augmentation (DDW, 2018). Many past PATTP and QMRA studies have used one or more of these

[3] The 1989 Surface Water Treatment Rule also provides protection against the growth of microorganisms in the distribution system by setting limits on the concentration of heterotrophic bacteria and *Legionella*.

pathogen groups (NRC, 1998; Ander and Forss 2011; Barker et al. 2013; Amoueyan et al. 2017; Chaudhry et al. 2017; Pecson et al. 2017; Soller et al. 2017a; Soller et al. 2018a).

Another strategy is to focus on pathogens that have the largest contribution to public health burden (Scallan et al. 2011) (Table A-1). From this lens, human *Norovirus* and pathogenic bacteria—including *Salmonella* and *Campylobacter* spp.—are also of interest. Past water reuse related QMRAs have included *Norovirus* (Ander and Forss 2011; Barker et al. 2013; Amoueyan et al. 2017; Chaudhry et al. 2017; Soller et al. 2017a; Soller et al. 2018a), human adenovirus (Soller et al. 2017a; Soller et al. 2018a), *Campylobacter jejuni* (Barker et al. 2013; Soller et al. 2017a; Soller et al. 2018a), and *Salmonella enterica* (Chaudhry et al. 2017; Soller et al. 2017a; Soller et al. 2018a).

Table A-1. Health Burden of Pathogens That Are Also Waterborne.
Source: Data from Scallan et al. 2011.

No.	Pathogen	Episodes	Hospitalizations	Deaths
1	*Norovirus*	20,796,079	55,825	569
2	*Giardia intestinalis*	1,121,864	3,289	31
3	*Salmonella* spp. (non-typhoid)	1,095,079	20,608	403
4	*Campylobacter* spp.	1,058,387	10,599	95
5	*Clostridium perfringens*	966,120	438	26
6	*Cryptosporidium* spp.	678,828	2,473	42
7	*Shigella* spp.	421,048	4,672	32
8	*Staphylococcus aureus*	241,188	1,063	6
9	*Toxoplasma gondii*	173,415	8,859	654
10	*STEC* non-O157	138,063	331	0

It should be noted that the appropriate selection of a smaller group of reference pathogens can obviate the need to directly measure a wider range of pathogens. For example, the oocysts of *Cryptosporidium* are both small (4-5 µm) and resistant to many chemicals compared to cysts of most other parasitic protozoa, making it the preferred reference pathogen to represent protozoa through separation processes (such as granular media filtration) and disinfection (including free chlorine, chloramine, and ozone). Consequently, setting treatment requirements based on the reduction of oocysts of *Cryptosporidium* provides a significant factor of safety for the removal of other protozoon pathogens that are either larger, more sensitive to disinfection, or both (e.g., *Giardia*). While both *Giardia* and *Cryptosporidium* are regulated pathogens, some recent studies have concluded that focusing on *Cryptosporidium* alone is sufficient because its smaller size and greater resistance to disinfection (Crook et al. 2013; Olivieri et al. 2016; Pecson et al. 2017). The same rationale was applied in the development of the treatment criteria for the 1989 Surface Water Treatment Rule – the use of virus and *Giardia* eliminated the need to also regulate bacteria, since the non-bacterial indicators are more resistant to treatment (Regli et al. 1991). Recent risk assessments have also confirmed that bacterial pathogens do not significantly contribute to overall risk relative to the other target pathogens.

The State Board has identified six critical knowledge gaps that must be addressed to support their DPR regulatory effort, with one gap related to the characterization of pathogen concentrations in raw wastewater (State Water Resources Control Board, 2016). As a result, the State Board is currently pursuing a pathogen monitoring campaign to develop an expanded dataset of raw wastewater pathogen concentrations (Table A-2). This second DPR research project (DPR-2)—undertaken by a TWG—has identified the following pathogens and surrogates for inclusion in this full-scale sampling campaign.

Table A-2. Pathogens and Surrogates Included in the DPR-2 Monitoring Campaign.

Pathogen / Indicator	Enumeration	Method
Enterovirus	Culture and molecular	EPA 1615
Adenovirus	Culture and molecular	Rigotto, C. et al. (2011) and Ko, G. et al. (2005)
Norovirus	Molecular	EPA 1615
Male-specific coliphages	Culture and molecular	EPA 1601 and 1602
***Giardia* cysts**	Microscopy	EPA 1693
***Cryptosporidium* oocysts**	Microscopy	EPA 1693

The pathogens and indicators included in the pathogen monitoring campaign include the three historical drinking water and potable reuse pathogens: enteric viruses, *Giardia*, and *Cryptosporidium*. The campaign will utilize traditional EPA methods for the enumeration of these pathogens, namely, microscopy-based methods for *Giardia* and *Cryptosporidium* (EPA 1693), and both cell culture and molecular methods for enterovirus (EPA 1615). While these enumeration approaches have pros and cons, using these techniques allows direct comparison of the new data with previous monitoring campaigns, many of which have used the same methods.

The campaign will also widen beyond the historically used pathogens to include a broader range of viruses evaluated with both culture (adenovirus) and molecular techniques (adenoviruses and noroviruses). Finally, male-specific coliphages will be used as a viral indicator and quantified with both EPA culture-based methods as well as a qPCR assay. Data from this study will be available to the DPR-1 TWG and Research Team for inclusion in the PATTP/QMRA.

TWG Recommendation:
The TWG recommends the evaluation of the following: (1) the existing drinking water pathogens (*Enterovirus*, *Giardia*, and *Cryptosporidium*) along with (2) a wider range of enteric viruses (namely, adenoviruses and noroviruses), and (3) a human viral indicator (coliphages). This group of pathogens and indicators represents the historically relevant pathogens along with an expanded set of contemporary and emerging pathogens. Furthermore, additional information on coliphage concentrations may be useful for PATTP as an indicator for the reduction of viruses through treatment.

A.3.2 Raw Wastewater Pathogen Data

As the starting point for the exposure analysis in the QMRA process, it is critical that estimates of reference pathogen concentrations represent what may occur in raw wastewater[4]. Assumptions that cause this dataset to be too conservative could result in treatment requirements that require unnecessary, costly infrastructure or operational features. On the other hand, assumptions that underestimate pathogen concentrations in raw wastewater could result in treatment requirements that are not sufficiently protective of public health. To carefully scrutinize pathogen estimates, the State Board has devoted one project, DPR-2, to developing quality data for pathogen concentrations in raw wastewater. This section will explore the following questions:

- What raw wastewater pathogen concentration data should be used?

[4] Multiple starting places may be selected for QMRA including raw wastewater or treated wastewater that has undergone primary or secondary treatment. Texas and Australia, for example, have selected secondary effluent as the starting place for their treatment requirements. In such cases, the pathogen concentrations in the secondary effluent would be the starting place for QMRA. In California's potable reuse regulations, all requirements have assumed raw wastewater as the starting place.

- How should raw wastewater pathogen concentration data be used?
- How should non-detect values in a dataset be handled?

A.3.2.1 What Raw Wastewater Pathogen Concentration Data Should Be Used?

Given the limited number of US-based studies of pathogens in raw wastewater, the work of Rose et al. (2004) is often used in QMRA studies (Amoueyan et al. 2017; Pecson et al. 2017). This Water Environment Research Foundation study evaluated raw wastewater concentrations of a number of pathogens (*Enterovirus*, *Giardia*, *Cryptosporidium*) and indicators (total and fecal coliform, *Enterococci*, *Clostridium perfringens*, male-specific and somatic coliphages). This data set has served as the basis for the crediting of pathogen removal through wastewater treatment plants engaged in potable reuse in California, and was used by the California DPR Expert Panel in their evaluation of DPR feasibility (Olivieri et al. 2016). While the Rose data have served as the historical pathogen dataset, methods have moved on since that study and the DDW has stated that they will no longer solely use that data as the basis for defining raw wastewater pathogen concentrations and assigning pathogen log reduction through treatment. This decision stems from a number of factors including the fact that the Rose dataset includes only 5-6 samples per treatment plant, which is fewer than the 20-24 samples that the State Board is now requiring for pathogen monitoring studies.

In the absence of a trusted and exhaustive dataset of raw wastewater pathogen concentrations or an agreed to process to select such data, it is difficult to know what data should be used. The QMRA process is sensitive to the assumptions made in each study for raw wastewater pathogen concentrations (Nappier et al. 2018) and various literature reviews have been performed or used to describe wastewater concentrations (Amoueyan et al. 2017; Chaudhry et al. 2017; Soller et al. 2017a; Soller et al. 2018a). However, what has not been well described is the inherent variation in reference pathogen concentrations (i.e., actual spatiotemporal variability) versus the uncertainties in their estimations.

The range in occurrence data in the literature could be attributed to several different factors including the methods used to enumerate pathogens, inefficient or poor method recovery, the size of the sewershed sampled from, the geographic location, the degree of water conservation within that geographic location, or the season samples were taken. For example, studies have predicted that the distributions of pathogens in very small communities may show much greater variability in pathogen densities. In large communities, the impact of outbreaks is dampened out and there is a relatively lower degree of contact between community members (Barker et al. 2013; Olivieri et al. 2016). Given the direct link between wastewater quality and public health in potable reuse scenarios, higher levels of treatment will be required for areas with higher raw wastewater pathogen concentrations and greater inherent variability in pathogen treatment performances.

Additionally, it should be noted that due to the difficulty of enumerating pathogens in raw wastewater, some studies have used pathogen concentrations from primary or secondary effluent. This choice also can impact the findings of QMRAs (Nappier et al. 2018).

As discussed above, the State of California is undergoing a research project (DPR-2) to gain a better understanding of the concentrations of reference pathogens present in raw wastewater. This research project will fill an important knowledge gap for potable reuse-related QMRAs. The pathogen monitoring being undertaken by the State of California as part of DPR-2 will be conducted in large California cities where agencies have expressed interest in pursuing DPR or are currently pursuing IPR.

TWG Recommendation

The TWG recommends that DDW use the raw wastewater pathogen data developed by DPR-2 TWG. The TWG anticipates that this dataset will include historic literature data in addition to the new data that will

be collected over the 12- to 18-month monitoring campaign that the State is undertaking from 2019 to 2021. The historical data that will be used in the dataset will have been scrutinized and filtered by the DPR-2 TWG to include data that meets the following criteria:

- Data from the US, Europe, Canada, or Australia
- Data for municipal wastewater (as opposed to industrial wastewater)
- Data collected after 2000
- Data collected with the newest methods available

The use of this dataset will ensure that treatment requirements for DPR are based on the best available raw wastewater pathogen concentration data. Furthermore, a large number of datapoints (>120) will be from California wastewater agencies whose pathogen concentrations have been enumerated with the updated standard operating procedure from DPR-2.

A.3.2.2 How Should Raw Wastewater Pathogen Concentration Data Be Used?

Collecting and compiling an appropriate dataset of raw wastewater pathogen concentrations for modeling is its own challenge, but it is followed by the question of how to use the data. In the past, treatment requirements have been determined using the peak concentration of the pathogen seen in wastewater (Hultquist 2016; Gerba et al. 2017). In the absence of a complete, trusted dataset, this was the approach most protective of public health, albeit potentially overly conservative. Selecting the peak pathogen concentration seen in the literature as the basis for determining treatment requirements may place an unnecessary burden on treatment systems—the odds of a peak concentration occurring are rare, yet systems are required to provide a very conservative level of protection at all times.

Other values for raw wastewater pathogen concentrations have been used in QMRA studies. Most agree that using an average concentration is not an appropriate assumption and not protective of public health due to the wide variability in pathogen concentrations that is typically observed (Gerba et al. 2017). Instead, studies have used a probability distribution to characterize raw wastewater pathogen concentrations. In some studies, minimum and maximum concentrations from the literature are used and assumed to fit a uniform or log uniform distribution (Soller et al. 2017a). However, other studies aggregate data from the literature and fit a distribution to the data using maximum likelihood estimation (MLE) (Pecson et al. 2017). The benefit of a probabilistic analysis using a distribution of data is the ability to capture a range of data and performance as opposed to singular estimates that may not be representative of the diversity in different sets of data (Olivieri et al. 2016). Typically, a Monte Carlo analysis is then used in QMRA, randomly selecting multiple samples from each reference pathogen's concentration distribution, simulating treatment performance (i.e., PATTP), and running the resulting concentration (or dose) through the dose-response model. The challenge is then to define the risk-based target as a percentile (say 95th percentile) for acceptability.

Generally, raw wastewater pathogen concentrations have been fit to a probability distribution, and typically the distributions have been modeled using a log-normal distribution (Rose et al. 1996; Koivunen et al. 2003; Lemarchand and Lebaron 2003; Barker et al. 2013; Chaudhry et al. 2017; Eftim et al. 2017) or gamma distribution (Ander and Forss 2011; Petterson and Ashbolt 2016), which lead to minor differences particularly if the relative standard deviations are less than one (Haas 1997). For example, in the Expert Panel Final Report on the evaluation of the feasibility of DPR, Olivieri et al. (2016) developed a lognormal distribution of the concentration of *Cryptosporidium* based on data from Rose et al. (2004) to use in their analysis.

TWG Recommendation

The TWG recommends that DDW use the dataset developed by the DPR-2 research project to develop distributions of raw wastewater pathogen concentrations. The distributions should be developed using MLE methods, the Akaike Information Criterion (AIC), or Bayesian Information Criterion (BIC). Multiple platforms including R, Matlab, and Crystal Ball have capabilities to perform distribution fitting. Using a distribution of raw wastewater pathogen concentration will allow DDW to understand the range of concentrations that are typically seen while still capturing extreme events on the tail ends of the distribution. Using the peak concentration is a conservative assumption that would result in conservative treatment requirements that may have significant impacts on the infrastructure and operational costs that would be required to pursue a DPR project.

A.3.2.3 How Should Non-detect Values in a Dataset Be Handled?

The occurrence of non-detects in a sample is affected by the source concentration, analytical sample size, and the analytical recovery profile for the sample matrix (Chik et al. 2018). When developing a dataset of raw wastewater pathogen concentrations, it is likely that some of the samples will yield a non-detect. A dataset that includes data that is either above or below the limit of detection is called a "censored" dataset. If the values are below the limit of detection (for which the true values of the data are unknown), the data are considered "left-censored." Left-censored datasets are common in environmental microbiology (Canales, R.A. et al. 2018). Traditional methods to address non-detects include substitution (replacing non-detects with a specific value) and omission (discarding the non-detect data), though those approaches can cause the data to be biased (Parkhurst and Stern 1998). In addition, non-detects can tell us something important about the dataset and can be used to help inform a probability distribution. Methods have been developed to utilize non-detect values (Helsel and Hirsch 2002; Helsel 2005).

In a critical review of how to handle non-detects in microbial datasets, Chik et al.(2018) summarized a few of the common practices:

- Omit the non-detects entirely
- Substitute the non-detects with the method detection limit
- Substitute the non-detects with half the method detection limit
- Assume the non-detects are zeros with random sampling error
- Use censored data techniques

Omitting the non-detects or substituting the non-detects are practices that result in biased distributions (Parkhurst and Stern 1998; Helsel 2005) and would result in overly conservative estimates of pathogen concentrations (Chik et al. 2018).

In a recent paper, Canales et al. (2018) evaluated five different approaches for handling low (10%) to severe (90%) left-censored data and determined that two methods relying on multiple imputation led to the lowest error and bias when compared to actual data. The approach has two steps: in the first, the uncensored data are used to estimate the parameters of a lognormal distribution based on MLE methods. The approach accounts for the fact that part of the dataset—i.e., the censored data below the limit of detection—are not included in the estimation when developing the parameters. As an example, Figure A-2 shows a left-censored dataset where approximately 25% of the values are below the limit of detection (LOD). The remaining values would then be used to estimate the lognormal distribution with MLE methods.

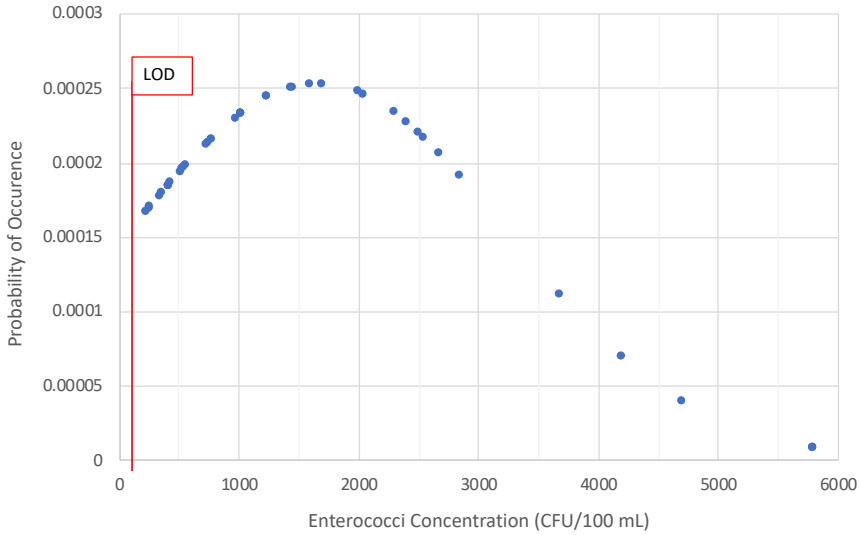

Figure A-2. Probability Plot of a Left-Censored Dataset of Environmental Enterococci Concentrations.

Once the distribution has been defined, the left-censored data can be assigned values through imputation. In brief, the modeled log-normal distribution can be randomly sampled until sufficient data below the LOD have been selected to replace the left-censored data. This "multiple imputation" approach provided the lowest error and bias compared to other approaches. Consequently, this approach may be useful particularly if the environmental datasets are well described by log normal distributions. It should be noted, however, that the TWG's recommendation is to use the modeled distributions rather than the discrete data points to more fully capture the range of possible values (see Section 3.2.2), in which case assigning values to the left-censored data is not necessary.

TWG Recommendation

The TWG recommends that non-detects in a raw wastewater pathogen concentration dataset be included in a probability distribution of the data using censored data techniques, such as the ones described in Canales et al. (2018). Censored data techniques have established methods and have been used in the industry in the past. The literature clearly shows that omitting the data or substituting the non-detect data with some version of the method detection limit biases the data in an inappropriate manner. While the censored data technique may be a conservative method for estimating microbial non-detects (Chik et al. 2018), the method of assuming that non-detects are zeros and applying random sampling error may not be conservative enough when considering the larger implications of using this dataset for a QMRA for direct potable reuse. The TWG would rather have slightly conservative estimates of raw wastewater pathogen concentrations and understand that there may be an inherent safety factor built into the analysis.

A.3.3 Enumeration Methods – Pros and Cons

Several analytical techniques can be used to enumerate pathogens in water samples, each with its own set of pros and cons. A description of three of the most commonly used techniques—culture assays, microscopy assays, and molecular assays—is provided in the following sections. Because the assays use different approaches for quantifying pathogen levels, the ideal assay for measuring the performance of a unit process may depend on the mechanism it employs for pathogen reduction (e.g., physical removal, disinfection, etc.), as described in Cangelosi, G.A. and Meschke, J.S. (2014). For any method, it is also important to consider method recovery (performance) and if the endpoint represents likely infectious pathogens.

A.3.3.1 Culture-Based Enumeration

Classical enumeration techniques rely on cell culture to determine the number of infectious pathogens present in a water sample. Cell culture quantifies the number of infectious pathogens by allowing them to reproduce in a population of host cells and cause an identifiable impact on the growth or morphology of those cells (e.g., cell death, changes in morphology, development of plaques, etc.). One benefit of cell cultures is that they assess the ability of a pathogen to perform **all** of the steps required for an infection, from 1) the initial identification and binding to the host, to 2) the entry of the pathogen or its genetic material into the host, to 3) the generation of an observable impact on the host. For this reason, cell cultures provide the greatest insight into the *infectivity* of the pathogen. This is an important criterion when the data are being used for risk assessment because only *infective* pathogens will impact public health. At this time, culture methods are the only technique capable of directly providing data on infectivity (Wigginton et al. 2018).

The major limitation of culture methods is that they have only been developed for a subset of the known human pathogens, and at that, do not detect all infectious forms. The organisms with developed culture methods may not be the most conservative indicators of risk or treatment performance. Furthermore, many methods require expensive equipment, highly-trained laboratory technicians, and extensive time periods to yield results. While bacterial assays are the most common and least predictive of the selected pathogens (Table A-2), viruses and protozoa typically require more complicated host cell systems typically involving tissue cultures (Wigginton et al. 2018).

Unfortunately, culture assays do not yet exist or are in their developmental stages for a number of important pathogens of public health concern. Norovirus, for example, is one of the key public health pathogens of concern for which a culture method has not yet been fully developed. Recently, new methods have been developed that may allow for the enumeration of norovirus by cell culture, though the methods remain in their infancy (Jones et al. 2014; Ettayebi et al. 2016). The use of these new methods is being explored in a current WRF 15-07 project. *Giardia* is another important pathogen for which there is no established culture method to estimate viability (Barash et al. 2017).

Culture methods have been developed for *Cryptosporidium*, though they are not as widely employed as the standard microscopy-based enumeration assays described in EPA 1623 and 1693 (Wigginton et al. 2018).

A.3.3.2 Microscopy-Based Enumeration

Pathogens can also be directly enumerated using microscopy-based methods. Typically, these methods require the concentration and purification of pathogens from water samples prior to visualization via microscopy. EPA 1623 and 1693 are two of the most frequently used microscopy-based methods that are used for the enumeration of *Giardia* cysts and *Cryptosporidium* oocysts. Microscopy methods benefit from the fact that they do not require the development of host cell cultures, and, therefore, have the potential to identify a wider range of pathogens. By eliminating the need for culturing, microscopy methods can also provide more rapid results than culture assays.

The negatives of microscopy include the general inability to examine pathogen infectivity, although vital stains (e.g., LiveDead™) provide an approximation. Consequently, the results from microscopy-based methods add further uncertainty when incorporated into risk assessments. As a conservative approach, it can be assumed that 100% of the pathogens enumerated microscopically are infective. Due to the physical constraints of visualizing small particles, light microscopy is also more common for the larger pathogens—such as protozoa and bacteria—and is not possible for virus-sized pathogens.

A.3.3.3 Molecular Enumeration

The use of molecular detection methods—such as quantitative PCR (qPCR) or digital PCR (dPCR)—has led to a large influx of data on pathogen concentrations in wastewater in the last two decades. The benefit of molecular methods is that they provide rapid, specific identification of pathogens without needing culture assays or microscopy. They accomplish this by targeting and quantifying the number of pathogen genomes present in the sample. Results of qPCR assays are typically reported in units of "genome copies" per mL or L. Typically, it is possible to identify target sequences in the pathogen's genome that are unique to that organism, allowing for highly specific identification. This specificity is an advantage of molecular techniques over cell culture and microscopy techniques.

The most important limitation of these methods is that the results are frequently difficult to relate to the number of infective pathogens present in the sample. Assumptions need to be made regarding what fraction of the genome copies in the sample are associated with infective pathogens (Haas 2020). For the last decade, multiple studies have documented the high degree of false-positives associated with PCR-based methods resulting from the presence of intact genomes within inactivated organisms (Nuanualsuwan and Cliver 2002; Pecson et al. 2009; Pecson et al. 2011; Wigginton et al. 2018; Hamza and Bibby 2019). This topic continues to be the focus of multiple research efforts. Mixed results are seen with modifications based on the use of propidium/ethidium monoazide to bind with inactivated pathogens' nucleic acid, so inhibiting subsequent qPCR for inactivated pathogens (Leifels et al. 2019).

For certain pathogens, however, molecular methods provide the only option for enumeration. One of the most important public health pathogens that can only be assayed through molecular methods is *Norovirus* (Wigginton et al. 2018). Challenges when incorporating *Norovirus* into QMRAs stem from the fact that there remains uncertainty regarding how to appropriately use molecular data in a QMRA, and which dose-response model or models are appropriate (NRC, 2012; Olivieri et al. 2016; Van Abel et al. 2017). The challenges of incorporating noroviruses into QMRA is detailed further in Section 5.2.1.

TWG Recommendation

The TWG recommends the use of culture-based enumeration methods—when available—as they provide the most straightforward indication of pathogen infectivity. In the absence of culture methods, both microscopy and molecular methods can be used to estimate pathogen concentrations, though any assumptions about the infectivity of the enumerated pathogens should be emphasized. If possible, efforts should be made to use the same pathogen quantification technique for both the raw wastewater and the development of the dose-response curves. The TWG recommends sensitivity analyses to evaluate the impact of different assumptions about pathogen infectivity in raw sewage and any deviations from the original feeding studies.

A.4 Treatment Train Performance

Several papers have developed methods to evaluate the treatment performance of DPR treatment trains using QMRA (Olivieri et al. 2016; Amoueyan et al. 2017; Chaudhry et al. 2017; Pecson et al. 2017; Soller et al. 2017a). However, there are different methods of evaluating performance that can yield varying degrees of associated risks. In this section, we describe different methods for assessing treatment performance.

A.4.1 Quantifying Pathogen Removal

In a DPR treatment train, there are many treatment processes most relevant to pathogen reduction. The key challenge is to quantify this removal/inactivation (termed 'pathogen reduction' in this review), which can be undertaken in several different ways.

Multiple studies have used human pathogens or microbial indicators to directly assess pathogen reduction performance (Olivieri et al. 1999). It is important to note that the direct measurement of pathogen or indicator reduction can provide perhaps the best estimate of the "actual" performance of the system. Direct measurements may not, however, be feasible for ongoing operational monitoring due to the long turnaround between the time when the water is sampled and when results are available. Due to the limitations of current pathogen monitoring methodologies, days to weeks may be needed to evaluate pathogen removal performance. These long delays can be problematic, particularly if the quality of the water needs to be monitored and verified on shorter timescales. Oftentimes, regulations require that unit processes be measured on an interval as frequent as once every 15 minutes, a constraint that limits the applicability of many microbial methods. In fact, the Expert Panel Final Report evaluating the feasibility of DPR suggests that all DPR systems have high frequency monitoring of surrogate constituents (Olivieri et al. 2016).

For this reason, it is important to differentiate between the "actual" level of pathogen removal and that which can be rapidly and continuously demonstrated. In lieu of direct pathogen measurements, surrogate water quality parameters are frequently used to provide a continuous evaluation of system performance. Combining data on microbial challenge studies with surrogate water quality parameters provides useful information on the relationship between the two measures (Zimmerman et al. 2016). Examples of surrogate use include turbidity to measure filter performance and disinfectant "CT" dose to quantify the degree of inactivation. Oftentimes, these surrogates have lower sensitivity (i.e., greater conservatism) than direct microbial methods, and thus may underestimate the actual level of public health protection that could be demonstrated in a microbial challenge study. Because they can provide a rapid and continuous demonstration of performance, however, surrogates are frequently used as the basis for the crediting of pathogen barriers.

Both of these methodologies for quantifying pathogen reduction have been used in QMRA studies. For example, Soller et al. (2017a) and Chaudhry et al. (2017) used pathogen reduction values from the literature to develop statistical distributions describing treatment process efficacy, or log removal values (LRVs). Whereas Pecson et al. (2017) calculated pathogen reduction from high-frequency surrogate monitoring data at a 1 MGD demonstration facility. The LRVs calculated in Pecson et al. (2017) were based on the California regulatory crediting scheme. The use of existing crediting schemes to evaluate treatment performance has also been used by Amoueyan et al. (2017) and Amoueyan et al. (2019).

In addition to pathogen reduction through treatment barriers, other factors affecting pathogen concentrations can be considered in a QMRA. Some studies assign pathogen decay rates based on values found in the literature that contribute to the reduction of pathogens through a treatment train (Lim et al. 2017) or through the environment (Amoueyan et al. 2017). Risk assessments have included varying the impacts of different assumptions (e.g., sensitivity analyses on storage and travel time in the environment) to quantify the benefits of IPR buffers relative to DPR. One issue with incorporating assumptions about die-off is that DDW generally does not recognize die-off in its crediting of pathogen reduction for potable reuse projects. For example, studies have evaluated the natural attenuation of pathogens in surface waters (Boehm et al. 2018), but in California no pathogen credit is assigned for the retention of purified water in the surface water augmentation projects. One notable exception is the crediting of virus inactivation at the rate of 1 log per month of retention time in the aquifer in groundwater recharge projects. While this is something that could be considered in the future, the fate of pathogens and rate of die-off through the environment are not yet well-understood. Moreover, this component of overall pathogen reduction will be insignificant in DPR applications that do not contain an environmental buffer.

A.4.4.1 TWG Recommendation

The TWG recommends that the PATTP/QMRA focuses on performance data that can be used to show regulatory compliance with pathogen reduction requirements. In most cases, this is synonymous with surrogate monitoring data that are required for existing crediting frameworks in lieu of direct pathogen measurements. Given the lower frequency of data collection, direct pathogen measurements may not capture the variability present in treatment performance. With conservative surrogate monitoring frameworks, a wider range of performance can be captured due to the high frequency of the monitoring. By developing the treatment requirements for DPR using similar high-frequency surrogate data, DDW will be able to directly compare the treatment requirements they develop to what a potential project may be proposing. In this way, there will not be the need for additional safety factors to be applied to treatment requirements.

A.4.2 Describing Performance

To effectively estimate risk, it is important to accurately characterize the operational performance provided by the treatment train. This means capturing periods when the treatment train is performing at or above its design criteria, but also periods of sub-optimal performance or overt failure when the train is failing to meet minimum requirements. The characterization of performance can be achieved in many ways, including through the use of point estimates or distributions of unit process performance. The selection of an appropriate distribution or point estimate is one of the most critical pieces of a QMRA (Nappier et al. 2018).

Generally, studies quantify performance through the use of either a) surrogates that relate pathogen reduction to indirect measurements of process performance (e.g., turbidity reduction), or b) through challenge studies in which pathogens or indicator organisms are directly measured into and out of a process. Once the data are collected, the performance of the unit processes are frequently described as either point estimates (i.e., single values of performance) or with distributions (i.e., ranges of values). Previous QMRAs have used the full gamut of possibilities to quantify and model performance. Site-specific surrogate performance data have been used to develop both point estimates (Amoueyan et al. 2017) and distributions of pathogen removal (Pecson et al. 2017). Both site-specific challenge studies (Olivieri et al. 1999) and ranges from the literature have been used (Chaudhry et al. 2017; Soller et al. 2017a) to develop performance distributions.

One principal benefit of site-specific data is that they provide the most accurate depiction of performance at a given site. At the same time, the data may be less applicable across facilities where differences in the treatment train design, operations, and maintenance may lead to significant variations in performance. In such circumstances, using performance data from the literature may provide a more broadly applicable view of performance. Nevertheless, this practice includes more variability than would be expected at any single facility (Smeets 2010). Caution should be used when aggregating performance data from the literature given that different jurisdictions may have different regulatory requirements that impact the shape and range of performance distributions. If an acceptable performance interval at Site 1 is unacceptable at Site 2, it would not be appropriate to use performance data from Site 1 to evaluate compliance at Site 2. For example, the UV disinfection of unrestricted-use recycled water in California requires a minimum dose of 100 mJ/cm^2 after granular media filtration. Using performance data from a facility with different UV dosing requirements would not be appropriate for aggregation into the dataset.

Several different distribution types have been used to describe performance of the unit processes. Chaudhry et al. (2017) used a combination of distributions (normal and uniform) along with point estimates to describe the performance of unit processes various treatment train. Soller et al. (2017a)

used uniform distributions based on minimum and maximum values seen in the literature for some treatment processes and used single point estimates for other treatment processes. In contrast, Pecson et al. (2017) used site-specific surrogate monitoring data from a year-long study and developed distributions using statistical methods to describe the performance of each unit process in a DPR treatment train. In some cases, point estimates of unit process performance have been used, particularly for processes whose performance cannot be easily measured or credited with existing frameworks, such as secondary treatment (Amoueyan et al. 2017).

To estimate the performance of the entire treatment train, Monte Carlo simulations are typically used to sample and aggregate the performance of the individual unit processes into distributions of the overall pathogen log reduction (Olivieri et al. 1999; Amoueyan et al. 2017; Pecson et al. 2017). The distribution of overall pathogen log reduction is then used in conjunction with raw wastewater distributions to create a distribution of treated water pathogen concentrations.

A.4.2.1 TWG Recommendation

The TWG recommends developing performance distributions based on the collection of high-frequency surrogate monitoring data that has been filtered appropriately to include the true variation in performance. The performance data should be equivalent to those specified under existing crediting frameworks to assign pathogen reduction credits (i.e., LRVs). For example, the translation from surrogate data (e.g., free chlorine CT) to pathogen reduction (e.g., virus inactivation) should be based on existing frameworks utilized in California (e.g., EPA free chlorine CT tables for virus inactivation). Once developed, the distribution of pathogen log reductions should be parameterized (i.e., modeled) based on vetted statistical methods. The distribution of treatment train performance should be developed using a Monte Carlo approach to sample from each of the individual unit processes making up the overall train.

The use of performance distributions based on site-specific surrogate monitoring will provide DDW with examples that can be used to develop treatment requirements. It will also allow DDW to begin to understand typical variability that may be seen in each unit process and develop an understanding of how much variability is acceptable while still being protective of public health.

A.4.3 Quantifying Failures

Multiple QMRA studies have shown that even short-duration failures can lead to a significant impact on the overall profile of risk (Haas and Trussell 1998; Pecson et al. 2017; Soller et al. 2018a). Given the importance of failures, it is perhaps surprising that there are few studies that have characterized the frequency, magnitude, and duration of failure events at wastewater and advanced treatment facilities (Ander and Forss 2011; Tng et al. 2015; Pecson et al. 2018).

Ander and Forss (2011) utilized a fault-tree analysis framework to describe the different types of failures that occur with common unit processes. The benefit of this framework is that it can be used in conjunction with a site-specific dataset to evaluate the treatment and risk impacts from a well-characterized set of failure assumptions. One of the limitations of this approach, however, is the raw data used to feed the assumptions in the fault tree. Amoueyan et al. (2017; 2019) utilized the Ander and Forss fault-tree analysis to model the failures in UF and pre-ozone processes. For other unit processes, such as UV, an arbitrary rate of failure was selected based on the lack of peer-reviewed literature information. In all cases, it was assumed that failures led to complete loss of treatment (i.e., failure led to 0-log inactivation).

The study by Tng et al. (2015) looked at the mechanical reliability of advanced water treatment facilities and concluded that only a small fraction of total mechanical failures would have an adverse impact on

water quality. From the data aggregated, they determined that two critical failures (i.e., those impacting water quality) would occur for every three unit processes in a treatment train per year.

Pecson et al. (2017) observed no failures impacting pathogen removal performance of the unit processes in their treatment train over a 12-month testing period. To account for rare failures (i.e., ones occurring at intervals longer than 12-months) and to add an extra layer of conservatism to the analysis, they also artificially introduced failure scenarios into the analysis. They assumed one critical failure per unit process per year (in line with other operating facilities and demonstration studies), and that all of the failures would result in full loss of pathogen reduction (i.e., 0-log LRV credit). The authors admitted that this catastrophic mode of failure is not likely to occur, but selected this assumption to be conservative. Finally, the duration of failure was varied to allow different assumptions about failure detection and response. The shortest period of failure was 15 minutes, i.e., the maximum amount of time in between measurements for a "continuously" monitored system. Failure assumptions extended up to 8 hours (one operational shift) and 24 hours. Soller et al. (2018b) also defined the probability, duration, and impact of various unit process failures based on actual performance data and then characterized public health risk. They noted that these short-duration (e.g., <15 minutes), off-specification events could drive annual risk in some instances.

Characterizing unit process interdependence is also important for understanding the impact of failures. Systems with a high degree of interdependence may experience cascading failures where a failure in one upstream unit process leads to the failure of downstream unit processes. Knowing whether a treatment train has high or low interdependence is critical for accurately modeling failure impacts. Pecson et al. (2017) showed that one DPR treatment train did not exhibit interdependence, allowing them to model failures as independent events. This is line with other studies as well (Haas and Trussell 1998; Olivieri et al. 1999). Other studies have modeled interdependence and the possibility of cascading failures. For example, Amoueyan et al. (2017; 2019) evaluated the impact of UF failures—and the resulting increase in TOC and UV absorbance—on downstream O_3 and UV processes.

A.4.3.1 TWG Recommendation

Based on the literature review, there is a general consensus that an understanding of process failures is an important knowledge gap for potable reuse. New information that becomes available to better characterize failures in terms of frequency, duration, and magnitude and the corresponding implications for pathogen reduction performance, should be evaluated and incorporated. In the meantime, failures should be introduced into the performance datasets, particularly if it was known that failures did not occur over the period which the data were collected. The absence of failures during shorter monitoring periods does not guarantee that rare failures will not occur over longer timescales.

The TWG also recommends further investigation into the possibility of cascading failures. While they were not observed in Pecson et al. (2017), they were modeled as a possibility in Amoueyan et al. (2017). Given the high degree of monitoring required for advanced treatment facilities, how likely is it that the failure of one unit process will not be detected before it impacts the next downstream process? For example, a failure in RO may impact the effectiveness of a downstream UV/AOP system by raising the UV absorbance of the RO product water. If the UV system is equipped with a continuous UVT meter that shuts the system down once the water quality drops below a minimum UVT, however, then how likely is it that the upstream failure would not trigger a failure response feature? This question should be addressed in conjunction with regulators at the State Board to determine whether this scenario should be modeled, or whether it can be addressed through existing data or future monitoring requirements.

A.5 QMRA Approach

Once the raw wastewater reference pathogens are selected, pathogen concentrations established, and treatment train performance modeled, a distribution of pathogen concentration in the effluent can be developed to characterize the exposure dose. Next, each reference pathogen's dose-response relationship is combined with the dose estimate to provide a distribution of risk to compare to the selected health-based risk target. This section will discuss each of these steps, as well as any other assumptions or decisions that are made in the QMRA process.

A.5.1 Pathogen Exposure

A.5.1.1 Exposure Pathways

Most studies have utilized 'static models' that focus on *primary* pathways of exposure, in particular the ingestion of pathogens in drinking water, and not on secondary exposure that may result by passing on infections by person-to-person or contaminated surfaces (fomites) (Pecson et al. 2017). Nonetheless, dynamic models have also been employed (Barker et al. 2013; Amoueyan et al. 2017). Further discussion on static versus dynamic models is given in Section 5.4.

TWG Recommendation

The TWG recommends that a static model focused on the primary pathway of exposure be used to develop treatment requirements. Secondary exposure to infected individuals will vary for different sectors of the public, and stricter treatment requirements would not protect against the secondary exposure pathways. Furthermore, secondary exposure has not been previously considered in the development of treatment requirements.

A.5.1.2 Drinking Water Pathogen Concentrations

In a treated water augmentation DPR scenario, the drinking water pathogen concentration would be equivalent to that of the DPR product water, or effluent (C_{eff}) of the advanced water treatment facility (AWTF). For the PATTP/QMRA evaluation, it is assumed that treated water augmentation will be the default scenario, i.e., modeling will not account for additional barriers in between the AWTF and consumers. C_{eff} can be estimated by adjusting the raw wastewater, or influent, concentration of the target pathogen(s) (C_{inf}) based on the overall treatment LRV, per the following equation:

$$C_{eff} = \frac{C_{inf}}{10^{LRV}}$$

Monte Carlo simulations can be used to generate both C_{inf} values (i.e., raw wastewater concentrations) and the overall LRV of the treatment train (from the aggregation of the individual unit process performance distributions) to develop a distribution for C_{eff}, the concentration in the final effluent.

TWG Recommendation

The TWG recommends that the approach discussed above be used to develop a distribution of effluent concentrations from the modeled AWTFs.

A.5.1.3 Drinking Water Consumption

QMRA studies have to make assumptions about the amount of water a person consumes each day in order to determine the exposure to a particular pathogen. There are two common approaches for modeling drinking water consumption:

- Modeling consumption based on a distribution:
  - Roseberry and Burmaster (1992);
  - EPA exposure factors handbook (EPA, 2011)

- Modeling consumption based on a point estimate:
  - 1 L per person per day (Olivieri et al. 2016)
  - 2 L per person per day (Amoueyan et al. 2017; Amoueyan et al. 2019)
  - 2.5 L per person per day, which represents the 90th percentile per capita water ingestion for adults based on the 2011 EPA distribution.

Other studies have conducted a sensitivity analysis to look at the impact of varying assumptions about drinking water exposure (Mons et al. 2007). Based on Pecson et al. (2017), the assumptions about drinking water exposure led to an approximate two- to three-fold difference in the overall risk estimates.

Different assumptions for drinking water consumption assumptions have been utilized in other risk assessments (Ander and Forss 2011). In a review of studies regarding drinking water consumption, Mons et al. (2007) concluded that in the absence of country-specific data, a Poisson distribution with an average of 3.49 glasses/day (with one glass being 250 mL) should be used as a conservative estimate. However, these more conservative estimates of drinking water consumption have been associated with more extreme conditions that are not representative of the municipal scale potable reuse envisioned for California (e.g., Barker et al. 2013) assumed 3 L per person per day in an Antarctic field station).

TWG Recommendation
The TWG recommends that the PATTP/QMRA tools developed by the Research Team include the ability to utilize different assumptions about drinking water consumption. At a minimum, the tool should include the ability to toggle between a distribution-based approach (Roseberry and Burmaster 1992; EPA, 2011) and a point-estimate approach (e.g., 1 L per day to up to 2.5 L per day in multiple aliquots per day).

A.5.1.4 Quantifying Exposure
The distribution of pathogens in C_{eff} can be converted to a distribution of doses based on the following equation:

$$Dose_{interval} = C_{eff} \times Volume\ consumed$$

Where C_{eff} is calculated as described above and "volume consumed" is based on the assumptions about consumption rate and the frequency of consumption events per day.

This approach was followed in Pecson et al. (2017) using a 15-min interval, and used in Soller et al. (2017a) based on a daily interval. Typically, this interval will be dependent on the frequency of the data available for treatment train performance.

Another consideration for drinking water consumption is the number of consumption events per day. Van Abel et al. (2014) showed that the risk of infection increased with the number of consumption events per day even if the daily intake volume remains consistent. However, given that in a distribution system, pulses of water will be delivered to different areas of the distribution system and each pulse may be diluted by a different pulse of water delivered at a different time, it is difficult to characterize the number of consumption events per pulse of water that leaves the treatment system and enters the distribution system.

TWG Recommendation
The TWG recommends that the dose be calculated at the same interval as the performance data are collected (e.g., every 15 minutes). In this way, the model will be consistently using the same time

interval throughout. The TWG recommends assuming that consumers are uniformly exposed to each interval of water produced by the treatment facility. For example, if the performance of the unit process was calculated hourly, and the total volume of water consumed per day was 2 liters, then each consumer would be exposed to 2 L / 24 intervals or 0.083 L each hour of the day.

A.5.1.5 Blending

Finally, an assumption must be made about the make-up of the overall drinking water supply. In evaluating the risk from DPR, it is important to note that many systems will continue to rely on existing and historical supplies (e.g., surface water), and will be supplemented with potable reuse supplies. Consequently, DPR supplies will frequently be blended with other water sources that will dilute the fraction of the potable reuse supply. Nonetheless, previous studies have assumed that the DPR water will be consumed unblended—i.e., without dilution from other supplies—since this provides the most conservative estimate of potable reuse exposure (Pecson et al. 2017; Soller et al. 2017a).

TWG Recommendation

The TWG recommends that DDW consider the impact of blending from a traditional water source (e.g., surface water) when developing treatment requirements. Raw water augmentation and treated water augmentation may have different blending scenarios that impact risk, and this should be taken into consideration.

A.5.2 Dose-Response Analysis

Dose-response relationships provide the link between exposure (e.g., from the consumption of an advanced treated effluent) and the probability of infection. Multiple dose-response functions are available for the pathogens of interest (Section 3.1), and multiple have been used in past QMRAs. The selection of the dose-response function can have a significant impact on the risk estimates (Messner et al. 2014; Schmidt 2015; Pecson et al. 2017; Soller et al. 2017a; Nappier et al 2018). Table A-3 summarizes some of the dose-response relationships used in recent studies.

Table A-3. Dose-Response Relationships Used for Various Pathogens in Recent QMRAs.

Pathogen	Dose-Response Model	Equation	Parameter Values	Used by
Adenovirus	**Exponential** (Crabtree et al. 1997)	$1 - e^{-rd}$	r =0.4172	Soller et al. 2018a; Soller et al. 2017a; Soller et al. 2017b
	Hypergeometric (Teunis et al. 2016)	$1 - {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 5.11 β = 2.8	Soller et al. 2018a; Soller et al. 2018b
Campylobacter jejuni	**Hypergeometric** (Teunis et al. 2005)	$1 - {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 0.024 β = 0.011	Soller et al. 2018a; Soller et al. 2018b; Soller et al. 2017a; Barker et al. 2013
	Beta-Poisson (Medema et al. 1996)	$1 - \left(1 + \frac{d}{\beta}\right)^{-\alpha}$	α = 0.145 β = 7.59	Van Abel et al. 2014; Soller et al. 2017b
***Cryptosporidium* spp.**	**Exponential** (EPA, 2006)	$1 - e^{-rd}$	r = 0.09	Soller et al. 2018a; Soller et al. 2018b; Pecson et al. 2017; Soller et al. 2017a
	Exponential (Barbeau et al. 2000; Zhang et al. 2012)	$1 - e^{-rd}$	r = 0.00419	Amoueyan et al. 2017; Chaudhry et al. 2017,
	Fractional Poisson (Messner and Berger 2016)	$P \times \left(1 - e^{\frac{-d}{\alpha}}\right)$	P = 0.737 a = 1	Soller et al. 2018a; Soller et al. 2017a; Pecson et al. 2017
	Beta-Poisson (Messner and Berger 2016)	$P = 1 - \left[1 + \frac{d}{\beta}\right]^{-\alpha}$	α = 0.116 β = 0.121	Pecson et al. 2017
	Exponential with Immunity (Messner and Berger 2016)		Values provided by M. Messner[1]	Soller et al. 2018a
Giardia lamblia	**Exponential** (Teunis et al. 1997)	$1 - e^{-rd}$	r = 0.0199	Soller et al. 2018a; Soller et al. 2018b; Soller et al. 2017a; Barker et al. 2013
Norovirus	**Hypergeometric** (Teunis et al. 2008)	$1 - {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 0.04 β =0.055	Soller et al. 2018a; Soller et al. 2018b; Soller et al. 2017a; Soller et al.

Pathogen	Dose-Response Model	Equation	Parameter Values	Used by
				2017b; Barker et al. 2013
	Fractional Poisson (Messner et al. 2014)	$P \times \left(1 - e^{\frac{-d}{\alpha}}\right)$	P = 0.72 a = 1106	Soller et al. 2018a; Soller et al. 2017a; Soller et al. 2017b; Chaudhry et al. 2017
	Weighted model (Soller et al. 2017b)			Soller et al. 2018a; Soller et al. 2017b
	Upper Bound – Hypergeometric (Teunis et al. 2008)	1 $- \ {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 0.04 β =0.055	
	Lower Bound – Fractional Poisson (Atmar et al. 2008; Atmar et al. 2014; Messner et al. 2014)	$P \times \left(1 - e^{\frac{-d}{\alpha}}\right)$	P = 0.72 a = 1106	
Rotavirus	**Beta-Poisson** (Ward et al. 1986)	$P = 1 - \left[1 + \frac{d}{\beta}\right]^{-\alpha}$	α = 0.253 β = 0.426	Pecson et al. 2017
Salmonella enterica	**Beta-Poisson** (Haas et al. 1999)	$1 - \left(1 + \frac{d}{\beta}\right)^{-\alpha}$	α =0.3126 β =2884	Soller et al. 2018a; Soller et al. 2018b; Soller et al. 2017a; Soller et al. 2017b; Chaudhry et al. 2017

d = dose

[1] 30,000 Markov Chain Monte Carlo parameter pairs were provided and used in the analyses

A.5.2.1 TWG Recommendation

The TWG recommends that the PATTP/QMRA tools developed by the Research Team include the ability to toggle between different dose-response functions and have the ability to enter user-defined functions. Specific recommendations for norovirus are provided in the next section.

A.5.2.2 Norovirus Dose-Response

Given its important public health burden, *Norovirus* is of great interest for both drinking water and potable reuse applications. One of the main challenges incorporating norovirus into risk assessments (and therefore into regulatory frameworks) stems from the fact that methods to assess norovirus infectivity remain elusive. While new human *Norovirus* culture methods show promise, they have not been developed sufficiently to assess infectivity of human noroviruses in wastewater and drinking water (Jones et al. 2014; Ettayebi et al. 2016). Consequently, *Norovirus* enumeration is currently limited to total viral estimations using molecular methods that provide quantification based on the number of genomic targets present in a sample[5]. The lack of correlation between genome copies and infectious units has been well-documented in the literature and is generally the largest impediment to the

[5] Different norovirus genogroups can be distinguished based on the selection of the primer and probe set.

application of molecular results into QMRA (Haas 2020). This issue is particularly problematic for the development of relevant dose-response functions for noroviruses.

Given norovirus' importance to public health, efforts have been made to work around the genome copy-to-infectious units (GC:IU) issue. For example, various challenge studies have been undertaken by exposing human volunteers to known doses of *Norovirus* genome copies. The data are then used to develop relationships between the probability of infection for exposure to known numbers of norovirus genome copies. In this framework, it is not necessary to characterize the ratio of genome copies to infectious units—as long as that ratio is constant, then characterizing the genome copies along in a sample is sufficient to predict the probability of infection.

One of the major limitations of this assumption, however, is that it remains unknown whether or not the GC:IU ratio that existed during the human challenge studies is identical to, similar to, or significantly altered in environmental matrices like wastewater and subsequent treatments. The human challenge studies have used either purified noroviruses that have been suspended in conditions amenable for archiving (high-protein veal infusion broth with bovine serum albumin), or freshly prepared stocks purified from the feces of infected individuals (Teunis et al. 2008; Seitz et al. 2011; Frenck et al. 2012; Atmar et al. 2014; Messner et al. 2014). To use the GC-based dose-response curves in potable reuse QMRAs, the GC:IU present during these feeding studies must be similar to the GC:IU ratios present in the raw wastewater. Confirming that this assumption is accurate is not straightforward.

The numerous conditions that can inactivate viruses have varying impact on the structure and integrity of the genome. Multiple studies have reported that the loss of infectivity does not correspond in a 1:1 manner with the loss in qPCR signals. In other words, intact genome copies remain enumerable by qPCR even after the viruses have been inactivated by treatment (Sobsey et al. 1998; Shin and Sobsey 2003; Duizer et al. 2004; Baert et al. 2008). This finding is predictable given that an intact genome is not the *only* requirement for virus infectivity – the virus must also maintain its ability to bind to its host cell and insert its genetic material within the host. These latter functions are not dependent on the genome, but on other viral components including the capsid and supporting protein infrastructure (Wigginton et al. 2012). Treatments that impair these non-genomic regions can also render viruses inactivated.

Consequently, it is not possible to confirm whether viruses that have been shed by infected human hosts and traveled to and throughout the wastewater treatment facility retain the same functionality than was present during the challenge studies. Some researchers have posited that most viruses detected by qPCR should be infective if they were recently excreted in feces (Gerba et al. 2017). In the absence of evidence, it appears likely that their exposure to the wastewater environment may also lead to the inactivation of at least a sub-population of viruses. Other studies have shown that virus survival may be impacted the presence of organic debris and the formation of viral aggregates. The impact of this inactivation on the GC:IU ratio remains a knowledge gap that is critical for correctly utilizing GC-based dose-response curves in QMRAs.

In the absence of such knowledge, QMRAs utilizing GC-based dose-response curves should evaluate a range of possible scenarios, ideally bookended by findings from the scientific literature (an example of this approach can be found in Haas et al. 2017). At one end, the most conservative assumption is that every genome copy represents an infectious virus. Studies that have assayed both GC and IU have shown that GC:IU ratios much greater than 1:1 can exist, which would ostensibly contradict this assumption. Some authors note, however, that this may be due to the fact that the culture assays are not enumerating all of the infectious virus (Gerba et al. 2017). A recent study of enteroviruses in the raw wastewater feeding the North City Water Reclamation Plant— assayed with both culture and molecular methods using EPA Method 1615—provides the most recent data on potential GC:IU ratios (Figure A-3).

Two notable points emerge: 1) the GC:IU ratio was consistently greater than 10,000:1 over the 21 raw wastewater samples collected during the yearlong campaign, and 2) significant variability of approximately four orders of magnitude was observed in this ratio, which ranged from 10^4:1 to 10^8:1. Even if the culture method were only detecting a fraction of the enteroviruses (e.g., 1-10%), the large magnitude of this ratio suggests that the GC:IU would still be significantly greater than 1:1. This suggests that the use of molecular data for raw wastewater concentrations in a QMRA may overestimate the concentration of pathogens in final drinking water and the public health risk, thereby leading to overly conservative treatment targets.

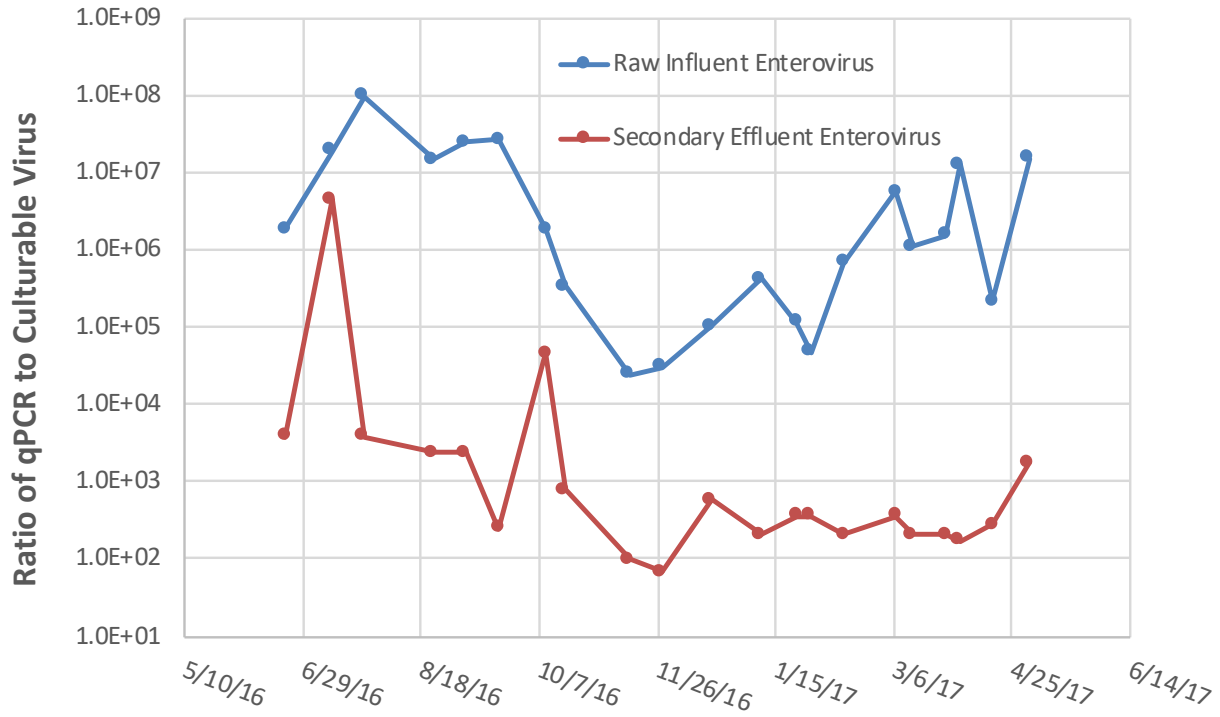

Figure A-3. Ratios of Genome Copies to Infectious Enteroviruses in the Raw Wastewater (Blue) and Secondary Effluent (Red) of the City of San Diego's North City Water Reclamation Plant.

TWG Recommendation

After evaluating the recent literature on this topic, Gerba et al. (2017) stated that "estimating ratios of infectious virus to genome copies detected by qPCR will probably never be known with certainty in the foreseeable future." Given the current state of the science, the TWG recommends that noroviruses (and other non-culturable pathogens, as needed) be included in potable reuse QMRAs using the GC-based dose-response curves. However, analyses must incorporate estimates of the uncertainty in the assumptions underlying its use. Recommendations from Van Abel et al. (2017) provide guidance to the use of the GC-based dose-response relationships regarding a) aggregation, b) susceptible populations, c) genogroup differences, and d) the use of multiple dose-response functions as part of the sensitivity analysis. The TWG also endorses the approach laid out by Van Abel et al. (2017) related to assumptions about infectious and noninfectious particles, namely, that this assumption be explicit in the reporting, and that a wide range of possible values be used when assessing risk based on GC-derived dose-response values. While the DPRisk tool does not include the ability to specify different GC:IU ratios, the impact can be evaluated by simply adjusting the raw wastewater concentration inputs. For example, if the unmodified dataset spans from 10^2 to 10^6 GC/L, adjusting this whole distribution down by an order of magnitude (i.e., to 10^1 to 10^5 GC/L) would account for a 10-fold increase in the ratio of GC:IU ratios. In

line with Van Abel et al. (2017), the TWG recommends that a range of assumptions from 1:1 to >10,000:1 be evaluated as part of the sensitivity analysis.

A.5.3 Risk Characterization

The two main risk targets used in the literature are a) the 10^{-4} infections per person per year and b) the 10^{-6} disability adjusted life years (DALYs) per person per year (Regli et al. 1991; World Health Organization, 1996; World Health Organization, 2006). Many studies undertaken in the US have used the 10^{-4} infections per person per year as the benchmark risk target (Chaudhry et al. 2017; Pecson et al. 2017; Soller et al. 2017a), whereas the DALY framework is more frequently used outside of the US (Barker et al. 2013). For acute gastrointestinal infections, the 10^{-6} DALYs represents a similar annual risk of infection (10^{-3}) as the 10^{-4} goal, particularly for organisms such as rotavirus and *Cryptosporidium* (World Health Organization, 1996; World Health Organization, 2006; Natural Resource Management Ministerial Council et al. 2008). Many studies report both values (Amoueyan et al. 2017; Pecson et al. 2017; Schoen et al. 2017). The study by Amoueyan et al. (2017) noted that the EPA LT2ESWTR does not achieve a single risk threshold (e.g., 10^{-4} annual risk) for *Cryptosporidium*, but instead a range of risks based on the concentration of oocysts in the source water and the required level of treatment for each bin classification.

Risk may be reported over several time periods including both annual risk and daily risk. Many studies will calculate the annual risk in order to compare to the common annual risk targets of 10^{-4} infections per person per year or 10^{-6} DALYs per person per year. Various starting points/timescales are used to annualize risk, although the overall approach is essentially the same. For example, one can develop risk estimates for intermediate time periods (e.g., daily, hourly, or 15-minute risk), and then aggregate those periods to account for the number of days, hours, or 15-minute periods in a year. Studies that annualize risk based on daily risk calculations frequently use the following equation:

$$P_{annual} = 1 - \prod_{n=1}^{365}(1 - P_{daily})$$

This methodology assumes that each exposure period results in a statistically independent risk of infection (Haas and Eisenberg 2001).

Shorter time periods—including 15-minute intervals—can also be used to aggregate 15-minute risk values into a single annual risk via the following equation:

$$P_{annual} = 1 - \prod_{n=1}^{35{,}040}(1 - P_n)$$

Where P_{annual} is a single annual probability of infection and P_n is a single 15-minute risk of infection. This approach was followed by Pecson et al. (2017).

Some studies also look at the cumulative risk of infection by simultaneously accounting for the risk of infection from all reference pathogens (Soller et al. 2017a; Soller et al. 2018a). This approach can provide greater accuracy if the risk from multiple pathogens is of the same order of magnitude. The cumulative risk can then be adjusted for the relevant timescale (e.g., converting from cumulative daily to cumulative annual risk).

$$P_{cumulative} = 1 - \prod_{n=1}^{i}(1 - P_i)$$

Where $P_{cumulative}$ is a cumulative probability of infection accounting for *i* reference pathogens simultaneously.

A.5.3.1 TWG Recommendation

To date, US regulations have utilized the "infections per person" framework over the DALY framework. The TWG recommends maintaining the use of the infections per person framework for consistency with previous drinking water and potable reuse regulations.

Based on input from the State Board in their *DPR Regulatory Framework*, the TWG is aware that the State Board would like to reduce the potential variability that could occur using an annual risk target by specifying a maximum daily risk objective. The acceptable daily risk would be calculated as the annual risk target of 10^{-4} infections per person per year divided by 365 days to yield a daily risk target of 2.7×10^{-7} infections per person per day. Meeting this daily risk target will ensure compliance with the annual risk target. The TWG recommends developing tools that allow for the evaluation of both the daily and annual risk values for comparison with their targets.

A.5.4 QMRA Process Assumptions

There are a few decisions regarding the mechanics of a QMRA that tend to vary between studies but are important to understand and keep consistent.

A.5.4.1 Static vs Dynamic Models

Many studies employ a static QMRA methodology (Olivieri et al. 1999; Pecson et al. 2017; Soller et al. 2017a; Soller et al. 2018a), while other studies use dynamic models (Eisenberg et al. 1996; Barker et al. 2013; Amoueyan et al. 2017). Static models are focused on the individual and assume there is a single exposure event (Soller et al. 2004). Dynamic models are non-linear, mathematical simulations of complex interrelated system elements, and one benefit of using them in potable reuse is that they allow modeling of temporal variability such as changes in population structure, water quality, and treatment performance. A dynamic model would also allow for direct system feedback linking disease prevalence within a community to pathogen concentrations in raw wastewater, for example. Table A-4, from Soller et al. (2004) below describes some of the key differences between a static and dynamic model.

Table A-4. Comparison of Static and Dynamic Risk Assessment.

Source: Soller et al. 2004.

Static Risk Assessment Model	Dynamic Risk Assessment Model
Static representation	Dynamic representation
Direct exposure (environment-to-person)	Direct and indirect exposure (environment-to-person and person-to-person)
Individual-based risk	Population-based risk
Assumes that the potential for secondary transmission of infection or disease is negligible.	Potential for secondary or person-to-person transmission of infection or disease exists.
Assumes that immunity to infection from microbial agents is negligible.	Exposed individuals may not be susceptible to infection or disease because they already may be infected or may be immune from infection due to prior exposure.
Dose-response function is the critical health component.	The dose-response function is important; however, factors specific to the transmission of infectious diseases may also be important.

TWG Recommendation

The TWG recommends the use of a static model. While a dynamic model is technically more rigorous, the number of assumptions required for a dynamic model is much greater than for a static model, and those assumptions might have greater uncertainty as well, potentially resulting in reduced accuracy of the QMRA. In some cases, static models can yield similar results to dynamic models (Soller and Eisenberg 2008). Furthermore, population dynamics and person-to-person exposures have historically not been considered when developing treatment requirements.

A.5.4.2 Stochastic vs Deterministic Models

Stochastic or probabilistic models incorporate probability distributions to provide an understanding of the full range of data that may be available. Deterministic models, such as the models originally used to develop the "12/10/10" framework, use point estimates and are restricted by the assumptions for each point estimate. However, sensitivity analyses can be used to inform the range of impact from each assumption.

The Expert Panel recommended the use of a probabilistic model to determine treatment requirements for DPR, and the State Board committed to evaluating probabilistic QMRA as a potential tool (Olivieri et al. 2016; State Water Resources Control Board, 2018).

TWG Recommendation

The TWG recommends the use of a stochastic model based on the input from the State Board and their Expert Panel. Without a stochastic model, conservative assumptions would always be made, and treatment requirements would likely be overly conservative.

A.5.4.3 Monte Carlo Simulations

Studies often utilize the Monte Carlo simulation approach within the QMRA process to create distributions of risk. The number of simulations that are done to create the distributions can affect the shape of these distributions, specifically the tail ends. Studies employing a Monte Carlo approach for QMRA have ranged from 1,000 simulations (Soller et al. 2017a; Soller et al. 2018a; Amoueyan et al. 2019) to 10,000 (Amoueyan et al. 2017) to 100,000 simulations (Chaudhry et al. 2017).

TWG Recommendation
The TWG recommends that the number of simulations done be numerous enough to capture rare events (over years). Without enough simulations, rare events may not get captured and will impact the tails of the distributions that are created—which are typically drivers in a QMRA (Pecson et al. 2017; Soller et al. 2018).

A.5.4.4 Unit Time Increments

QMRA will also require that assumptions be made about the time steps used for both the performance evaluation and the risk assessment. One option is to use 15-minute time-steps for the performance monitoring interval given the fact that potable drinking water applications are frequently required to provide "continuous" monitoring of process performance, where "continuous" is defined as no less than once every 15 minutes. Most surrogate monitoring systems are capable of measuring values at least every 15 minutes (e.g., disinfectant residual meters, turbidimeters, TOC and conductivity meters, etc.). A 15-minute interval has been used in previous QMRA studies (Pecson et al. 2017).

Another option is to use a daily interval. This time increment is used in numerous studies (Barker et al. 2013; Soller et al. 2017a; Soller et al. 2018a; Amoueyan et al. 2019). Daily values for treatment performance and water consumption are often more commonplace than shorter time intervals, although that trend is shifting with broad implementation of advanced treatment and online monitoring. One shortcoming of using a daily increment is the inability to understand the impact of short duration (15-min) failures on risk. On the other hand, some scenarios may not require the resolution of a 15-min timescale, so it is important to understand the implications of timescale on the specific scenario being modeled.

TWG Recommendation
The TWG recommends using a 15-min time increment for both the treatment train performance and risk assessment. Using a 15-min time increment will allow DDW to understand the impacts of short-duration failures and will be able to set treatment requirements and base regulations on the impact these failures may have on risk.

A.6 Linking Performance and QMRA Results

Ultimately, the goal of this research project (DPR-1) is to provide DDW with the necessary tools to implement a probabilistic method (QMRA) to evaluate and confirm the treatment requirements for DPR (Figure A-4). In this literature review, the TWG has discussed the multiple steps that are required to develop such tools and explored the various assumptions and decisions that can be made at each step. However, there are still decisions to be made by DDW about treatment requirements, surrogate monitoring for awarding LRVs, and acceptable levels of risk for DPR. The relationship between treatment performance and resulting risk is obvious; yet there are subtleties that DDW should consider when using these probabilistic methods to confirm acceptable levels of treatment.

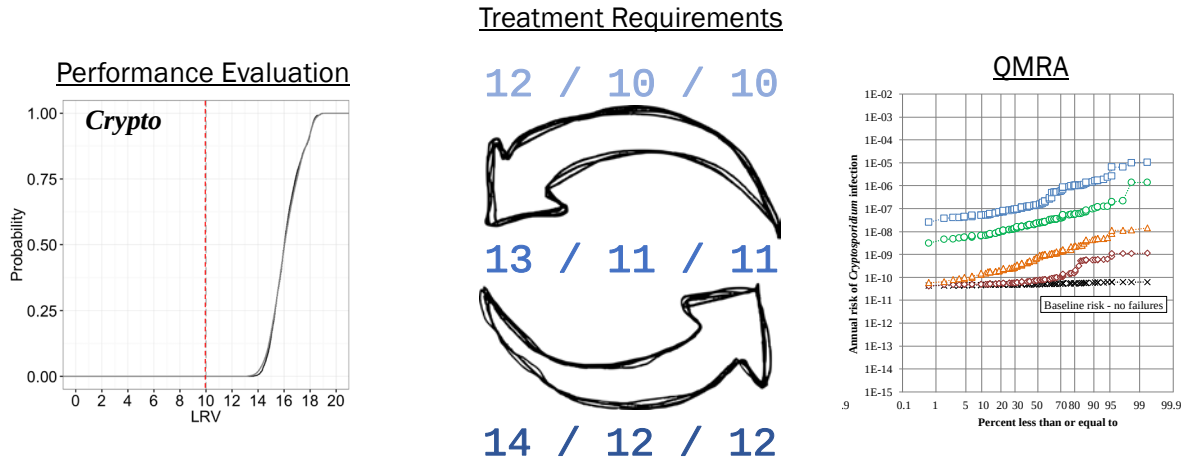

Figure A-4. Relationship Between Probabilistic Analysis of Treatment Train Performance and Quantitative Microbial Risk Assessment.

The nature of probabilistic methods is that they provide distributions. DDW will need to consider distributions of performance, either per unit process or per treatment train. These treatment performance distributions may have different variability depending on how they are operated. DDW should consider what amount of variability in treatment performance is acceptable. For example, if an MF process should be providing 4-log removal of *Cryptosporidium*, DDW might consider the following questions:

- Should the process be required to meet the 4-log requirement at the 95th percentile value or the 50th percentile (median) value or some other percentile?
- How wide can the distribution be? Or in other words, should there be multiple thresholds for performance (at the 5th percentile, 25th percentile, etc.)?
- What are the implications of off-specification conditions (e.g., LRV = 0)?

When evaluating the impacts of treatment performance, DDW should consider and understand how variability in treatment performance impacts risk.

In addition, DDW should consider the impact of treatment failures on risk. Considerations here include the magnitude, duration, and frequency of failures. By either imparting some failure into the model, or back-calculating the tolerance for failure in modeled scenarios, DDW can begin to understand the tolerance for treatment failures given different treatment requirements (Soller et al. 2017a; Amoueyan et al. 2019). Not only should treatment failures be considered, but DDW should take note of the number of treatment processes that should be required to meet the risk threshold during failure events. It has been demonstrated that an increase in the number of processes reduces the probability that a critical failure will occur (Pecson et al. 2015).

The tools developed from this research project should provide DDW with the ability to develop distributions of risk (either daily risk or annual risk or both). These distributions of risk will show at what percentage of the time the risk is below the selected risk threshold. DDW should evaluate the distributions of risk and understand how changes in treatment performance impact these distributions. Failures will have impacts on risk; as will the variability in treatment performance without failures. DDW will need to consider the following questions, and more, when developing treatment requirements:

- What is the tolerance for risk?
- Does the risk threshold need to be met at all times? Or at some percentile value?
- Should the risk compliance goal be some order of magnitude below the risk threshold to account for failures in treatment? In other words, should there be a safety factor incorporated to account for potential failures?
- Are the risk thresholds achievable with the selected treatment requirements?

The TWG suggests that DDW look closely at the risk curves for each pathogen as treatment requirements are developed. It is likely that for certain treatment trains, one pathogen will clearly drive the need for additional treatment either because it is present at higher concentrations in raw wastewater, or because it is harder to treat using the selected treatment processes. However, DDW should have standards for treatment for each pathogen that correspond to the associated risks for that pathogen. If a certain pathogen ultimately drives the risk for a particular treatment train, possibly requiring additional treatment, the QMRA for that combination of pathogen and treatment should be carefully reviewed to ensure that all assumptions are reasonable and that an appropriate level of conservatism has been considered.

Finally, as DDW begins to understand how treatment performance and failures impact risk, they will need to determine how to incorporate any conclusions into regulations. The tools provided here will provide more granularity than may be necessary to include in regulations. Rather than specify acceptable performance variability for each treatment process, DDW could choose to include a safety factor of some degree that would account for any variability that may occur in treatment.

A.7 Conclusions

This literature review has evaluated each step of the QMRA process and the TWG has provided recommendations at each of these steps for how to proceed. In some instances, the TWG has recommended one clear path (Section 3.1); however, for other steps of the QMRA, the TWG has recommended that DDW explore how different choices may impact the results of a risk assessment (Section 5.2). The goal is to develop a method that is consistent and uniform and appropriate for development of regulations on DPR in California. This literature review will aid the development of QMRA and PATTP tools that can ultimately be used by DDW and other stakeholders to inform the DPR decision-making and regulatory processes.

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APPENDIX B

Guidance Document for DPRisk

B.1 Project Definition and Background

In 2010, California Senate Bill 918 tasked the California State Water Resources Control Board (State Board) with evaluating the feasibility of developing water recycling criteria for direct potable reuse (DPR). The legislation subsequently launched a series of coordinated efforts:

- a DPR Expert Panel with 12 members from academia, industry, and government;
- a $6-million DPR Research Initiative (2012-2016);
- publication of a comprehensive summary report (Olivieri et al. 2016);
- legislation (Assembly Bill 574) seeking final DPR regulations by 2023; and
- an additional $1.4-million research initiative into remaining knowledge gaps for DPR.

As part of the $1.4-million initiative, the State Board commissioned a Technical Working Group and Research Team to develop a computer-based tool that could be used to quantify and characterize pathogen risk in DPR applications. This project became known as DPR-1 and culminated in the development of DPRisk—the focus of this Guidance Document. This tool was expected to encompass quantitative microbial risk assessment (QMRA) and probabilistic assessment of treatment train performance (PATTP). These processes are critically important in identifying the log reduction values (LRVs) necessary for adequate protection of public health from waterborne pathogens. This tool could ultimately be used by anyone interested in characterizing the performance of a DPR system, but it was specifically envisioned for regulators and other stakeholders to use this tool to inform the development of risk-based criteria for the design and operation of DPR systems in California.

B.2 Historical Context

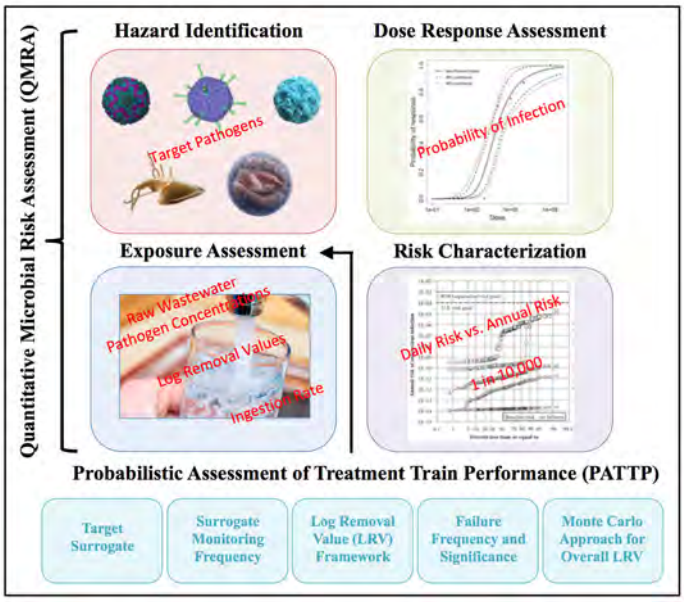
The primary goal of municipal drinking water treatment is to design, maintain, and operate drinking water systems that are redundant, robust, and resilient, thereby ensuring reliable protection of public health (Pecson et al. 2015). The two main groups of contaminants of public health concern are toxic chemicals and pathogenic microorganisms. Even in municipal wastewaters, typical concentrations of most chemicals will not exert an immediate health effect, but long-term exposure may result in adverse health outcomes. In other words, brief exposures to toxic chemicals may be less relevant for understanding health impacts than average lifetime concentrations, or *chronic* exposures. In contrast, pathogens can initiate an infection after a single exposure event—even when someone is exposed to only a single microorganism—and therefore represent an *acute* threat to public health. Scallan et al. (2011) identified the top 10 pathogens contributing to the public health burden in the United States in 2011 (see following table). This collection of bacteria, viruses, and protozoa provides a starting point for identifying priority pathogens in drinking water applications.

In the U.S., existing drinking water regulations target a small group of pathogens (*Giardia* and *Cryptosporidium*), broader pathogen groups (enteric viruses), and microbial indicators (e.g., total coliform and *E. coli*). Although routine monitoring of total coliform and *E. coli* in finished drinking water is feasible, the concentrations of bacterial, viral, and protozoan pathogens are often so low that routine monitoring is insufficiently sensitive to ensure adequate protection of public health (Macler and Regli, 1993; Regli et al. 1991; Trussell et al. 2013). Instead, mitigating pathogen risk requires an LRV approach, essentially establishing the minimum degree of pathogen reduction that must be demonstrated through

an engineered treatment train. For example, the U.S. Environmental Protection Agency's Surface Water Treatment Rules established baseline LRVs of 4/3/2 for viruses, *Giardia*, and *Cryptosporidium*, respectively (EPA, 2006a, 1998, 1989). More recently, the California Division of Drinking Water established baseline LRVs of 12/10/10 for viruses, *Giardia*, and *Cryptosporidium* in potable reuse applications employing groundwater augmentation.

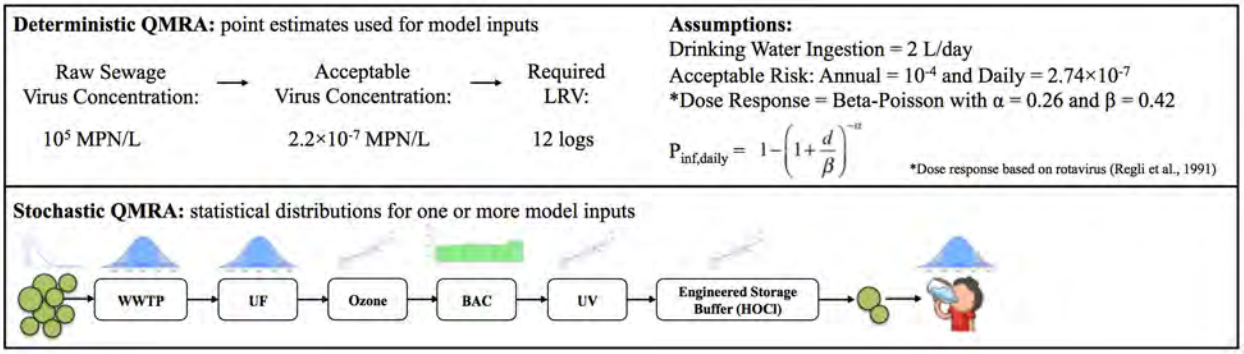
No.	Pathogen	Episodes	Hospitalizations	Deaths
1	Norovirus	20,796,079	55,825	569
2	*Giardia intestinalis*	1,121,864	3,289	31
3	*Salmonella* spp. (non-typhoid)	1,095,079	20,608	403
4	*Campylobacter* spp.	1,058,387	10,599	95
5	*Clostridium perfringens*	966,120	438	26
6	*Cryptosporidium* spp.	678,828	2,473	42
7	*Shigella* spp.	421,048	4,672	32
8	*Staphylococcus aureus*	241,188	1,063	6
9	*Toxoplasma gondii*	173,415	8,859	654
10	*STEC* non-O157	138,063	331	0

Pathogen LRV targets are often determined as part of a QMRA, in which experimental data are combined with mathematical models and relevant assumptions to estimate the required reduction of a particular microbial hazard (Haas et al. 1999; WHO, 2016). QMRA is often described as a 4-step process involving (1) hazard identification, (2) exposure assessment, (3) dose response assessment, and (4) risk characterization. In part because of the water industry's focus on broad implementation of potable reuse, the recent literature has made significant advancements in each step of the QMRA process, including integration of PATTP.

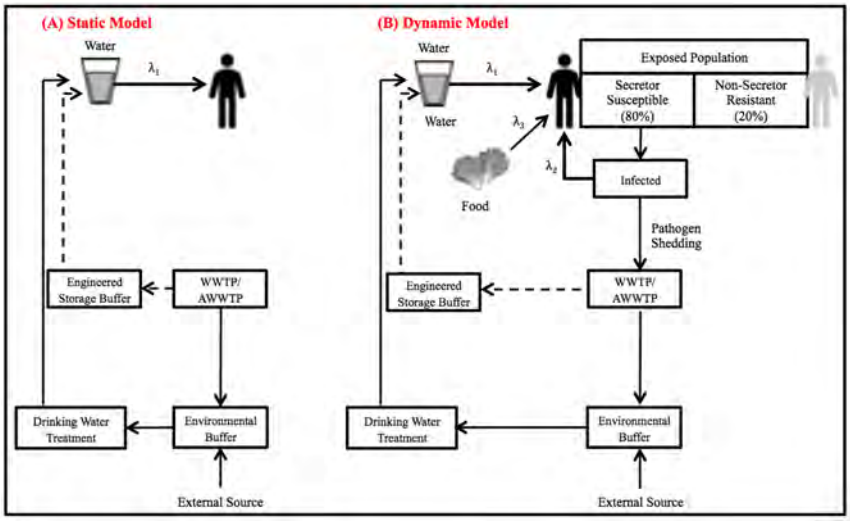


QMRA can be used to estimate risk for a specific scenario, or if a target risk is predetermined, QMRA can be used to identify the desired water quality or level of treatment (e.g., the overall LRV for a treatment train). QMRAs that involve fixed inputs are deterministic, but more sophisticated, stochastic QMRAs incorporate statistical probabilities (or distributions) to capture variability in datasets. This is often accomplished using a 'Monte Carlo' approach in which the distributions are sampled numerous times (e.g., 10,000 simulations) to capture a wide range of possible scenarios. These differences are illustrated in the following figure, which also shows how a deterministic QMRA was used to develop California's pathogen LRV targets for indirect potable reuse via groundwater augmentation. The basis for these regulations was an annual risk of 1 in 10,000 (or 10^{-4})—a benchmark that has been used extensively in the drinking water industry and is now the foundation of many potable reuse regulatory frameworks. One objective of DPRisk was to provide California regulators with

an opportunity to consider stochastic, or probabilistic, scenarios (e.g., PATTP) in the development of the DPR regulations.

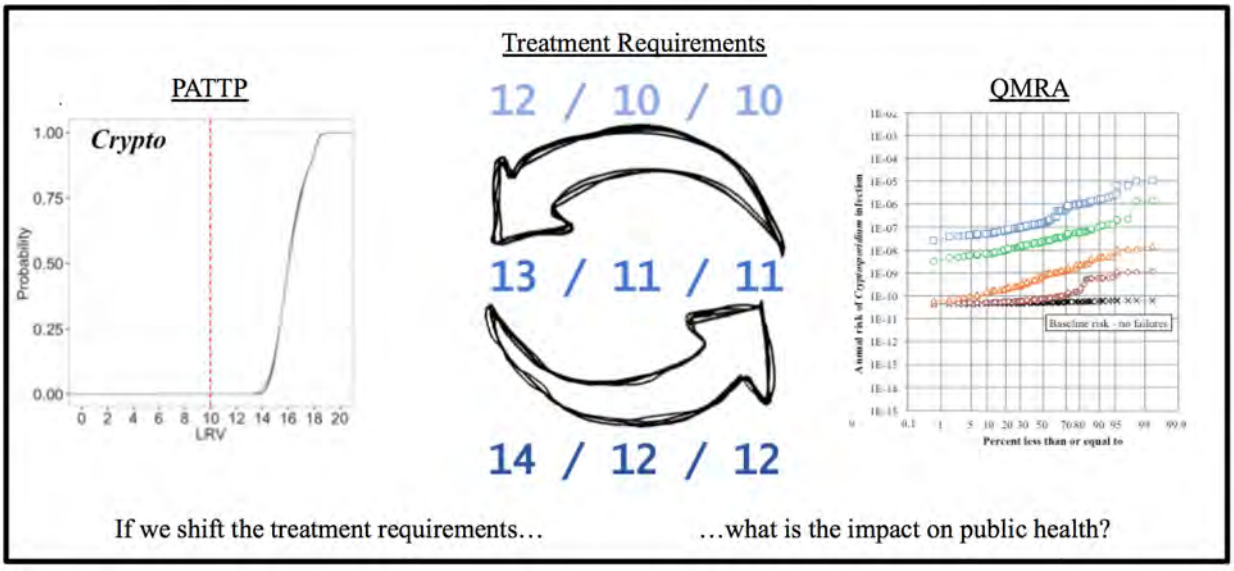


Another QMRA consideration is the appropriateness of a static vs. dynamic model. Static models are focused on the individual and calculate the probability of infection as a single exposure event with minimal (if any) time dependence or system feedback (Soller & Eisenberg, 2008). Dynamic models are non-linear, mathematical simulations of complex interrelated system elements and often consider multiple epidemiological states (e.g., susceptible, exposed, infected, diseased, recovered) and exposure pathways (e.g., person-to-person and person-to-environment-to-person) (Amoueyan et al. 2020). One benefit of using a dynamic QMRA in potable reuse is the ability to model temporal variability in population structure, water quality, and treatment operations and performance. Specifically, a dynamic model allows for direct system feedback linking infections and disease prevalence within a community to pathogen concentrations in raw wastewater (Amoueyan et al. 2020). There are situations in which dynamic modeling might be preferred (Soller & Eisenberg, 2008), but because dynamic models often require complex epidemiological inputs that may not be fully defined in the literature, static models are often assumed to be suitable and even preferred in many instances. Accordingly, static models dominate the literature (Amoueyan et al. 2017, 2019; Olivieri et al. 2016; Pecson et al. 2017; Soller et al. 2017, 2018a) and have been the primary source of information for the development of treatment requirements and regulations.



Even when focusing exclusively on static modeling, the process of performing a QMRA incorporating PATTP still involves multiple steps that can be approached in different ways and for unlimited scenarios. Moreover, the public can be exposed to a number of pathogens simultaneously, and the potable reuse industry includes an ever-expanding suite of treatment trains operating under various conditions. This results in countless modeling frameworks and, more importantly, wide-ranging conclusions that could potentially affect policy and regulatory and engineering decision-making. Therefore, it is often prudent

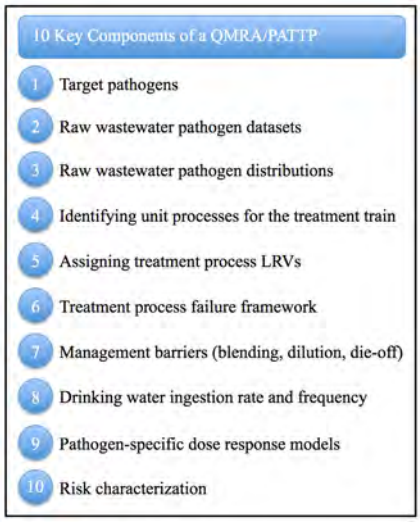
for stakeholders to adapt QMRA models to their own systems to account for site-specific factors that cannot be captured with a more generalized approach (Amoueyan et al. 2019).



A benefit of DPRisk is that it can be accessed by a wide range of users (e.g., students, researchers, consultants, regulators, and utility personnel) to generate direct QMRA comparisons using a single easy-to-use framework. But as noted earlier, the original intent of DPRisk and this Guidance Document was to facilitate the QMRA and PATTP processes so that critical stakeholders could evaluate various policy, regulatory, and treatment alternatives, either for generalized systems or more specific applications. For example, DPRisk could be used to answer any of the following questions:

- Are the specified risk thresholds achievable with a specific treatment train?
- What are the risk implications of a treatment process meeting a specified performance target at the 95th, 50th (median), or 5th percentile—or some other percentile?
- What are the risk implications of a treatment process operating with stringent oversight and tight tolerance vs. a treatment process operating with limited oversight and greater fluctuations in performance?
- What are the implications of an off-specification or failure condition with varying magnitude (e.g., 100% vs. 50% reduction in LRV), frequency (e.g., 3 times per year vs. 1 time per year), and/or duration (e.g., 24-hr event vs. 15-min event)?
- What is the tolerance for a certain operational condition (e.g., failure duration) before a risk benchmark is exceeded (e.g., annual risk of 10^{-4} or daily risk of 2.7×10^{-7}), and can this information help establish the required monitoring frequency for a critical control point (CCP)?

B.3 Overview of DPRisk



DPRisk was developed with significant flexibility to allow for its adaptation to a wide variety of modeling scenarios. The source code can be used as-is, either through the established web-based platform or on a local computer, or updated over time to reflect the industry's evolving understanding of pathogen concentrations, treatment reliability, epidemiological considerations, etc. The original version of the tool was developed using RStudio's freely available, web-based Shiny platform. RStudio provides open source software that allows the user to leverage the R statistical language (https://www.r-project.org/), which is increasingly being used for QMRA and the analysis of complex microbiological data (e.g., metagenomics applications). The free Shiny add-on (https://shiny.rstudio.com/) allows for interactive web-based user interfaces. The underlying code can be run on a variety of Unix platforms, Windows, and MacOS machines, or hosted on fee-based cloud services such as Shinyapps.io (https://www.shinyapps.io/). Additional details on how to access DPRisk can be found in the DPR Research section of the California State Water Resource Control Board's website at https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/direct_potable_reuse.html.

This DPRisk Guidance Document is divided into 10 key components of a QMRA/PATTP. These are summarized in the following sections, followed by a series of case studies to demonstrate use of the tool and how examples from the QMRA literature can be reproduced in DPRisk. For successful utilization of DPRisk, it is expected that the user has a general understanding of the QMRA process and is somewhat familiar with probability distributions. For more detailed information on the various aspects of QMRA/PATTP, the user should also refer to the literature cited throughout the Guidance Document.

B.4 Step 1: Target Pathogens (Hazard Identification)

B.4.1 Background

The first task in undertaking a PATTP/QMRA is known as hazard identification and involves identifying the pathogen(s) of greatest relevance to the application in question. Past studies have addressed a wide range of applications and pathogens, including recreational exposure to *Giardia* (Eisenberg et al. 1996); comparisons of norovirus exposure via drinking water, food, and person-to-person transmission (Amoueyan et al. 2020); and inhalation of aerosolized *Legionella* (Hamilton et al. 2019), among many other examples. In identifying target pathogens, one option is to focus on those with prescribed LRVs mandated by existing regulations. Under the U.S. EPA's Surface Water Treatment Rules, LRVs are specified for three groups of pathogens: 4-log enteric virus, 3-log *Giardia*, and 2-log *Cryptosporidium* removal and/or inactivation (EPA, 2006a, 1999, 1998). These same three pathogen groups were targeted by the original Groundwater Replenishment Reuse Regulations in the State of California (DDW, 2014)—commonly described as the 12/10/10 framework. Hence, many past PATTP and QMRA studies have focused on one or more of these pathogens (Amoueyan et al. 2017, 2019; Ander and Forss, 2011; Barker et al. 2013; Chaudhry et al. 2017; NRC, 1998; Pecson et al. 2017). Other studies have expanded the list to also include bacterial pathogens such as *Salmonella* and *Campylobacter* (Amoueyan et al. 2019; Soller et al. 2017; 2018a, 2018b).

It should be noted that strategic selection of a smaller group of reference pathogens can obviate the need to consider a broader range of targets. For example, *Cryptosporidium* oocysts are both smaller (4-5 µm) and more resistant to chemical disinfectants than many other protozoan parasites. Consequently, *Cryptosporidium* can be used as a conservative reference pathogen when estimating LRVs for a broad range of protozoan parasites in the context of physical separation (e.g., granular media filtration, low pressure membrane filtration) and oxidative disinfection processes (e.g., free chlorine, chloramine, and ozone) (NWRI, 2013; Olivieri et al. 2016; Pecson et al. 2017). This was the approach recommended by a panel of public health experts who proposed an alternative 12/10/9 LRV framework for enteric viruses, *Cryptosporidium*, and total coliform bacteria (as a surrogate for bacterial pathogens) (NWRI, 2013). In effect, it was assumed that achieving 10-log removal/inactivation of *Cryptosporidium* would adequately address risks associated with *Giardia*.

B.4.2 Integration into DPRisk

DPRisk focuses solely on primary transmission of waterborne enteric pathogens through oral ingestion of contaminated drinking water. The tool may have sufficient flexibility to consider other pathogens and exposure routes (e.g., incidental recreational ingestion), but the tool was designed with a specific focus on DPR applications. The Raw Wastewater Pathogen Concentration input (under Model Specification) includes *Cryptosporidium*, *Giardia*, and three enteric viruses (enterovirus, adenovirus, and norovirus) as the default target pathogens. This was intended to maintain consistency with California's potable reuse regulations and to allow the user to leverage newly developed datasets characterizing raw wastewater pathogen concentrations. Specifically, in conjunction with DPR-1, the State Board also sponsored a separate research team to conduct a comprehensive raw wastewater monitoring campaign. That project became known as DPR-2 (Pecson et al. 2021), and the results from that study are summarized in this Guidance Document (described in the next two sections). Finally, to provide greater flexibility, DPRisk also allows for a user-defined target pathogen.

B.5 Step 2: Raw Wastewater Pathogen Datasets

B.5.1 Background

For the exposure assessment in a potable reuse QMRA, it is common to use raw wastewater pathogen concentrations as the starting point. Due to difficulties in enumerating pathogens in raw wastewater or in an effort to dampen concentration variability, alternative reference points such as primary effluent, secondary effluent, or even the finished effluent from a conventional wastewater treatment plant have also been used (TWDB, 2015). Regardless of the starting point, if the pathogen concentration is not accurately represented (e.g., in terms of observed variability and magnitude), the resulting model output will not be representative of real-world conditions and may lead to erroneous conclusions. For example, overly conservative assumptions might result in unnecessary treatment requirements and costly infrastructure. On the other hand, underestimating pathogen concentrations (e.g., failing to consider seasonal spikes) might lead to engineering and regulatory decisions that do not adequately protect public health.

In the absence of a trusted and exhaustive dataset or an accepted process to select such data, it is difficult to know what data should be used. Recent literature reviews and QMRAs have developed or identified a number of viable datasets (Amoueyan et al. 2017, 2019; Chaudhry et al. 2017; Eftim et al. 2017; Hamilton et al. 2018; Soller et al. 2017, 2018a), but the available literature still fails to completely

capture inherent spatiotemporal variability. This is in part because pathogen monitoring is difficult and costly, particularly at the scale and frequency required to develop a full and accurate characterization of raw wastewater pathogen concentrations. Therefore, QMRAs often rely on limited datasets and/or simplifying assumptions, but the results can be highly sensitive to the assumptions made at this stage (Nappier et al. 2018).

Occurrence data are affected by myriad factors, including the methods used to enumerate pathogens and characteristics of the sample itself (e.g., sample type, geographic location, and sampling time). Variables linked to geographic location include the size of the sewershed, the types of flows into the system (e.g., industrial, commercial, residential), and even the degree of water conservation within the community. Pathogen concentrations in small communities or more isolated settings (e.g., building-scale reuse) are expected to show greater variability, while concentrations in larger communities likely experience a dampening effect due to the blending of diverse flows (Barker et al. 2013; Olivieri et al. 2016). With respect to temporal factors, pathogen concentrations might exhibit intraday, day-to-day, and seasonal variability, all of which are affected by use patterns, changes in the level of endemic disease within a community, and outbreak conditions.

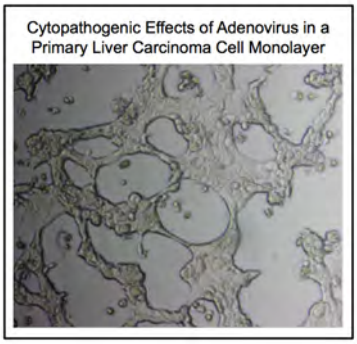
Rose et al. (2004) reported concentrations of multiple pathogens (enteroviruses, *Giardia*, and *Cryptosporidium*) and indicators (total/fecal coliform, enterococci, *Clostridium perfringens*, and coliphages) in the raw and treated wastewater of U.S. facilities. This dataset has been used as the basis for crediting pathogen reduction through wastewater treatment, as an important resource in evaluating DPR feasibility in California (Olivieri et al. 2016), and as part of numerous QMRA studies (Amoueyan et al. 2017; Amoueyan et al. 2019; Pecson et al. 2017). Realizing that a broader database of pathogen concentrations was necessary, the State Board commissioned a comprehensive wastewater sampling campaign over 14 months and in collaboration with the following agencies: San Francisco Public Utilities Commission, City of San Diego, City of Los Angeles Sanitation and Environment, Los Angeles County Sanitation Districts, and Orange County Sanitation/Water District. The targets, enumeration techniques, and methods are summarized below, and additional method details are included in Pecson et al. (2021). This study serves as the basis for the default pathogen data for DPRisk, as will be described later.

Pathogen / Indicator	Enumeration	Method[1]
Enterovirus	Culture; molecular	EPA 1615
Adenovirus	Culture; molecular	Ko et al. (2005); Rigotto et al. (2011)
Norovirus	Molecular	EPA 1615
Male-specific coliphages	Culture; molecular	EPA 1601 and 1602
Giardia cysts	Microscopy	EPA 1693
Cryptosporidium oocysts	Microscopy	EPA 1693

[1]Methods were optimized as part of DPR-2; final method details are available in Pecson et al. (2021).

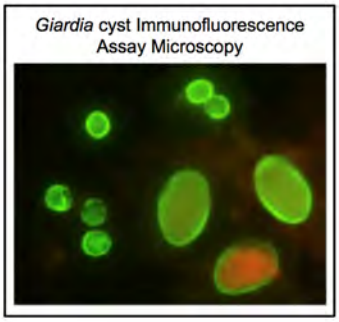
Before using occurrence data, it is important to understand differences in enumeration approaches, specifically culture vs. microscopy vs. molecular assays. Because these assays vary in their approach to detection and quantification, it is important to understand the implications of using certain datasets to characterize raw wastewater pathogen concentrations or to model the performance of a particular treatment process (e.g., physical removal vs. inactivation) (Cangelosi and Meschke, 2014). It is also important to consider critical details such as equivalent sample volume and method recovery, and from a public health perspective, it is important to understand how the method endpoint correlates with the dose response model used later in the QMRA.

B.5.1.1 Culture Methods



Classical virus enumeration techniques rely on cell culture to determine the number of infectious viral particles in a water sample. Cell culture assesses the ability of a viral particle to perform all steps necessary for an infection, including (1) initial binding to a host cell receptor, (2) entry of the virus or its genetic material into the host, (3) and use of the host cell metabolic machinery for viral replication. From a methods perspective, cell culture assays are designed so that viral replication within the population of host cells elicits an identifiable change in the growth or morphology of those cells (e.g., cell death, changes in morphology, or development of plaques). For these reasons, cell culture provides the most direct insight into the *infectivity* of a virus. This is an important criterion for QMRA because only infectious pathogens will generally impact public health. The major limitations of cell culture are that corresponding methods have only been developed for a subset of the known human pathogens, and the methods that do exist generally require expensive equipment, highly-trained laboratory technicians, and extensive incubation periods (Wigginton et al. 2018). Norovirus is a prime example of a target pathogen that cannot be cultured efficiently. There has been recent success in developing an infectivity method, but the required host cell system is highly complex and currently lacks reproducibility (Ettayebi et al. 2016; Jones et al. 2014).

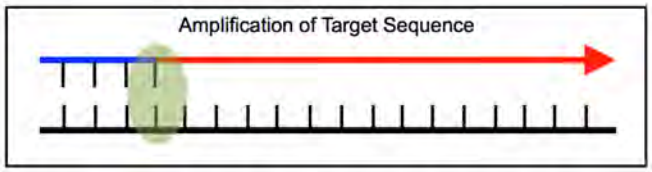
B.5.1.2 Microscopy Methods



With respect to the protozoan parasites, *Giardia* has no established cell culture method (Barash et al. 2017), and while *Cryptosporidium* has a cell culture method, use of microscopy is a more common approach. Quantification of *Giardia* cysts and *Cryptosporidium* oocysts is typically accomplished with EPA Method 1623 for water and EPA Method 1693 for wastewater, both of which involve concentration by filtration or centrifugation, purification with immunomagnetic separation, and detection and quantification with immunofluorescence assay microscopy. Because microscopy methods do not require preparation and infection of host cells, they are able to provide more rapid results. However, microscopy is hindered by a general inability to examine pathogen infectivity, which ultimately adds further uncertainty when the corresponding data are incorporated into QMRAs. As a conservative approach, it can be assumed that 100% of the pathogens enumerated by microscopy are infectious.

B.5.1.3 Molecular Methods

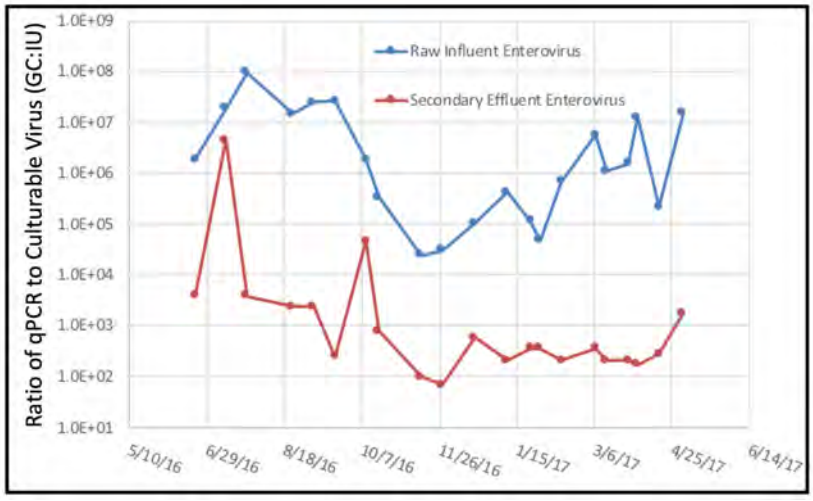
The use of quantitative polymerase chain reaction (qPCR) and now droplet digital PCR (ddPCR) has led to an influx of pathogen concentration data for various water matrices, including raw wastewater. This has been compounded by the renewed focus on wastewater-based epidemiology during the COVID-19 pandemic. Molecular methods provide rapid and specific pathogen detection—and even simultaneous detection of multiple pathogens—without the need for culture assays or microscopy. This is accomplished by identifying specific target sequences within genetic material (i.e., RNA or DNA) and quantifying the number of target genomes present in a sample. Pathogen concentrations are then reported in units of 'gene copies' or 'genome copies' (gc) per volume. The primary limitation of standard molecular methods is the inability to differentiate infectious vs. inactivated target microorganisms. In fact, molecular methods are sometimes



even unable to differentiate intact cells or viral particles from extracellular or 'free' nucleic acid. This is a key consideration when performing a QMRA because molecular data might significantly overestimate the concentration of infectious pathogens, potentially leading to overly conservative risk characterizations. Multiple studies have documented the presence of intact genomes within inactivated organisms (Hamza and Bibby, 2019; Nuanualsuwan and Cliver, 2002; Pecson et al. 2011, 2009; Wigginton et al. 2018). The use of integrated cell culture PCR (ICC-PCR) or qPCR (ICC-qPCR) (Gerrity et al. 2008; Ko et al. 2005) provides some indication of infectivity, and nucleic acid binding agents (e.g., propidium/ethidium monoazide) can also be used to differentiate genetic material in 'live' vs. 'dead' cells. However, the results from these methods are not always reliable (Leifels et al. 2019). For pathogens that have no established culture or microscopy methods (e.g., norovirus), molecular methods provide the only option for enumeration. But again, there remains uncertainty regarding how to appropriately use molecular data in a QMRA and whether certain dose response models should be used in conjunction with molecular data (NRC, 2012; Olivieri et al. 2016; Van Abel et al. 2017).

B.5.1.4 Attempts to Link Viral Molecular Data to Infectivity

Inactivation mechanisms have varying impact on genome structure and integrity. Studies have reported that loss of infectivity—or infectious units (IU)—during treatment does not necessarily correspond with a similar reduction in genome copy counts. In other words, genome copies may be enumerable by qPCR even after viruses have been inactivated (Baert et al. 2008; Duizer et al. 2004; Shin and Sobsey, 2003; Sobsey et al. 1998). This would theoretically result in higher GC:IU ratios with higher levels of treatment. This finding is predictable given that an intact genome is not the only requirement for virus infectivity. The virus must also maintain its ability to bind to a host cell and insert its genetic material—functions that are dependent on the integrity of the capsid, envelope (if applicable), and related proteins (Wigginton et al. 2012). Some researchers have suggested that viruses detected with molecular methods should be infectious if they were recently excreted in feces (Amoueyan et al. 2019; Gerba et al. 2017), though it appears likely that their exposure to the wastewater environment would lead to at least some level of rapid inactivation.



Based on the discussion above, it might appear that GC:IU ratios might be sufficiently close to 1:1 in raw wastewater to justify use of molecular data in QMRAs. However, there is historical evidence to the contrary. A recent study of enteroviruses in San Diego wastewater employed EPA Method 1615 and directly compared culture and molecular data. Two notable points emerged from the analysis: (1) GC:IU ratios were consistently higher for raw wastewater ($>10^4$:1) than secondary effluent ($>10^2$:1) and (2) wide ranges were observed for raw wastewater (ranging from 10^4:1 to 10^8:1) and secondary effluent (ranging from 10^2:1 to 10^7:1). Considering point (1), these findings contradict the earlier hypothesis that minimum GC:IU ratios occur in raw wastewater and then increase monotonically with treatment. Some authors note this may be due to systematic undercounting of infectious viruses when using culture methods (Gerba et al. 2017), but qPCR is also susceptible to interference and low recoveries, particularly in complex matrices such as raw wastewater.

Nevertheless, even if culture methods were only recovering a fraction of infectious enteroviruses (e.g., 1-10%), the high GC:IU ratios in the San Diego study suggest the true ratio would still be significantly greater than 1:1. ***Therefore, without a GC:IU adjustment, the use of molecular data in a QMRA may significantly overestimate pathogen concentrations in the final drinking water, leading to conservative treatment targets.***

At this time, correlations between molecular and culture data and the implications for utilizing dose response curves based on molecular data remain a critical knowledge gap, and that will likely be true for the foreseeable future (Gerba et al. 2017). In the absence of such knowledge, QMRAs utilizing genome copy data should evaluate a range of possible scenarios, ideally bookended by findings from the scientific literature. A comprehensive example of this approach can be found in Haas et al. (2017), which assessed sewer worker risk from Ebola virus in untreated hospital wastewater assuming GC:IU ratios of 1:1 (most conservative scenario) or a uniform distribution ranging from 10^3:1 to 10^4:1. Van Abel et al. (2017) also provides guidance on the use of molecular norovirus data in the context of pathogen aggregation, susceptibility within a population, genogroup differences, and the use of multiple dose response functions as part of the sensitivity analysis. Van Abel et al. (2017) notes that assumptions related to GC:IU ratios should be explicitly reported in a QMRA and that a wide range of possible values should be considered as part of a sensitivity analysis.

B.5.2 Integration into DPRisk

In the absence of system-specific data, it is recommended that DPRisk users rely on the raw wastewater pathogen datasets developed as part of DPR-2 (Pecson et al. 2021). The DPR-2 data were generated with methods that were specifically optimized for five California raw wastewaters, achieved a high detection frequency for all targets (94%), accounted for sample-specific recovery, and adhered to stringent QA/QC criteria. The resulting DPR-2 distributions also incorporated historical data from the literature that satisfied several criteria, namely inclusion of recovery adjustments and reported detection frequencies >50%. By directly comparing culture and molecular data for enterovirus and adenovirus, DPR-2 was also able to propose ranges and distributions for GC:IU ratios, which are summarized in the next section.

There may still be instances in which the user would prefer to use alternative data. Therefore, DPRisk allows for raw data inputs or user-defined parameters for common statistical distributions. DPRisk does not restrict the user in any way so it is important to use caution when selecting and incorporating a particular dataset and drawing conclusions from the tool output.

B.6 Step 3: Raw Wastewater Pathogen Distributions

B.6.1 Background

Once a pathogen concentration dataset is selected, it is important to understand how to incorporate the data into a QMRA. Potable reuse treatment requirements in the U.S. were historically based on what was believed to be peak pathogen concentrations in raw wastewater (Gerba et al. 2017; Hultquist, 2016). A similar approach was used in the development of the World Health Organization (WHO) and Australian guidelines for potable reuse and water recycling (see summary table below). At the time, this deterministic (i.e., point estimate) approach was believed to be the most protective of public health, particularly given the

Uncertainty: An input parameter characterized by a lack of data or an incomplete understanding. Can be reduced or eliminated with additional data or with improved methods.

Variability: An input parameter best described by a data distribution rather than a point estimate due to natural deviations over time and space. Cannot be reduced but can be better characterized.

uncertainty surrounding pathogen concentration data. However, some viewed this approach as overly conservative in that basing treatment requirements on peak concentrations might place an unnecessary burden on treatment systems. The odds of a peak concentration occurring are rare, yet under this framework, systems must provide a very conservative level of protection at all times. Other point estimates, such as the median or average, are often avoided because they do not adequately capture the *variability* in concentrations commonly observed (Gerba et al. 2017).

Framework	Virus Conc. (log_{10} per L)	*Giardia* Conc. (log_{10} per L)	Crypto Conc. (log_{10} per L)	Bacteria Conc. (log_{10} per L)
California[1]	5	5	4	N/A
WHO	4.3 (norovirus)	N/A	3.4	3.8 (*Campylobacter*)
Australia[2]	3.9 (rotavirus)	N/A	3.3	3.8 (*Campylobacter*)

[1] maximum observed; [2] 95th percentile

An alternative that is commonly applied in QMRAs involves the use of statistical distributions that have been fit to pathogen concentration datasets. This stochastic approach is more effective at capturing the entire range of possible outcomes for a particular estimate (Olivieri et al. 2016; Schoen et al. 2017). The distribution might be as simple as a uniform (or log_{10}uniform) distribution, which exhibits an equal probability for all values between a defined minimum and maximum. More complex distributions can be fit using maximum likelihood estimation (MLE), which can be accomplished with common mathematical/statistical software programs. With MLE, the parameters used to describe a dataset are obtained by maximizing a likelihood function—analogous to determining the slope and vertical intercept for a best-fit linear regression. In the QMRA literature, pathogen concentrations have often been represented by uniform distributions (Amoueyan et al. 2019; Soller et al. 2017), lognormal distributions (Barker et al. 2013; Chaudhry et al. 2017; Eftim et al. 2017; Koivunen et al. 2003; Lemarchand and Lebaron, 2003; Rose et al. 1996), and gamma distributions (Ander and Forss, 2011; Petterson and Ashbolt, 2016).

'Non-detects'—or left-censored data—are a common feature of many pathogen concentration datasets, with their frequency being dependent on a range of factors including the source water, equivalent sample volume, and analytical recovery (Chik et al. 2018). In some cases, non-detects are discarded or replaced with other values, such as the method detection limit (MDL), but such assumptions can result in bias affecting the conclusions drawn from a QMRA (Parkhurst and Stern, 1998). Non-detects provide important information about the dataset and should be used to inform the selection of an appropriate probability distribution (Helsel and Hirsch, 2002; Helsel, 2005). Chik et al. (2018) summarized several common practices for dealing with non-detects:

- Omit the non-detects entirely;
- Use an appropriate substitute (e.g., MDL, MDL/2, MDL/$\sqrt{2}$);
- Assume the non-detects are zeros with random sampling error; or
- Use censored data techniques.

Canales et al. (2018) tested several of the approaches listed above and also considered MLE, Kaplan-Meier (KM) estimation, and two forms of multiple imputation (MI). Each method was evaluated against varying degrees of censoring. For the MI approach, the study assumed (1) the entire dataset, including the left-censored data, followed a lognormal distribution or (2) the left-censored data followed a uniform distribution. After comparing against a known dataset, Canales et al. (2018) found that the two

MI approaches were superior in terms of estimating censored data and also resulted in slightly conservative risk estimates, which might be preferred for the development of potable reuse regulations.

B.6.2 Integration into DPRisk

The user first selects a target pathogen in the Raw Wastewater Pathogen Concentration section of the tool interface. The user then selects an enumeration method (i.e., culture, molecular, microscopy) and defines the distribution for the raw wastewater concentration (in organisms per L). The selection of an enumeration method is simply provided for user reference and is noted in the tool output, but it does not have any specific functionality.

As noted earlier, it is recommended that the user rely on the DPR-2 datasets, all of which were fit to lognormal distributions. For *Cryptosporidium*, *Giardia*, and enterovirus, data from DPR-2's 14-month sampling campaign were supplemented with data from the literature. Imputation was also used to assign values to left-censored data points. The resulting distributions are characterized in the following table, and additional details are available in the final report for DPR-2 (Pecson et al. 2021). These distributions are assumed to be broadly representative of municipal systems receiving primarily domestic wastewater, although there are some differences in comparison with the recent literature. For example, the enterovirus culture, adenovirus culture, and *Giardia* microscopy concentrations are considerably higher than the literature, while the enterovirus and adenovirus molecular data are generally lower. *Cryptosporidium* concentrations are generally in alignment with the published literature, and the norovirus GII molecular data are very consistent with the reported distribution for North America in Eftim et al. (2017). However, some distributions in Eftim et al. (2017) were higher due to geographic or seasonal differences, and the maximum reported concentration was 9.17 $\log_{10}$ gc/L, which may not be captured when using the recommended DPR-2 distribution.

Pathogen	Method	Units	Lognormal Distribution		Based on 10,000 Simulations		
			Base *e* μ	Base *e* σ	50th	99th	max
Enterovirus[1]	Culture	MPN/L	7.4	2.3	1.6×10^{3}	3.3×10^{5}	1.0×10^{7}
Enterovirus[1]	Molecular	gc/L	11.7	2.5	1.2×10^{5}	3.8×10^{7}	1.7×10^{9}
Adenovirus	Culture	MPN/L	6.4	2.3	5.8×10^{2}	1.2×10^{5}	3.9×10^{6}
Adenovirus	Molecular	gc/L	9.9	3.7	1.9×10^{4}	9.9×10^{7}	2.6×10^{10}
Norovirus GIA	Molecular	gc/L	8.8	2.3	6.4×10^{3}	1.3×10^{6}	4.2×10^{7}
Norovirus GIB	Molecular	gc/L	8.3	2.3	3.9×10^{3}	8.0×10^{5}	2.6×10^{7}
Norovirus GII	Molecular	gc/L	9.2	2.8	9.5×10^{3}	6.2×10^{6}	4.3×10^{8}
Giardia[1]	Microscopy	cysts/L	9.2	0.9	9.8×10^{3}	7.8×10^{4}	3.1×10^{5}
Cryptosporidium[1]	Microscopy	oocysts/L	4.4	1.4	8.0×10^{2}	2.0×10^{3}	1.7×10^{4}

Source: Pecson et al. 2021.
[1]Parameters reflect combined distributions (DPR-2+literature).

As explained on the next page, it is important to note that some datasets are described using a base *e* lognormal distribution, which is the DPRisk default, while others are described using a base 10 lognormal distribution (DPR-2 final report). Therefore, the values reported in the table differ by a factor of 2.303 from the values reported in DPR-2. Using published parameters for a base 10 lognormal distribution in DPRisk will significantly underestimate raw wastewater pathogen concentrations and the corresponding risk estimates. It is recommended that the user always verify that the raw wastewater concentration outputs from DPRisk match expectations based on the input distribution and original literature or data source.

Base e (ln) vs. Base 10 (log) Logarithms

Raw wastewater pathogen concentrations are often described by lognormal distributions. This raises an important distinction between base e (or natural) logarithms and base 10 logarithms. A lognormal distribution describes a dataset in which the *natural* logarithms of the data points are normally distributed about a mean (lognormal mean = μ) with a certain standard deviation (lognormal standard deviation = σ). For DPRisk, the default lognormal mean for *Giardia* is 9.2, which corresponds with a concentration of $e^{9.2} \approx 10{,}000$ cysts/L. The corresponding base 10 logarithm is 9.2/2.303 = 4.0, which corresponds with a concentration of $10^{4.0} = 10{,}000$ cysts/L. Two additional points:

The lognormal mean (μ) is not the same as the overall mean (m) of the dataset. Similarly, the lognormal standard deviation (σ) is not the same as the overall standard deviation (s) of the dataset. A general relationship between these terms is as follows, although MLE is still the preferred approach for identifying the best-fit parameters for a lognormal distribution:

$$\mu = \ln\left(\frac{m^2}{\sqrt{s^2+m^2}}\right)$$

$$\sigma = \sqrt{ln\left(\frac{s^2}{m^2}+1\right)}$$

A lognormal distribution will be skewed on an arithmetic scale but will exhibit a typical 'bell curve' on a log scale.

It is important to remember the distinction between base e and base 10 throughout the QMRA process. For example, treatment processes modeled with kinetics may often be described with base e rate constants, while LRVs are typically base 10. Care should be taken when modeling and interpreting data in this context. This Guidance Document will point out these nuances as needed.

In DPRisk, there are three ways to define the raw wastewater distribution:

1. Defining the parameters of a user-specified lognormal distribution. This is the approach when using the lognormal distributions from DPR-2 (i.e., the parameters summarized in the previous table). If a point estimate is desired—rather than a distribution—the user can specify μ as the natural logarithm of the point estimate concentration (or multiply a $\log_{10}$ concentration by 2.303) and specify σ as 0. For example, the maximum norovirus concentration reported in Eftim et al. (2017) was 9.17 $\log_{10}$ gc/L or 1.48×10^9 gc/L. The corresponding DPRisk input for μ would be $9.17\times2.303 = 21.2$ or $\ln(1.48\times10^9) = 21.1$, and σ would be 0.
2. Uploading a raw wastewater pathogen concentration dataset that is assumed to follow a lognormal fit. The tool will use MLE to identify the lognormal mean and lognormal standard deviation that best describe the dataset. The data file should be uploaded as a .csv file with a single column and column heading. Once the upload is complete, the tool will preview the first several rows of data to allow for user verification.
3. Uploading a .csv file that has already been curated with 10,000 raw wastewater pathogen concentrations, which will be used 'as-is' by the tool. If the user is interested in modeling a distribution other than DPRisk's default distribution (e.g., a uniform or gamma distribution), this option allows the user to generate a dataset outside of DPRisk and then upload the data into the tool (see Section B.17, Case Study 3). If fewer than 10,000 data points are provided, the tool will sample with replacement until 10,000 data points are generated.

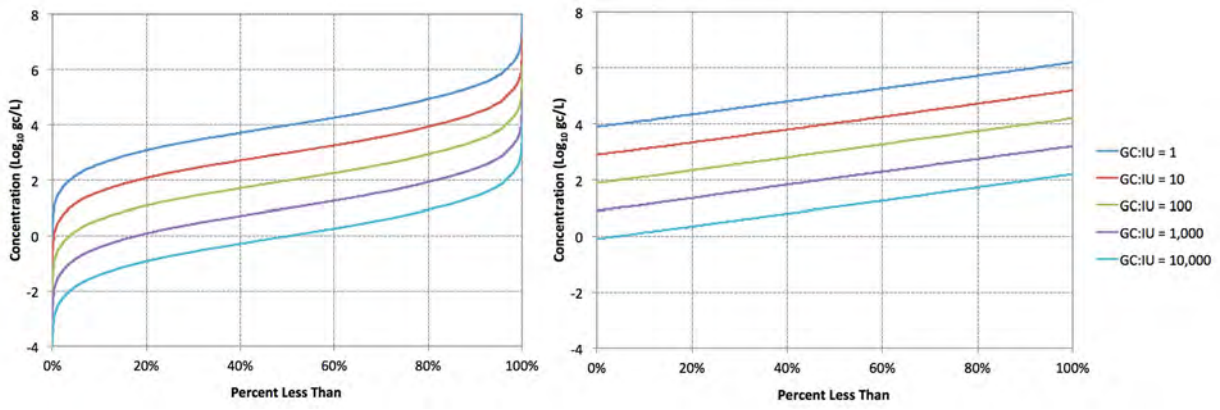
Again, DPRisk does not restrict the user in any way during parameter selection so it is important to use caution when characterizing raw wastewater pathogen concentrations. The final output from the tool will include a summary of descriptive statistics (e.g., mean, standard deviation, minimum/maximum,

critical percentiles) and a plot of the cumulative distribution. It is recommended that the user evaluate this output to ensure it matches expectations/realistic conditions and accurately describes the raw data (if available).

B.6.2.1 Adjusting Molecular Data for Infectivity

One final note is related to the use of molecular data, specifically in relation to the GC:IU ratio. For the aforementioned City of San Diego enterovirus study, the GC:IU ratios for raw sewage ranged from 10^4:1 to 10^8:1. The values for DPR-2 were considerably lower, with enterovirus ranging from 10^0:1 to 10^4:1 and adenovirus ranging from 10^0:1 to 10^5:1. While DPRisk does not include a feature for specifying a GC:IU ratio, the impact can be evaluated by adjusting the raw wastewater concentration inputs across multiple scenarios (i.e., a sensitivity analysis on GC:IU ratio) or by integrating the GC:IU ratios into an LRV framework. Three potential approaches are described below.

The first option is to run an initial modeling scenario with a baseline concentration distribution (e.g., a lognormal distribution with the default DPR-2 parameters). As will be described later, DPRisk's QMRA output includes a downloadable parameter set file containing 10,000 raw wastewater concentrations. The user can then divide each concentration by the desired GC:IU ratio. For example, a GC:IU ratio of 10^2:1 means that for every 100 genomes detected by molecular methods, only 1 represents an infectious virus. After dividing each concentration by 100, the 10,000 data points could be transferred to a new .csv file, which could then be used as a raw wastewater concentration input file for a subsequent modeling scenario. This process could be repeated, each time dividing the original concentrations by a new GC:IU ratio, until a sufficient range had been captured.



Examples of this iterative approach for norovirus are shown in the preceding figure, with the left side representing adjustments to a lognormal distribution (Eftim et al. 2017) and the right side representing adjustments to a $\log_{10}$ uniform distribution (Soller et al. 2018b). More details about $\log_{10}$uniform distributions are provided in Section B.17. One important note is that concentrations in the DPRisk input file should not be log-transformed; the data should be actual concentrations in gc/L. The preceding graphs only show $\log_{10}$-transformed data for clarity.

The second option allows the user to bypass manual adjustments to the raw wastewater concentrations. Instead of dividing each concentration in the DPRisk output file, the user can simply incorporate the GC:IU adjustment as a 'Management Barrier' LRV (management barriers are described later in Section 7). In DPRisk, simulated failures are not applied to management barriers so the GC:IU adjustment would occur regardless of the user inputs for the failure framework. With this approach, the user could select any of the management barriers and input (a) a point estimate LRV, (b) a uniform distribution for the LRVs spanning a desired GC:IU range, or (c) even a normal distribution for the LRVs describing observed

GC:IU ratios (e.g., from DPR-2). For any of these options, the values should be base 10, or $\log_{10}$ reductions. For (a), a GC:IU ratio of 100 would correspond with a point estimate LRV of $\log_{10}(100)$ or 2.0. For (b), the user could define the range for the uniform distribution to align with the adenovirus data from DPR-2 (i.e., 10^0:1 to 10^5:1), which would correspond with LRVs ranging from 0 to 5. For (c), the user could select a "zero-truncated normal distribution" for the management barrier LRV and define the mean and standard deviation with parameters derived from DPR-2, which are summarized in following table.

Management Barrier LRVs for GC:IU Ratio	Pathogen	Distribution	Min	Max	Distribution	Mean	St. Dev.
	Enterovirus	Uniform	0	4	Normal	2.12	1.02
	Adenovirus	Uniform	0	5	Normal	2.44	1.28

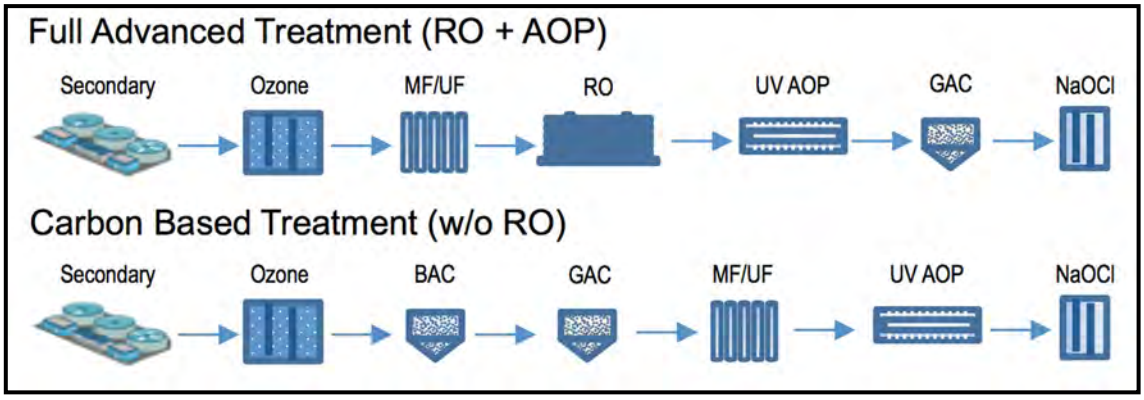
Source: Pecson et al. 2021.
All values are $\log_{10}$.

The third option is to simply adjust the input parameters defining the raw wastewater pathogen concentration. For example, when using a lognormal distribution, the μ, or lognormal mean, should be reduced by ln(GC:IU). So, for a μ of 9.2 (i.e., norovirus from DPR-2), a GC:IU ratio of 10 would require the input to be reduced by ln(10) or 2.3, resulting in a revised μ of 9.2 – 2.3 = 6.9. A GC:IU ratio of 100 would require the input to be reduced by ln(100) or 4.6, resulting in a revised μ of 9.2- 4.6 = 4.6, and so on. No change is required for the lognormal standard deviation (or σ). Again, the user should verify that the DPRisk output for raw wastewater pathogen concentrations matches expectations based on the simulated GC:IU ratio(s).

B.7 Step 4: Identifying Unit Processes for the Treatment Train

B.7.1 Background

The first step in developing the PATTP is to identify the unit processes comprising the treatment train of the advanced water purification facility (AWPF). To date, very few systems have been tested, permitted, and/or operated in a DPR configuration, although future DPR systems will likely be similar (perhaps with additional engineered barriers) or even identical to existing IPR treatment trains. Two hypothetical examples are shown below:



Once the unit processes are identified, the next step is to determine how the performance, or more specifically the LRV, of each unit process can be modeled. In some instances, unit processes have been modeled as point estimates, but several recent papers have incorporated PATTP into the QMRA (Amoueyan et al. 2017, 2019; Chaudhry et al. 2017; Olivieri et al. 2016; Pecson et al. 2017; Soller et al. 2017). The different approaches range from using uniform or normal distributions for observed

pathogen reduction (Amoueyan et al. 2019; Chaudhry et al. 2017; Soller et al. 2017) to statistical distributions based on surrogate metrics of treatment process performance (Pecson et al. 2017).

Directly measuring pathogen reduction by a unit process would provide the best estimate of actual treatment performance, but this is impractical due to method limitations. Instead, treatment performance is often estimated based on widely accepted correlations (e.g., disinfectant CT relationships) or the results of challenge tests with surrogate microorganisms. For example, spiking of MS2 bacteriophage is commonly used to estimate enteric virus reduction during disinfection or by media/membrane filtration. However, it is not currently practical to adapt this challenge study approach to operational monitoring, so other surrogate parameters that are conducive to online monitoring have been identified, validated, and implemented.

The literature provides a wealth of data that can be used to develop correlations between microbial challenge studies and a wide range of surrogate water quality parameters (Zimmerman et al. 2016). Surrogate metrics include turbidity removal or pressure decay tests for microfiltration (MF) and ultrafiltration (UF); reductions in electrical conductivity (EC), total organic carbon (TOC) concentration, fluorescence, sulfate, and strontium for nanofiltration (NF) and reverse osmosis (RO); and disinfectant 'CT' to quantify microbial inactivation. These surrogates often have lower sensitivity (i.e., greater conservatism) than direct microbial methods and thus underestimate the actual level of public health protection that could otherwise be demonstrated in a microbial challenge study. Nevertheless, surrogates offer rapid demonstration of performance, which is often required for crediting LRVs for pathogen barriers. DPR systems in particular are expected to be equipped with high-frequency monitoring of surrogate constituents, preferably in an on-line configuration, so that LRV credits can be tracked and awarded in near real-time (Olivieri et al. 2016).

B.7.2 Integration into DPRisk

The following table summarizes the unit processes available to the user in DPRisk and the default performance metrics for estimating pathogen reduction. The default performance metrics are provided for user reference and do not have any specific functionality in the tool. Specific relationships between the default performance metrics/surrogates and the final LRV point estimate/statistical distribution are described in greater detail in the next section. These defaults are not meant to comprise an exhaustive list of all treatment processes ever integrated into an AWPF; instead, the defaults focus primarily on treatment processes awarded LRVs under California's regulatory framework for potable reuse. Also, the descriptions/titles of the default treatment processes impart no specific functionality in the tool. They are simply provided for convenience in terms of treatment train characterization and LRV accounting. To allow for greater flexibility, the user has the option of specifying up to two custom treatment processes. Because IPR and future DPR systems will likely include some degree of blending and storage or travel time, the tool also allows for integration of an environmental or engineered storage buffer that can be used to simulate blending, dilution, and pathogen die-off. This will be discussed in greater detail in Step 7: Management Barriers.

Unit Process	Typical PATTP Approach or Metric
Secondary Biological Treatment	Point Estimate or Statistical Distribution
Membrane Bioreactor (MBR)	Statistical Distribution or WaterVal Framework
Ozone (Pre-Ozone and Post-Ozone)	Ozone CT
Biological Activated Carbon (BAC)	None
Membrane Filtration (i.e., MF or UF)	Surrogate-based LRV (e.g., PDT, Turbidity)
Reverse Osmosis (RO)	Surrogate-based LRV (e.g., EC, TOC, FI, Sr, Sulfate)
UV/Advanced Oxidation Process (AOP)	UV Dose
Chlorine (Pipeline and Contactor)	Free Chlorine CT
Coagulation/Flocculation/Sedimentation/Filtration	Turbidity
Custom Process 1	N/A
Custom Process 2	N/A

CT = concentration × time, EC = electrical conductivity, FI = fluorescence intensity, HRT = hydraulic retention time, PDT = pressure decay test, Sr = strontium, TOC = total organic carbon.

B.8 Step 5: Assigning Treatment Process Log Reduction Values

B.8.1 Background

To effectively estimate risk, it is important to accurately characterize the operational performance of the treatment train. This means capturing periods when the treatment train is performing at or above its design criteria, but also periods of sub-optimal performance or overt failure when treatment is failing to meet minimum requirements. The characterization of performance can be achieved in many ways, including through use of point estimates or distributions of unit process performance. The selection of an appropriate distribution or point estimate is one of the most critical pieces of a QMRA (Nappier et al. 2018), and it is important to consider whether the PATTP should be based on site-specific data or aggregated data across a number of studies and/or sites.

The use of site-specific data might not be appropriate when generalizing risk across a broad range of scenarios and locations, while the more generalized approach may not capture subtle differences in treatment train design, operations, and maintenance at a specific facility. This can lead to significant variations in performance and risk characterization (Smeets, 2010). In fact, jurisdictions often have different regulatory requirements that impact the design and operational criteria of a given treatment process. The use of site-specific data is warranted when seeking the most accurate depiction of performance and risk at a given location, particularly when the site adheres to strict operational performance criteria to maximize public health protection.

B.8.2 Integration into DPRisk

The user defines the LRV framework in the Treatment Train section of the DPRisk interface. DPRisk does not include any default performance data or LRV estimates because treatment processes are often operated under a wide range of conditions. In the absence of default settings, it is recommended that users rely on established disinfectant CT relationships or performance distributions based on high-frequency surrogate monitoring data from pilot- and full-scale potable reuse systems. Many examples are provided in the QMRA literature (Amoueyan et al. 2019; Chaudhry et al. 2017; Soller et al. 2017, 2018a, 2018b). In addition, published data from the North City Demonstration Pure Water Facility are publicly available and are also incorporated into Case Study 2 (Pecson et al. 2017). For the City of San Diego case study, translations from surrogate data (e.g., TOC reduction by RO) to pathogen reduction (e.g., virus LRV) were based on the existing potable reuse regulatory framework in California. Coupled

with a Monte Carlo approach, these relationships can be used to characterize expected variability in treatment process performance and pathogen LRV.

DPRisk includes the following three options to characterize treatment performance:

1. The user has the option of characterizing the performance of individual processes.
2. The user can specify an overall LRV point estimate for the treatment train.
3. The user can upload a data file curated with 10,000 LRVs for the overall treatment train, which will be used 'as-is' by the tool. If selected, the data file should be a single-column .csv file with a column header. This option is useful if the user would like the overall LRVs to follow a specific distribution or to sample the observed performance of a specific system. If fewer than 10,000 data points are provided, the tool will sample with replacement until 10,000 data points are generated.

For option (1), each of the following is available for individual treatment processes:

1. The user has the option of specifying the parameters of a uniform distribution (i.e., minimum and maximum), zero-truncated normal distribution (i.e., mean and standard deviation), or inverse Gaussian distribution (i.e., μ and λ). These were selected as defaults in part because they were some of the more common distributions reported in the QMRA literature. For alternative distributions, see option (3).
2. The user can specify an LRV point estimate for the treatment process in question.
3. The user can upload a data file curated with 10,000 LRVs for the treatment process in question, which will be used 'as-is' by the tool. If selected, the data file should be a single-column .csv file with a column header. This option is useful if the user would like the LRVs to follow a statistical distribution that is not included in DPRisk's default settings or to sample the observed performance of a specific treatment process. If fewer than 10,000 data points are provided, the tool will sample with replacement until 10,000 data points are generated.

To generalize the underlying code for DPRisk, it was necessary to limit user input to LRVs rather than trying to incorporate the myriad process-specific surrogate parameters. In some cases, the user may only have surrogate performance data available, such as free chlorine CTs, UV doses, or influent and effluent TOC concentrations from an RO process. To facilitate use of DPRisk, the table on the following page provides guidance on how to convert common surrogate performance data to LRVs. These conversions are generally consistent with California's regulatory framework. Once the corresponding LRVs are determined, the LRV data can be fit to a statistical distribution outside of DPRisk, and the best-fit distribution and associated parameters can be specified in the tool. Alternatively, the LRVs can be uploaded into DPRisk as a .csv file with 10,000 data points. Again, if fewer than 10,000 data points are provided, DPRisk will randomly sample with replacement from the data provided. The figure above shows an example in which the user has decided to specify LRVs for individual treatment processes. In this example, secondary biological treatment is modeled as a uniform distribution with a minimum LRV of 1.0 and a maximum LRV of 2.0, and the MBR is modeled with an LRV of 0 because it is not included in the hypothetical treatment train. Additional examples will be shown in the case studies at the end of the Guidance Document. For treatment processes that should be excluded from the analysis, the corresponding LRV must be specified as a point estimate of 0 (i.e., the default setting for all treatment

processes). Consistent with the California regulatory framework, DPRisk limits all LRVs determined from a statistical distribution to a maximum of 6.0. This LRV cap does not apply to user input files or to point estimates. For each underlying data point, DPRisk calculates the pathogen concentration in the AWPF product water according to the following equation, where C_{raw_sewage} is the raw wastewater pathogen concentration (as determined from Step 3: Raw Wastewater Pathogen Distributions) and LRV_{Total} is the sum of the LRVs for the individual treatment processes (when applicable).

$$C_{AWPF\_effluent} = C_{raw\_sewage} \times 10^{-LRV_{Total}}$$

Unit Process	Common LRV Frameworks[1]	Source
Secondary	Point Estimate or Probability Distribution	N/A
MBR	Virus: LRV = 1.5 *Giardia*/*Cryptosporidium*: LRV = 2.0 Bacteria: LRV = 4.0	WaterVal (2017a)
Ozone[2]	Virus: LRV = $2.1744 \times (1.0726)^{Temp} \times CT$ *Giardia:* LRV = $1.038 \times (1.0741)^{Temp} \times CT$ *Cryptosporidium:* LRV = $0.0397 \times (1.09757)^{Temp} \times CT$	EPA (2010)
Free Chlorine[3]	Virus: LRV = See CT Table on following page *Giardia*: LRV = $\frac{CT}{0.361 \times \left(-2.261 + e^{(2.69 - (0.065 \times Temp) + (0.111 \times C) + (0.361 \times pH))}\right)}$ *Cryptosporidium*: LRV = 0	WaterVal (2017b) EPA (1999)
UV/AOP[4]	Virus: LRV = (0.0238 × UV Dose) – 0.3905 (based on adenovirus) *Giardia:* LRV = (0.1617 × UV Dose) + 0.8853 *Cryptosporidium:* LRV = (0.1671 × UV Dose) + 0.7603	EPA (2006b)
BAC	LRV = 0	Assumed for CA
Coag/Floc/Sed/Filt	LRV = 0	Assumed for CA
Membrane Filtration[5]	Virus: LRV = 0 *Giardia*/*Cryptosporidium*: LRV = $\log\left(\frac{Q_p \times ALCR \times P_{atm}}{\Delta P_{test} \times V_{sys} \times VCF}\right)$	Assumed for CA EPA (2005)
RO	LRV (all pathogens) = $-\log\left(\frac{Surrogate_{out}}{Surrogate_{in}}\right)$	Assumed for CA
DWTP (not specifically included in DPRisk)	Virus: LRV = 4 *Giardia*: LRV = 3 *Cryptosporidium*: LRV = 2	EPA Surface Water Treatment Rules
Total LRV	$LRV_{Total} = LRV_1 + LRV_2 + \ldots + LRV_N$	N/A

[1]LRV is assumed to be the same for adenovirus, enterovirus, and norovirus; [2]Temperature in °C and ozone CT in mg-min/L; [3]Free chlorine CT in mg-min/L, temperature in °C, and chlorine residual C in mg/L; [4]UV dose in mJ/cm^2; [5]Q_p = filtrate flow rate (gpm), ALCR = air liquid conversion ratio, P_{atm} = atmospheric pressure (psia), ΔP_{test} = measured decay rate (psi/min), V_{sys} = volume of pressurized air in the system (gallons), VCF = volumetric concentration factor (dimensionless).

pH	Log_{10} inactivation	≤ 0.2 NTU					≤ 2 NTU					≤ 5 NTU				
		5°C	10°C	15°C	20°C	25°C	5°C	10°C	15°C	20°C	25°C	5°C	10°C	15°C	20°C	25°C
≤7	1	4	3	2	2	1	4	3	2	2	1	4	3	2	2	1
	2	5	4	3	2	2	5	4	3	2	2	6	4	3	2	2
	3	7	5	4	3	2	7	5	4	3	2	7	5	4	3	2
	4	8	6	4	3	2	9	6	4	3	2	9	7	5	3	3
≤7.5	1	7	5	4	3	2	7	5	4	3	2	8	6	4	3	2
	2	10	7	5	4	3	10	7	5	4	3	13	9	6	5	4
	3	13	9	7	5	4	13	9	7	5	4	16	12	9	6	5
	4	16	11	8	6	4	16	11	8	6	4	21	15	11	7	6
≤8	1	9	7	5	3	3	10	7	5	4	3	12	9	6	4	3
	2	14	10	7	5	4	15	10	7	5	4	19	13	9	7	5
	3	18	13	9	7	5	19	13	10	7	5	25	18	13	9	7
	4	23	16	12	8	6	23	16	12	8	6	32	23	16	11	8
≤8.5	1	11	8	6	4	3	12	9	6	5	4	14	10	7	5	4
	2	17	12	9	6	5	19	13	9	7	5	21	15	11	8	6
	3	23	16	12	9	6	25	17	13	9	7	29	21	15	10	8
	4	29	21	15	10	8	31	22	16	11	8	37	26	18	13	9
≤9	1	13	9	6	5	3	14	10	7	5	4	15	10	7	5	4
	2	20	14	10	7	5	22	16	11	8	6	23	16	12	8	6
	3	28	19	14	10	7	30	21	15	11	8	32	23	16	11	8
	4	35	25	17	12	9	38	27	19	13	10	41	29	20	14	10

B.9 Step 6: Treatment Process Failure Framework

B.9.1 Background

Deviations in treatment process performance might include (1) typical operational variability, (2) periodic off-specification events, and (3) low-probability failures. Depending on the extent of monitoring, the treatment performance datasets described in the previous section might only capture a subset of these possibilities. So, it is important to consider how to handle failure conditions—specifically their magnitude, duration, and frequency—as part of the QMRA/PATTP. By either imparting some failure into the model, or characterizing the tolerance for failure in modeled scenarios (i.e., observed LRV redundancy), stakeholders can begin to characterize the resiliency of a given system.

Multiple QMRAs have shown that even short-duration failures can lead to a significant impact on the overall risk profile (Amoueyan et al. 2019; Haas and Trussell, 1998; Pecson et al. 2017; Soller et al. 2018b). Although recent studies have begun to characterize the frequency and duration of off-specification or failure events (Ander and Forss, 2011; Pecson et al. 2018; Soller et al. 2018b; Tng et al. 2015), it is still difficult to quantify the true magnitude of a failure. Some studies show that pathogen LRVs are still relatively high even during simulated failures. In fact, Pecson et al. (2018) noted that the probability of a UV failure of sufficient magnitude to cause a change in pathogen LRV might be on the order of 10^{-11}, and a similar conclusion was reached in Tng et al. (2015). Therefore, including catastrophic failures in a QMRA, such as those resulting in an LRV of 0, may overestimate the risk for a given system. Moreover, such catastrophic failures are unlikely to occur because DPR systems will likely require fail-safe protocols to mitigate or eliminate the impacts of such events. Nevertheless, these rare events that might be as short as 15 minutes can drive annual risk estimates for drinking water systems (Soller et al. 2018b). This underscores the importance of treatment process verification (e.g., monitoring

surrogate parameters at critical control points) to rapidly identify and respond to off-specification or failure conditions (Amoueyan et al. 2019).

In addition to catastrophic failures, engineered processes never achieve ideal hydraulic conditions. This means that treated water can experience a wide range of hydraulic residence or exposure times, which has implications for disinfectant CT, UV dose, storage/travel time, etc. This highlights the importance of fully characterizing the hydraulics of natural and engineered systems. In the absence of this information, one can assess the sensitivity of risk to normal operational variability by 'experimenting' with the statistical distributions used to model certain parameters (e.g., increasing the standard deviation of a normally-distributed LRV). This concept is incorporated into Case Study 1 (Section B.15).

Characterizing unit process interdependence is also important for understanding the impact of failures. Systems with a high degree of interdependence may experience cascading failures, or 'domino effects,' where a failure in an upstream unit process leads to the failure or diminished performance of downstream unit processes. Knowing whether a treatment train has high or low interdependence is critical for accurately modeling failure impacts. Amoueyan et al. (2017; 2019) incorporated cascading failures into the QMRA by simulating changes in water quality resulting from an upstream failure that would adversely impact downstream treatment performance. However, the final risk calculations were more sensitive to individual and compound failures (i.e., simultaneous catastrophic failures) rather than simulated interdependence. Pecson et al. (2017) also showed that FAT trains exhibited minimal interdependence, allowing modeling of failures as independent events. Similar conclusions were reached in Haas and Trussell (1998) and Olivieri et al. (1999).

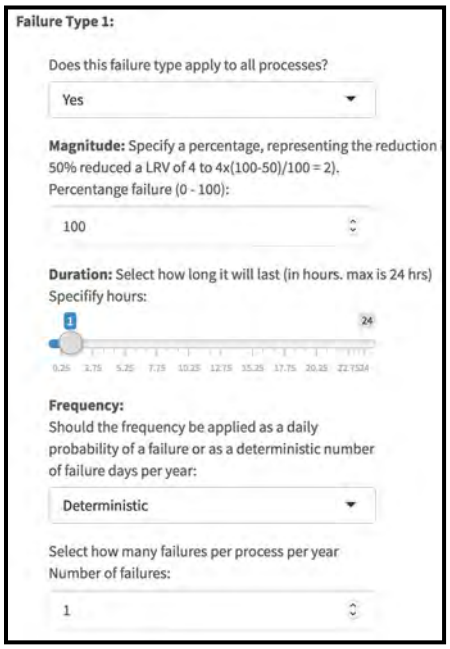
There is a general consensus that an understanding of process failures is an important knowledge gap for potable reuse. New information that becomes available to better characterize failures in terms of magnitude, duration, and frequency and the corresponding implications for pathogen reduction should be evaluated and incorporated into QMRAs/PATTPs. In addition to capturing typical variability in treatment process performance, off-specification events or failures should be considered in stochastic modeling, regardless of whether they were actually observed during a particular monitoring period. This is because the absence of failures during shorter monitoring periods does not guarantee the absence of rare failures over longer timescales. Moreover, by considering off-specification events and failures, it is then possible to quantify the resilience of a system and demonstrate the importance of on-line surrogate monitoring and response protocols.

B.9.2 Integration into DPRisk

The user defines the failure framework in the Treatment Failure section of the DPRisk interface. DPRisk allows the user to define global failure characteristics, define failures for individual or multiple engineered treatment processes, or to exclude failures entirely. Under the global setting (see figure below), failure characteristics are applied similarly across all of the engineered treatment processes included in the model scenario, although process-specific failures are still 'sampled' independently. Failures are **not** applied to management barriers (see next section on description of management barriers). The user has the option of defining up to 6 failure types based on their magnitude, duration, and frequency:

- **Magnitude:** percent reduction in LRV (0-100%).
  - Example: The user specifies a failure magnitude of 70%, which means a treatment process will operate at 30% of normal conditions during a simulated failure. If that treatment process is typically awarded an LRV of 6.0, the corresponding failure LRV would be (100-70)/100×6.0 = 0.3×6.0 = 1.8.

- **Duration:** number of hours over which a failure occurs (specified as a consecutive block of 15-min intervals, with the block being assigned randomly within the failure day).
  - Example: 30-min failure duration = setting of 0.5 hours.
  - Example: 1-hour failure duration = setting of 1 hour (see figure).
  - Example: 24-hour failure duration = setting of 24 hours.
- **Frequency:** the user can specify a deterministic frequency or daily probability. The failures may occur independently (i.e., single failure) or concurrently (i.e., compound failure), as determined by Monte Carlo simulations of 15-minute time intervals.
  - Deterministic: every treatment process ***will*** fail "X" number of times per year.
  - Probabilistic: each process has "X" ***daily*** probability (between 0 and 1) of failure.

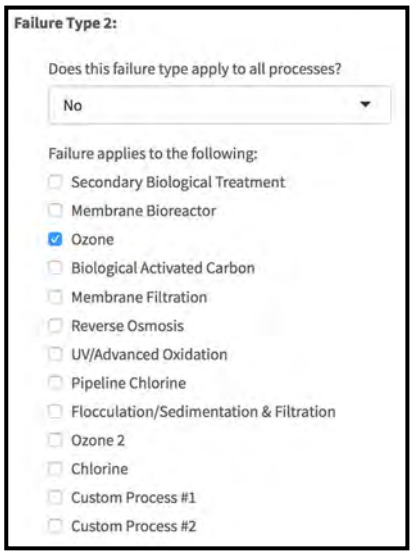


For deterministic failure frequencies, the tool selects a random day (or days) to assign a failure, and for stochastic failure frequencies, the tool assigns failures based on probabilistic sampling of all days in the simulation. A user might select a stochastic probability of failure of 0.01, which means each process has a 1% probability of failure on any given day. This equates to a *probable* failure frequency of approximately 3-4 times per year (i.e., 0.01 failures/day×365 days/year = 3.65 failures/year). With the deterministic approach, the tool *forces* failures to occur at the specified frequency. The probabilistic approach might provide a better representation of actual conditions, assuming failures are adequately characterized to identify reasonable probabilities, while the deterministic approach might be a better option to understand the implications of a specific failure scenario by forcing it to occur (i.e., eliminating the confounding factor of probability). Additional discussion on the link between failure probability and the recommended number of failure simulations is provided in Step 10: Risk Characterization.

When failures are identified, the specified magnitude (i.e., reduction in LRV) and duration are also assigned to that day. As will be discussed later, DPRisk's underlying model structure is based on 15-minute time intervals. For failure durations less than 24 hours, the reduction in LRV is applied to a random block of 15-minute intervals corresponding with the specified failure duration. If the treatment train involves multiple unit processes, failures for the various unit processes are sampled independently, which may lead to compound (or simultaneous) failures. Moreover, if multiple failure *types* are specified, each failure type is sampled independently. In the event of a compound (or simultaneous) failure of different types for the same unit process, the LRV is adjusted for both failures unless the LRV has already been reduced to 0.

As will be discussed later [see Step 8: Drinking Water Ingestion (Exposure Assessment)], users have the ability to specify the number of ingestion/consumption events per day, with the default setting being 96 (i.e., every 15 minutes) for consistency with DPRisk's 15-minute calculation framework. When fewer than 96 ingestions are specified, there will be certain periods of the simulated day (i.e., certain 15-minute time intervals) for which there are no exposures. Due to the random nature of the failure assignments, it might be possible for a failure to occur—even with a deterministic frequency—but be allocated to a 'no-exposure' time interval. These failures will have no impact on risk unless the duration is sufficiently long so that it aligns with a subsequent ingestion event. Therefore, in establishing input

parameters, the user must consider the potential interrelatedness of failure duration, failure frequency, and ingestion frequency, perhaps by conducting relevant sensitivity analyses.



It is unlikely that all unit processes are characterized by the same magnitude, duration, and frequency of failure, so there may be a preference to model process-specific failure characteristics rather than using a global failure approach. This is useful for distinguishing a process that might have a low probability of failure versus one with a high probability of failure, or perhaps a process with a high probability of low magnitude failures versus one with a low probability of high magnitude failures. When individual unit processes are defined (Treatment Train tab) and the "Conduct failure analysis" option is selected (Treatment Failure tab), the tool will automatically provide the option of applying a failure type to all processes (i.e., global failure approach) or only to selected unit processes (see ozone example in figure). All other parameter options remain the same for the process-specific failure option.

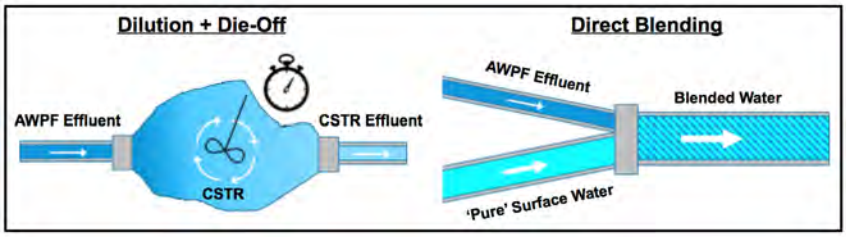
The industry has not yet developed a comprehensive understanding of how failure magnitude, duration, and frequency vary by process. There are some data in the literature describing failure frequencies and durations, but it is not yet clear how pathogen LRVs (i.e., failure magnitudes) are impacted during those low probability events (if at all). In the absence of more comprehensive datasets, failure characterization and subsequent data interpretation and/or policy decision-making should be done with caution. The following table provides some guidance on modeling process *variability* versus *failure* for individual treatment processes. As noted earlier, process variability is unavoidable but should be minimized in full-scale treatment to adequately manage public health risk. The effects of variability are primarily addressed through the statistical distribution used to award LRVs to a particular treatment process. On the other hand, off-specification conditions and/or failures represent discrete events that might result in a significant change in process performance over varying lengths of time. In the literature, off-specification events are sometimes described as short-term conditions resulting in sub-optimal performance (i.e., partial reductions in LRVs) (Soller et al. 2018b), while failures are often described as complete (i.e., 100%) reductions in LRV. The values in this table can be used as a starting point for specifying global or process-specific failures in DPRisk.

Unit Process	Failure Type and Probability	Failure Duration	Source
Secondary	Variability: distribution on LRV	N/A	N/A
MBR	Variability: distribution on LRV	N/A	N/A
Ozone	Variability: ozone CT/LRV distribution Off-spec: P = 0.025 Failure: P = 0.000325 Failure: P = 0.0022	N/A 15 min 24 hr 30 min	N/A Soller et al. (2018b) Amoueyan et al. (2019) Ander and Forss (2011)
Free Chlorine	Variability: chlorine CT/LRV distribution Failure: P = 0.0021	N/A 90 min	N/A Ander and Forss (2011)
UV/AOP	Variability: UV dose/LRV distribution Failure: P = 0.002 Failure: P = 0.0001 or 0.0005	N/A 15 min 30 min	N/A Soller et al. (2018b) Pecson et al. (2018)
Membrane Filtration (MF and UF)	Variability: PDT/LRV distribution Off-spec: P = 0.021 Failure: P = 0.0029	N/A 15 min 45 min	N/A Soller et al. (2018b) Ander and Forss (2011)
RO	Variability: surrogate distribution Failure: P = 0.018	N/A 15 min	N/A Soller et al. (2018b)

B.10 Step 7: Management Barriers (Blending, Dilution, and Die-off)

B.10.1 Background

In some contexts, blending and dilution can be used interchangeably, but for this Guidance Document and for the DPRisk tool, 'blending' refers to complete and instantaneous mixing with a *pathogen-free* water supply, while 'dilution' refers to more complicated mixing regimes. Dilution is often characterized through hydraulic modeling of engineered treatment systems (e.g., computational fluid dynamics in a UV reactor) or hydrodynamic modeling of reservoirs under variable meteorological conditions.



Potable reuse can theoretically span an endless range of blending/dilution scenarios, although existing regulatory frameworks include some degree of specificity regarding these requirements. In California, the recycled water contribution (RWC) in a groundwater augmentation project is essentially an allowable blending ratio determined by TOC concentration (TOC_{max} = 0.5/RWC). On the other hand, reservoir augmentation applications must demonstrate compliance with certain dilution requirements (>10:1 or 100:1), generally through use of hydrodynamic modeling informed by tracer studies. Future DPR applications will likely involve raw water augmentation (i.e., blending prior to drinking water treatment) or treated water augmentation, either by blending with finished drinking water or direct distribution to a consumer. Typically, pathogen LRVs are not awarded for blending or dilution in IPR systems so dilution-related LRVs may not be awarded in future DPR systems. However, accounting for

blending or dilution as part of a QMRA might provide value in terms of estimating potential conservatism.

Pathogen reduction through blending/dilution can be supplemented with estimates of pathogen die-off in an environmental buffer (Amoueyan et al. 2019; Lim et al. 2017), but again, environmental die-off is rarely recognized in regulatory frameworks. No pathogen credit is awarded for the storage of purified water in reservoir augmentation projects in California, but 1-log virus reduction is credited for every month of travel time in groundwater augmentation projects. Pathogen die-off is still not well understood, which leads to considerable uncertainty in a QMRA, but there is a growing knowledgebase on this topic (Boehm et al. 2018; 2019). In general, this is less significant for DPR applications because of the limited interaction with the environment and reduced time between treatment and distribution, but there may be exceptions. In California, reservoir augmentation requires a minimum theoretical retention time ($V_{EndOfMonth}/Q_{Total}$) of 2 months, and systems with retention times shorter than 2 months would likely require permitting under DPR regulations. Therefore, die-off might still contribute a significant LRV in some raw water augmentation scenarios, but for treated water augmentation, it might be more appropriate to consider blending in the absence of die-off. In any case, this offers another opportunity to characterize a potential degree of conservatism by incorporating die-off into a QMRA.

B.10.2 Integration into DPRisk

Pathogen LRVs for blending, dilution, and die-off are not commonly included in potable reuse regulatory frameworks, but DPRisk allows for their implementation through the Management Barriers tab. Similar to the engineered treatment processes, these management barriers are integrated in an LRV format to ensure consistency with the QMRA framework and to allow for maximum flexibility. **However, DPRisk does not apply an LRV cap nor failures to the management barriers**.

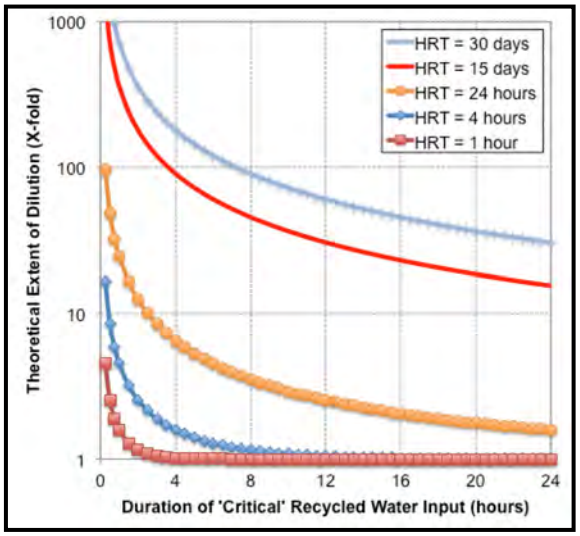
As noted earlier, blending can be described as complete and instantaneous mixing with a secondary water supply, such as source water upstream of a drinking water treatment facility, finished drinking water, or groundwater. This secondary water supply is often assumed to be free of pathogens, although this may not always be accurate as some source waters are known to contain pathogens (Amoueyan et al. 2019). As with the aforementioned engineered treatment processes, blending can be characterized in DPRisk as (1) a point estimate, (2) a statistical distribution, or (3) an input file curated with 10,000 data points. For compatibility with the DPRisk framework, the blending ratio should be described as an LRV. As shown in the following example, a recycled water contribution (RWC) of 10% (or 0.10) would correspond with an LRV of 1.0.

RWC = 10% = 0.10 Blending LRV = $-\log_{10}(0.10)$ **Blending LRV = 1.0**	Blending Ratio = 9:1 Blending LRV = $-\log_{10}[1/(9+1)]$ **Blending LRV = 1.0**	Extent of Blending = 10X Blending LRV = $-\log_{10}(1/10)$ **Blending LRV = 1.0**

Hydrodynamic or hydraulic modeling coupled with tracer studies may be needed to accurately characterize dilution in a particular potable reuse scenario. This type of data can be transformed into an LRV distribution and uploaded into DPRisk (see Section B.16, Case Study 2). In the absence of these data, estimating dilution assuming an ideal completely stirred tank reactor (CSTR) may be an adequate alternative. If desired, response retention time (RRT) can be integrated into the CSTR approach to consider the implications of treatment process failure and monitoring frequencies at critical control points. A theoretical dilution ratio can be calculated for a CSTR using the following equation:

$$\text{Theoretical Extent of Dilution (X)} = \frac{C_0}{C} = \frac{1}{1 - e^{-t/\tau}}$$

where t = duration of 'critical' recycled water input, τ = theoretical hydraulic residence time (HRT) in the environmental buffer or engineered storage buffer (i.e., V/Q), and X = the 'X'-fold dilution achieved in the scenario. One way of defining the duration of 'critical' recycled water input could be the longest time between measurements at the critical control points. When considering failures, the duration of 'critical' recycled water input could alternatively be described as the failure duration. Longer failures correspond with inputs of off-specification recycled water over longer durations, which should decrease the LRV awarded for dilution. The preceding figure shows examples of theoretical dilution ratios for HRTs ranging from 1 hour (engineered storage buffer) to 30 days (environmental buffer) and failure durations ranging from 15 minutes to 24 hours. In the absence of site-specific data, 15 minutes might be a reasonable default for the duration of the 'critical' recycled water input. The dilution LRV can be calculated according to the equation below when using this CSTR approach. The dilution LRV can then be integrated into DPRisk as (1) a point estimate, (2) a statistical distribution, or (3) an input file curated with 10,000 data points.



$$\text{Dilution LRV} = -\log_{10}(1/X) = -\log_{10}\left(1 - e^{-t/\tau}\right)$$

Die-off is generally modeled as first order decay (base e) using rate constants from the literature (Boehm et al. 2018; Boehm et al. 2019) and the following equation:

$$-\ln\left(\frac{N_t}{N_0}\right) \text{ or } -\ln\left(\frac{C_t}{C_0}\right) = k_i t$$

where N_t = number of organisms at time t, N_0 = number of organisms at time 0, C_t = concentration of organisms at time t, C_0 = concentration of organisms at time 0, k_i = base *e* first order rate constant for die-off of pathogen *i* (units = time^{-1}), and t = time. For consistency with typical QMRA frameworks, it is necessary to convert the base *e* pathogen reduction to base 10, which can be accomplished as follows:

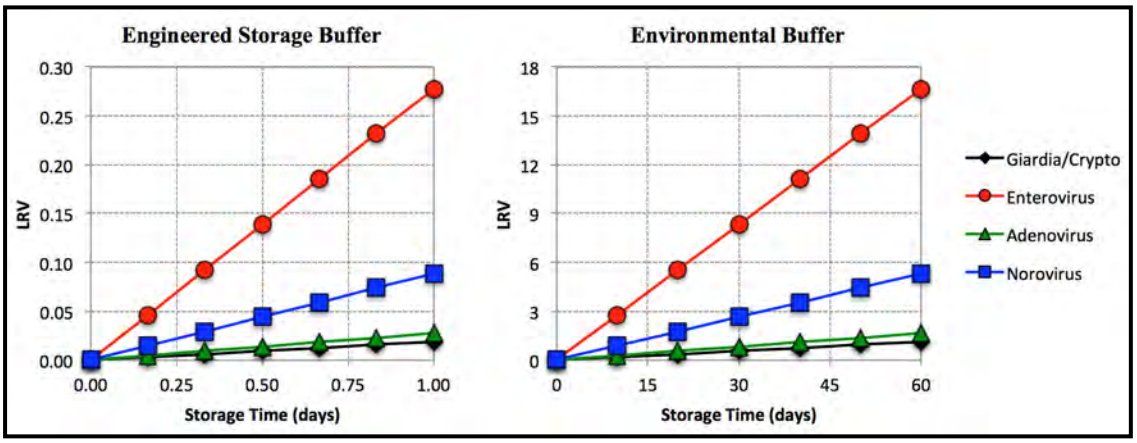
$$\text{LRV} = -\log_{10}\left(\frac{N_t}{N_0}\right) \text{ or } -\log_{10}\left(\frac{C_t}{C_0}\right) = \frac{k_i t}{2.303}$$

Die-off is technically a function of a number of variables, including salinity, temperature, pH, and sunlight exposure, although exact relationships are often uncertain. Boehm et al. (2019) provides a comprehensive review of pathogen die-off and presents empirical regression models to quantitatively describe some of these relationships. But even when controlling for a certain variable, such as temperature, the die-off rate constants often span multiple orders of magnitude, calling into question whether there is a sufficient number of high-quality datasets available for complete and accurate characterization. The following table provides a summary of the die-off rate constants from Boehm et al. (2018; 2019), in addition to identifying statistical distributions that can potentially be integrated into a Monte Carlo simulation to capture some of the inherent uncertainty/variability. Using the identified base *e* means/medians in conjunction with the aforementioned equations, the corresponding figure illustrates the LRVs that might be expected for a range of DPR scenarios. The figure demonstrates that the expected LRVs for the target pathogens might be insufficient to warrant inclusion in a QMRA when assuming an engineered storage buffer with a theoretical hydraulic retention time of up to 24 hours. On

the other hand, reservoirs with storage times up to 2 months might warrant inclusion of a die-off LRV or at least recognition of additional conservatism if die-off is excluded.

Pathogen	N	Base *e* Mean[1] (d^{-1})	Lognormal Dist. (d^{-1}) μ	σ	Source
Giardia	14	0.044	-3.132	2.211	Boehm et al. (2018)
Cryptosporidium	22	0.041	-3.201	1.842	Boehm et al. (2018)
Virus (all)	8	0.155	-1.865	1.152	Boehm et al. (2018)
Enterovirus[2,3]	96	0.640	-0.446	1.054	Boehm et al. (2019)
Pathogen	**N**	**Base *e* Median (d^{-1})**	**Range (d^{-1}) Min**	**Max**	**Source**
Adenovirus[2]	8	0.063	0.021	0.288	Boehm et al. (2019)
Norovirus[2,4]	5	0.205	0.020	0.368	Boehm et al. (2019)

[1]Calculated as e^{μ} with μ from reported lognormal distribution; [2]Includes reported values for experiments performed with culture methods and in freshwater (no distinction for temperature); [3]Determined from maximum likelihood estimation in Matlab; [4]Based on experiments with murine norovirus.



The die-off LRV can ultimately be integrated into DPRisk as (1) a point estimate, (2) a statistical distribution, or (3) an input file curated with 10,000 data points. The point estimate would be the most straightforward approach but would only incorporate a single die-off rate constant and a single storage time. The statistical distribution or input file would allow for a Monte Carlo-type approach by capturing the variability in reported die-off rate constants and/or storage time for a given DPR scenario.

Assuming inclusion of management barriers, DPRisk calculates the pathogen concentration in the finished drinking water as follows:

$$C_{drinking\_water} = C_{AWPF\_effluent} \times 10^{-(LRV_{blending} + LRV_{dilution} + LRV_{die\text{-}off})}$$

B.11 Step 8: Drinking Water Ingestion (Exposure Assessment)

B.11.1 Background

QMRAs must include assumptions about the amount of water a person consumes each day in order to determine the exposure to a particular pathogen. There are two common approaches for modeling drinking water consumption: (1) modeling consumption based on a distribution (EPA, 2011; Roseberry and Burmaster, 1992) or (2) modeling consumption based on a point estimate. Common point estimate assumptions include 1 L per person per day (Olivieri et al. 2016); 2 L per person per day (Amoueyan et al. 2019); 2.5 L per person per day, which represents the 90th percentile value for adults based on EPA (2011); and even 3 L per person per day at an Antarctic field station (Barker et al. 2013).

As an artifact of probability-based calculations, the frequency of ingestion can also have a significant impact on the final risk characterization, even when the total volume remains constant (Van Abel, N. et al. , 2014). For example, Amoueyan et al. (2019) calculated daily risk based on a single 2-L ingestion, Soller et al. (2018b) calculated daily risk based on a 2-L volume ingested as eight 250-mL aliquots throughout the day, and Pecson et al. (2017) calculated risk based on a lognormally distributed daily ingestion volume divided evenly across 96 time intervals (i.e., every 15 minutes). The implications of different ingestion frequencies are illustrated in the following hypothetical example. By filling up a pitcher of water multiple times throughout the day, there is a higher probability of capturing the effects of a failure condition, assuming that condition is not detected and diverted at the treatment facility. That being said, it is still possible for the single aliquot to align with a failure condition, which would then impart a higher risk due to the greater ingestion volume. A failure condition aligning with only one of four (or more) aliquots might impart a lower risk because it is partially mitigated by the dilution effect. In any case, ingestion frequency can potentially have significant implications for risk estimates.

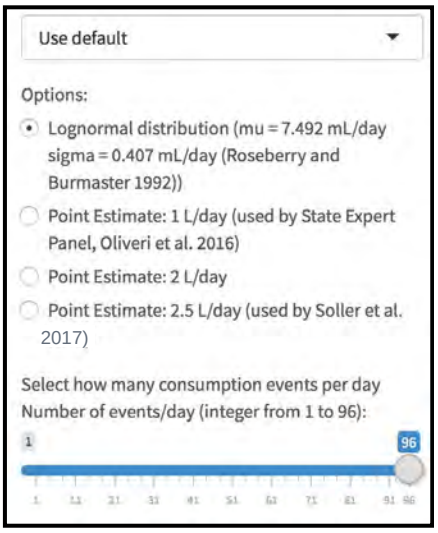
Assumptions:
(1) Treatment train with 3 independent unit processes
(2) Each unit process has a 0.1% failure probability
(3) Probability of all unit processes operating successfully = 0.997
$(0.999)\times(0.999)\times(0.999) = 0.997$
(4) N = number of times pitcher is filled in a given day

Scenario 1: Fill up 4 L at one time
Probability of successful operation = $0.997^N = 0.997^1 = 0.997$
Probability of treatment train failure = 1 - 0.997 = 0.003 = 0.3%

Scenario 2: Fill up 1 L at 4 different times
Probability of successful operation = $0.997^N = 0.997^4 = 0.988$
Probability of treatment train failure = 1 - 0.988 = 0.012 = 1.2%

Probability of off-spec drinking water is 4 times higher with 4 aliquots vs. 1 aliquot

B.11.2 Integration into DPRisk



DPRisk allows the user to specify ingestion volume as a lognormal distribution, a point estimate, or an input file curated with 10,000 data points (e.g., to consider an alternative statistical distribution). All non-default inputs should be based on units of **mL per day.** Alternatively, the user has the option of selecting from a list of four default ingestion volumes, specifically the lognormal distribution from Roseberry and Burmaster (1992), a point estimate of 1 L/day, a point estimate of 2 L/day, or a point estimate of 2.5 L/day. The lognormal distribution from Roseberry and Burmaster (1992) was also used in Pecson et al. (2017) and is characterized by $\mu = 7.492$ and $\sigma = 0.407$; the mean of this lognormal distribution corresponds with an ingestion volume of $e^{7.492} = 1{,}794$ mL/day. In addition to defining the daily ingestion volume, the user can select the number of ingestion (or consumption) events per day, from 1 to 96 (or every 15 minutes). The daily ingestion volume is then divided by the specified number of daily ingestion events and coupled with the estimated drinking water pathogen concentration to determine the interval-specific pathogen dose (see equation below). Additional details related to the tool calculation methodology are described in Step 10: Risk Characterization. Theoretically, this flexibility in defining ingestion volume and frequency allows for QMRAs targeting a wide range of exposures and applications, including large-volume drinking water ingestion versus small-volume (incidental) ingestion of recreational water. Coupled with a user-defined dose response model (see next section), it might even be possible to model aerosol inhalation of respiratory pathogens, although this application is not addressed in the Guidance Document and may require further tool development for specific applications.

$$\text{Dose (\# of pathogens)} = C_{drinking\_water}\ \text{(pathogens/L)} \times \frac{\text{Daily Ingestion Volume (mL/day)}}{\text{1000 (mL/L)} \times \text{N (ingestions/day)}}$$

B.12 Step 9: Pathogen Dose Response Models (Dose Response Assessment)

B.12.1 Background

Dose response relationships provide the link between exposure to a pathogen (i.e., dose) and the probability of infection. These relationships can be developed directly through animal studies and human clinical studies or indirectly through epidemiological/outbreak studies (EPA, 2014). Dose response models rarely distinguish for susceptible subpopulations (e.g., demographic differences such as age and immunocompromised status), although some QMRAs adjust the ingestion volume as a function of age. Also, the severity of the response (i.e., illness) is often addressed independently of the dose response (i.e., probability of infection) and is generally assumed to be independent of dose, although this is not always the case in reality (EPA, 2014). The severity of the response, which is linked to pathogen virulence and accounts for differences in morbidity and mortality, is discussed in greater detail in Step 10: Risk Characterization. Additional information on common dose response models, including the critical details that should be provided to justify use of a certain dose response model, is available in EPA (2014). This Guidance Document focuses only on commonly accepted dose response models for waterborne pathogens in drinking water applications.

Dose response functions sometimes vary widely within the same pathogen group (e.g., different bacteria or viruses), and even a single pathogen can be described by multiple functions, sometimes with

significant implications for risk estimates (Messner et al. 2014; Nappier et al. 2018; Schmidt, 2015; Soller et al. 2017). For example, Soller et al. (2017) and Amoueyan et al. (2019) showed that certain dose response models cause the final risk calculation to increase by up to several orders of magnitude. For a simple exponential model, even the value selected for the dose response parameter can cause risk to change by orders of magnitude (Amoueyan et al. 2017). Therefore, the dose response model can be a significant source of uncertainty in a QMRA. Examples for two different bacterial pathogens and three different dose response models for *Cryptosporidium* are shown in the table below. For a hypothetical concentration of 1×10^{-5} cells or oocysts per L (or 1 per 100,000 L) and a one-time ingestion volume of 2 L, the corresponding probability of infection would be 4×10^{-7} for *Campylobacter*; 2×10^{-9} for *Salmonella*; and 2×10^{-5}, 2×10^{-6}, or 8×10^{-8} for *Cryptosporidium*, respectively. This shows that the selection of a certain dose response model or parameter can lead to significantly different risk estimates for different types of pathogens, or even for the same pathogen.

Pathogen	Model	Probability of Infection[1]	Parameter	References
Campylobacter jejuni	Beta-Poisson	$1-\left(1+\frac{d}{\beta}\right)^{-\alpha}$	α = 0.1450 β = 7.59	Medema et al. (1996)
Salmonella enterica	Beta-Poisson	$1-\left(1+\frac{d}{\beta}\right)^{-\alpha}$	α =0.3126 β =2884	Haas et al. (1999)
Cryptosporidium	Beta-Poisson	$1-\left[1+\frac{d}{\beta}\right]^{-\alpha}$	α = 0.116 β = 0.121	Messner & Berger (2016)
	Exponential	$1-e^{-rd}$	r = 0.09	Haas et al. (1999)
	Exponential	$1-e^{-rd}$	r = 0.00419	Haas et al. (1999)

[1] d = dose (number of pathogens)

For QMRAs, it is important to consider a range of available dose response functions, particularly for final risk characterization and decision-making. It is also important to consider whether certain dose response models are compatible with early QMRA assumptions—norovirus being a prime example. As mentioned earlier, one of the challenges with incorporating norovirus into a QMRA (and into regulatory frameworks) stems from the difficulty in assessing its infectivity. Although some culture methods are emerging, norovirus enumeration is currently limited to molecular methods based on quantification of genome copies. The lack of a standard correlation between genome copies and infectious units is generally the greatest impediment to integrating molecular data into QMRAs, and also in the development of dose response functions.

Efforts have been made to work around the GC:IU issue. For example, various challenge studies have been undertaken by exposing human volunteers to known doses of norovirus genome copies, thereby facilitating development of genome copy-based dose response models. In this framework, it is not necessary to characterize the GC:IU ratio as long as that ratio is constant. One of the major limitations of this assumption, however, is that it remains unknown whether the GC:IU ratio from a human challenge study is similar to the ratio for an environmental matrix, such as a raw sewage or treated water. Human challenge studies often employ purified virus stocks that have been suspended in conditions amenable for archiving, or freshly prepared from the feces of infected individuals (Atmar et al. 2014; Frenck et al. 2012; Messner et al. 2014; Seitz et al. 2011; Teunis et al. 2008). Therefore, there may be significant differences in GC:IU ratio at various stages of treatment and ultimately exposure.

B.12.2 Integration into DPRisk

The following table summarizes the dose response models and parameters that are integrated into DPRisk's default configuration. When a particular pathogen is selected in Step 1: Target Pathogens,

these defaults auto-populate in the dose response tab. For adenovirus, norovirus, and *Cryptosporidium*, the user must select one of the default dose response options. There are also two options for user-defined dose response models: (1) selecting one of the default dose response models listed in the table below and specifying a point estimate for each dose response parameter or (2) selecting one of the default dose response models and providing an input file curated with 10,000 values for each dose response parameter.

Pathogen	Dose Response Model	Equation[a]	Parameter	References
Adenovirus	Exponential	$1 - e^{-rd}$	r =0.4172	Crabtree et al. (1997)
	Exact Beta-Poisson[b]	$1 - {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 5.11 β = 2.8	Teunis et al. (2016)
Enterovirus	Beta-Poisson[c]	$1 - \left[1 + \frac{d}{\beta}\right]^{-\alpha}$	α = 0.253 β = 0.426	Ward et al. (1986)
Norovirus	Exact Beta-Poisson[b] (Upper Bound; disaggregated)	$1 - {}_1F_1(\alpha, \alpha+\beta, -d)$	α = 0.04 β =0.055	Teunis et al. (2008)
	Fractional Poisson (Lower Bound; aggregated)	$P \times \left(1 - e^{\frac{-d}{\alpha}}\right)$	P = 0.72 α = 1106	Messner et al. (2014)
Cryptosporidium	Exponential	$1 - e^{-rd}$	r = 0.09	EPA (2006a)
	Exponential	$1 - e^{-rd}$	r = 0.00419	Haas et al. (1999)
	Fractional Poisson	$P \times \left(1 - e^{\frac{-d}{\alpha}}\right)$	P = 0.737 α = 1	Messner & Berger (2016)
	Beta-Poisson	$1 - \left[1 + \frac{d}{\beta}\right]^{-\alpha}$	α = 0.116 β = 0.121	Messner & Berger (2016)
	Exponential with Immunity	$P \times \left(1 - e^{-rd}\right)$	P = 0.737 r = 0.608	Messner & Berger (2016)
Giardia lamblia	Exponential	$1 - e^{-rd}$	r = 0.0199	Teunis et al. (1997)

[a]d = dose; [b]Also described as Hypergeometric; [c]Based on rotavirus for consistency with U.S. EPA's Surface Water Treatment Rule and California regulations.

B.13 Step 10: Risk Characterization

B.13.1 Background

Risk characterization involves the integration of the preceding steps and assumptions into a final risk estimate that can then be evaluated against various benchmarks. The first step in this process is to calculate the probability of infection for a given condition. To calculate the pathogen dose that should be incorporated into a dose response model, one must multiply the pathogen concentration in the finished/blended drinking water and the volume of water consumed at a given time. As noted earlier, the pathogen concentration in the finished drinking water ($C_{drinking\_water}$) depends on the assumed distribution of the raw wastewater pathogen concentration (C_{raw_sewage}); the degree of attenuation achieved by the engineered treatment barriers (i.e., the overall LRV or LRV_T); and the degree of blending, dilution, and/or die-off. The resulting distribution of $C_{drinking\_water}$ is then converted to a distribution of doses by accounting for the volume of water consumed and the frequency of ingestion. Once the dose is known, the final risk estimate (or probability of infection) for the specified time interval can be determined from the aforementioned dose response model.

In a QMRA, these data combinations are determined from 'Monte Carlo' simulations—a phrase describing the repeated sampling of data from assumed statistical distributions or underlying datasets. The number of data points in the underlying parameter set or the number of simulations might range from 1,000 (Amoueyan et al. 2019, 2020; Soller et al. 2017, 2018a, 2018b) to 10,000 (Amoueyan et al. 2017) to 100,000 (Chaudhry et al. 2017) to 1,000,000 (Pecson et al. 2017). However, the number of simulations alone does not fully characterize the resolution of a QMRA. For example, when trying to capture rare or extreme events with low probabilities, a QMRA that focuses on daily risk might require 1,000,000 simulated days. On the other hand, a QMRA that focuses on 15-minute risks might still require 1,000,000 data points to capture the low probability events, but that would equate to ~10,000 days because of the 96 time intervals per day. Therefore, it is important to consider the structure of the model to fully understand whether sufficient data sampling has occurred to have confidence in the final risk estimates.

Risk can actually be calculated for any time interval, including annual, daily, hourly, or even 15-minute intervals. One of the most common benchmarks for risk characterization is the annual risk of infection of 10^{-4}, which requires an adjustment from shorter time intervals to annual risk. For example, many QMRAs use daily risk as the foundation of the simulation, which subsequently requires converting daily risk to annual risk as follows:

$$P_{annual} = 1 - \prod_{n=1}^{365} (1 - P_{daily,n})$$

This methodology assumes that each exposure period results in a statistically independent risk of infection (Haas and Eisenberg, 2001). Risks calculated for shorter time periods (e.g., 15 minutes) can also be converted to daily or annual risks. The equations for 15-minute time intervals, for which there are 96 intervals in a day and 35,040 intervals in a year, are shown below. In this equation, P_{annual} is a single annual probability of infection, P_{daily} is a single daily probability of infection, and P_{15} is a single 15-minute risk of infection (Pecson et al. 2017).

$$P_{daily} = 1 - \prod_{n=1}^{96} (1 - P_{15,n})$$

$$P_{annual} = 1 - \prod_{n=1}^{35,040} (1 - P_{15,n})$$

Some studies even look at the cumulative risk of infection by simultaneously accounting for the risk of infection from all reference pathogens (Amoueyan et al. 2019; Soller et al. 2017, 2018b). In the equation below, $P_{cumulative,n}$ is the cumulative probability of infection for a given time interval accounting for N reference pathogens simultaneously.

$$P_{cumulative,n} = 1 - \prod_{i=1}^{N} (1 - P_{i,n})$$

The cumulative approach provides greater accuracy if the risks from two or more pathogens are of the same order of magnitude. In cases where a single pathogen dominates the risk calculation, the cumulative risk and pathogen-specific risk will generally be indistinguishable. If cumulative risk is

desired, the cumulative risk should first be calculated for the smaller time interval and then extrapolated to any time interval of interest.

The two main risk targets noted in the literature are 10^{-4} infections per person per year and 10^{-6} disability adjusted life years (DALYs) per person per year (Regli et al. 1991; WHO, 1996, 2006). For some enteric pathogens (e.g., rotavirus and *Cryptosporidium*), the 10^{-6} DALY target yields an equivalent annual risk of ~10^{-3} infections per person per year (NRMMC, 2008; WHO, 1996, 2006). The DALY framework simultaneously accounts for risk of infection and the health burden associated with the infection, including years lived with disability and life years lost. In other words, the DALY framework acknowledges that not all infections are created equal, with more virulent pathogens imparting a greater health burden than others. Many studies in the U.S. focus on 10^{-4} infections per person per year as the benchmark or target risk (Chaudhry et al. 2017; Pecson et al. 2017; Soller et al. 2017), whereas the DALY framework is more frequently used outside of the U.S. (Barker et al. 2013).

These approaches have resulted in varying LRV frameworks for potable reuse, as summarized in the following table. With revised assumptions for raw sewage concentration, dose response model, etc., Soller et al. (2018a) suggested that the LRVs required to achieve the 10^{-4} annual risk benchmark might actually be higher than 12/10/10—perhaps as high as 15/11/11.

Source	Basis	Reference	Virus LRV	*Crypto* LRV	*Giardia* LRV	Bacteria LRV
CA[a]	10^{-4} annual risk	Raw WW	12	10	10	--
NWRI[b]	10^{-4} annual risk	Raw WW	12	10	--	9[f]
TX[c]	10^{-4} annual risk	WWTP Effluent	8	5.5	6	N/A
WHO[d]	10^{-6} DALYs/year	Raw WW	9.5	8.5	--	8.5[g]
Australia[e]	10^{-6} DALYs/year	Raw WW	9.5	8	--	8.1[g]

[a]DDW (2014); [b]NWRI (2013); [c]TWDB (2015); [d]WHO (2017); [e]NRMMC (2008); [f]Total coliform; [g]*Campylobacter*

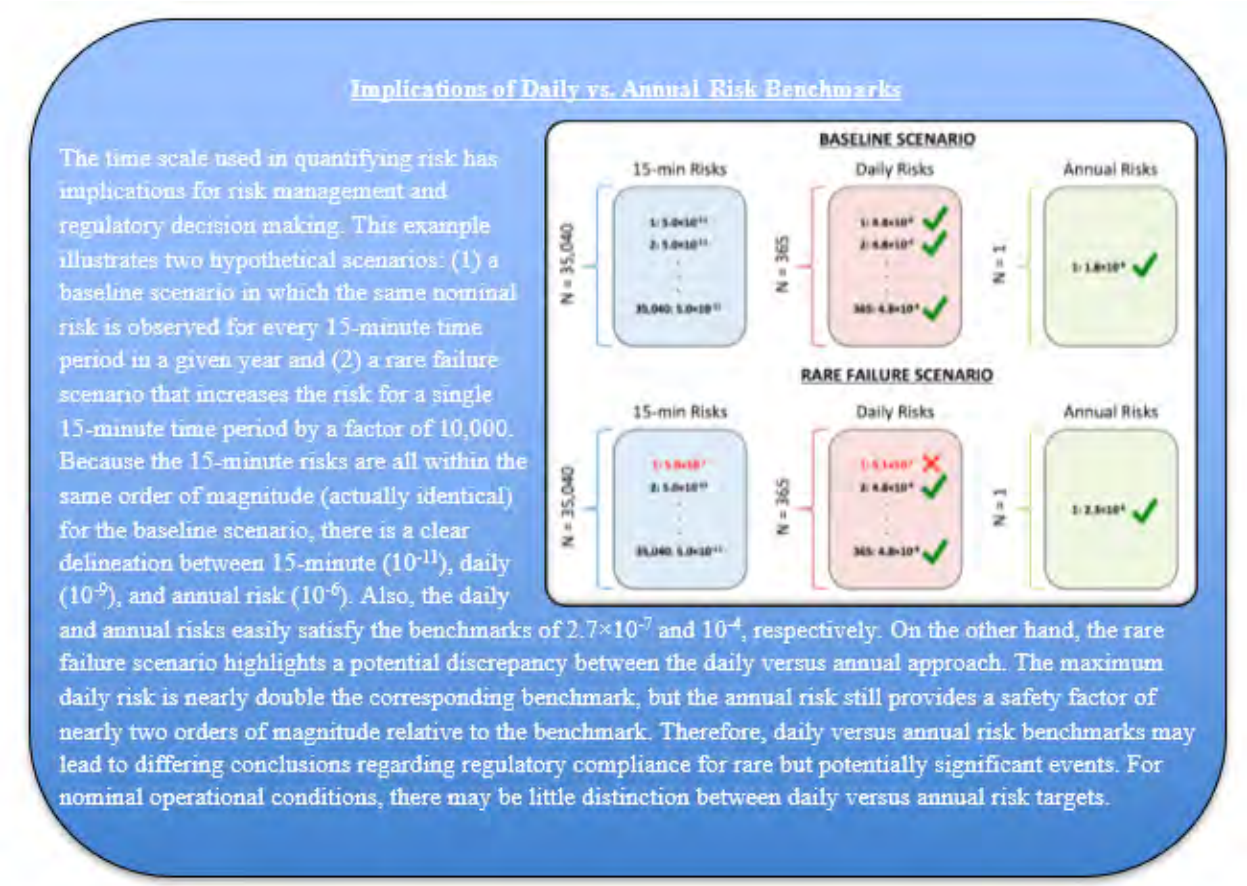
Another metric that is becoming common in the U.S. is a daily risk benchmark of 2.7×10^{-7}, which equates to the annual risk benchmark of 10-4 divided evenly across 365 days. However, it is important to note the following nuance in shifting from annual risk to daily risk, or even when comparing daily risk to 15-minute risk. The purified water from a well-operated DPR system that meets expected regulatory requirements will likely achieve risk levels that are orders of magnitude below the annual risk benchmark. Compliance will then be driven by low probability conditions that might occur only on a small number of days throughout the year (Soller et al. 2018b). In contrast, the aforementioned daily risk benchmark assumes the risk remains relatively flat at ~2.7×10-7 every day of the year. In this case, the daily risk (~10-7) and annual risk (~10-4) differ by nearly 3 orders of magnitude. But with rare events, the highest daily risk and the corresponding annual risk may actually be quite similar in magnitude because of the manner in which annual risk is calculated (see preceding equations). In other words, when extrapolating daily to annual risk, the final value generally does not reflect the vast majority of daily risk estimates and is instead driven by only a few data points—or possibly even a single data point. In a practical sense, this means that when low probability events are driving risk estimates, full compliance with a daily risk benchmark may not be necessary to achieve compliance with the corresponding annual risk benchmark. Figure 2 in Soller et al. (2017) illustrates this concept, along with a related observation for combined daily risk:

- The highest daily risk estimate essentially drives the annual risk estimate, which is why there is little visual separation between that data point and the horizontal red line. If the daily risks were shifted vertically so that the highest daily risk was just above 2.7×10^{-7}, the system would technically be in

non-compliance with the daily risk benchmark. However, that system would still be providing a safety factor spanning nearly 3 orders of magnitude when compared against the annual risk benchmark of 10^{-4}.

- The combined daily risk for this treatment scenario essentially follows a single pathogen (norovirus) because the contributions from other pathogens are negligible in comparison. This is an artifact of the equation/approach used to calculate the combined pathogen risk. Results may differ when evaluating other treatment trains or when incorporating different QMRA conditions/parameters, but in this case, calculating a cumulative (or combined) risk of all pathogens would be unnecessary.

The preceding example demonstrates that there may be scenarios in which daily versus annual risk benchmarks lead to differing conclusions regarding regulatory compliance. This possibility should be considered as part of future decision-making efforts. This is explored in greater detail in the following graphic.



B.13.2 Integration into DPRisk

For consistency with U.S. drinking water regulations and specifically potable reuse regulations in California, DPRisk focuses on the more general 'probability of infection' framework, rather than the 'disability adjusted life year' (DALY) framework. The tool specifically focuses on the 10^{-4} annual risk benchmark and the corresponding daily risk benchmark of 2.7×10^{-7} infections per person per day. As noted earlier, the daily and annual risks are computed by the tool as follows, with N representing the number of daily ingestion events:

$$P_{daily} = 1 - \prod_{n=1}^{N} (1 - P_n)$$

$$P_{annual} = 1 - \prod_{n=1}^{365\times N} (1 - P_n)$$

By default, the tool outputs these data relative to various statistical/percentile values (e.g., mean, standard deviation, minimum/maximum, 99th percentile) in tabular and graphical form to aid in identifying critical compliance thresholds. Because the tool focuses on only one pathogen at a time, there is no estimate of combined pathogen risk. However, the raw data output from the tool can be downloaded by the user, paired with model runs targeting other pathogens, and used to compute combined pathogen risks for various time intervals.

The tool also generates a benchmark profile of treatment train performance using the equations below. The resulting distribution is meant to represent the LRVs needed to achieve an annual risk of *exactly* 10^{-4}. The tool actually calculates the benchmark LRV for each combination of raw wastewater pathogen concentration and ingestion volume in an underlying 10,000-point parameter set (this parameter set is described in greater detail below). For each combination in the underlying parameter set, the tool assumes the raw wastewater pathogen concentration and ingestion volume are constant across all time intervals in the year (i.e., 365×N ingestion events per day) and then calculates the required LRV for that combination to achieve the 10^{-4} annual risk. In effect, the LRVs are calculated based on the interval-specific benchmark risk [i.e., $10^{-4}/(365\times N)$], so the benchmark LRVs are actually independent of the ingestion frequency selected by the user. Because the interval-specific risk is assumed to be constant across the entire year, while an actual simulation includes different data combinations for the various intervals, the benchmark may overestimate or underestimate the LRVs that are actually required in some instances. Therefore, the LRV benchmark curve should only be interpreted as an approximation of treatment requirements.

$$P_{annual\ benchmark} = 10^{-4} = 1 - \prod_{i=1}^{365\times N} \left[1 - D_r\left(\frac{V}{N} \times 10^{\text{Log } C_i \text{ - } LRV_{Benchmark}}\right)\right]$$

or simplified as follows based on the DPRisk calculation approach:

$$\frac{P_{annual\ benchmark}}{365\times N} = \frac{10^{-4}}{365\times N} = D_r\left(\frac{V}{N} \times 10^{\text{Log } C_i \text{ - } LRV_{Benchmark}}\right)$$

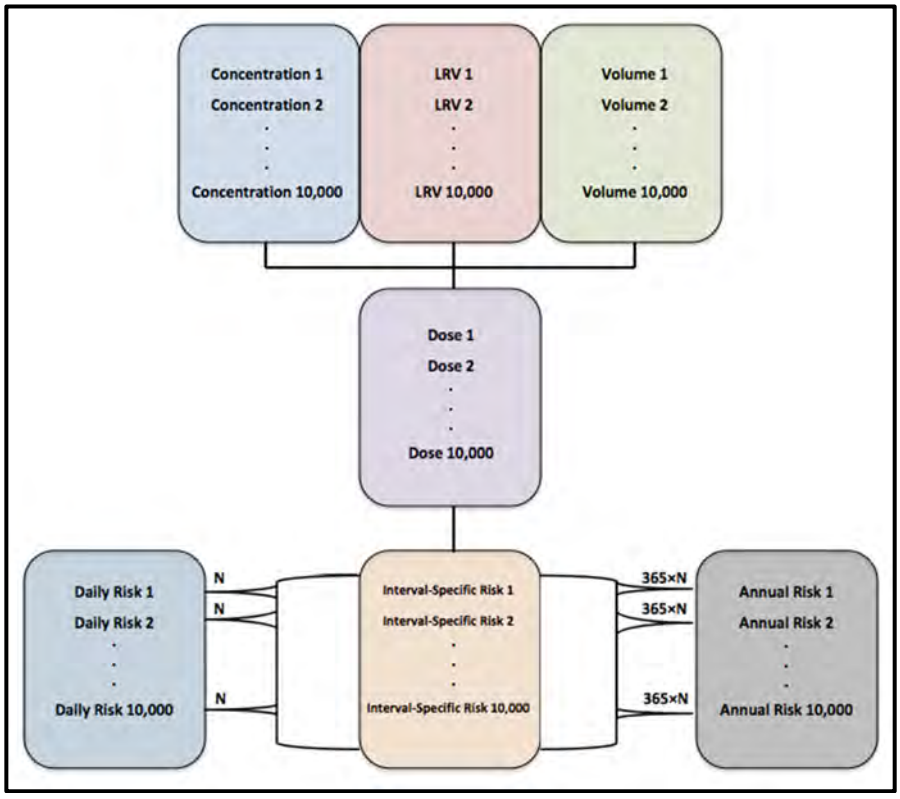
where, $P_{annual\ benchmark}$ = annualized tolerable infection risk,

D_r = dose response function,
V = daily ingestion volume from underlying parameter set,
N = number of daily ingestion events,
C = pathogen concentration in raw wastewater from underlying parameter set,
$LRV_{Benchmark}$ = required overall LRV to achieve tolerable infection risk.

Note: The benchmark LRV feature is only available when using a default dose response relationship. This is because the inverse of the dose response relationship for the benchmark annual risk has been solved off-line for each of the dose response defaults, and the resulting data array has been uploaded into the tool to reduce computer processing time. The tool then uses that array to solve for the

benchmark LRVs using the concentration/ingestion combinations generated for a given scenario. Therefore, benchmark LRVs are not calculated when a user-defined dose response relationship is selected.

The overall algorithm is illustrated in the following figure. The computations of the benchmark profile of treatment train performance and the daily and annual risks are all based on an underlying 10,000-point parameter set. In other words, the tool generates a combination of 10,000 raw wastewater pathogen concentrations, 10,000 LRVs for each unit process and management barrier (summed together to develop 10,000 overall LRVs), and 10,000 water ingestion volumes (accounting for daily ingestion volume and frequency). Together, these 'triplets' are used to compute 10,000 pathogen doses, which are then coupled with the specified dose-response function to arrive at 10,000 probabilities of infection. Each probability of infection represents the interval-specific risk, as determined by the ingestion frequency. In other words, for 96 ingestion events per day (i.e., every 15 minutes), each probability of infection represents a 15-minute risk, and for 1 ingestion event per day, each probability of infection actually represents a daily risk.



In some cases (e.g., benchmark profile of treatment train performance), the results generated by the tool are pulled directly from these 10,000 data combinations. But for the *daily* and *annual* risk calculations, additional Monte Carlo samplings are performed. Specifically, the tool randomly samples N probabilities of infection from this underlying parameter set to calculate the daily risk according to the aforementioned equation, with N representing the number of ingestion events per day. This process is repeated an additional 10,000 times to generate a distribution of daily risks. This same process is used to generate a distribution of annual risks, except that each annual risk is based on a bootstrapped Monte Carlo sampling (i.e., sampling with replacement) of 365×N probabilities of infection from the underlying parameter set. Again, this process is repeated 10,000 times to generate a distribution of annual risks. The use of 10,000 data points is a common target in the QMRA/PATTP literature and is expected to

capture an adequate number of data combinations to fully characterize the no-failure scenarios—out to 99.99%.

The failure framework also follows the same general approach, except that the tool samples 35,040 probabilities of infection for each failure simulation (i.e., 15-min time intervals spanning an entire year). The 35,040 data points are then subdivided into 365 days to generate corresponding daily risks. Therefore, each failure simulation represents 365 days, or 1 year. In contrast, the annual and daily risk samplings in the 'no-failure' framework are completely independent; this has no significant impact on risk characterization, however. In the failure framework, the tool then zeroes out the exposure in random time intervals for consistency with the daily ingestion rate. For example, if there is only one ingestion event per day, then a random selection of 95 (out of 96) exposures will be changed to zero for each day's worth of data. If there are 96 ingestion events per day, then no data are modified. The tool then randomly assigns failures (consistent with the specified failure magnitude and frequency) to individual intervals or contiguous intervals (consistent with the specified failure duration), with each interval representing a 15-minute block of time. As noted earlier, this may result in ingestions and failures that do not align with each other, although this depends on how the ingestion frequency and failure duration are defined (see Section B.17). The interval-specific, daily, and annual risks are then recalculated to reflect these changes.

In contrast with the 'no-failure' framework (fixed at 10,000 samplings), the user can specify the number of Monte Carlo simulations (or years) used to develop the risk distributions for failure conditions. This setting can be modified in the Configure section of the tool interface. By default, the tool is set to **100 failure simulations**, which should achieve adequate risk characterization for most applications while also requiring reasonable computer processing time. However, this setting may need to be increased to capture low probability events (e.g., low probability failure of a single unit process or a simultaneous failure of multiple unit processes), depending on the characteristics of the user-defined scenario.

If the frequency of treatment failure is specified as probabilistic, and assuming an average frequency of one day per year, the daily probability of failure in DPRisk would be specified as 0.00274 (i.e., 1/365). Since each Monte Carlo simulation represents a year (i.e., 35,040 15-min time points allocated to 365 days), then each Monte Carlo simulation would capture one failure per treatment process on average. Although each treatment process in the treatment train would likely fail at some point within the simulated year, the probability of two treatment processes failing simultaneously would be very low. For a treatment train with two independent unit processes, each with a daily failure probability of 0.00274, the probability of both processes failing on the same day would be 7.51×10^{-6} (i.e., 0.00274×0.00274). Capturing that kind of compound failure would require ~133,198 simulated days (i.e., $1/7.51\times10^{-6}$) or ~365 Monte Carlo simulations (i.e., 133,198 days/365 days per simulation). Following this same approach, capturing the simultaneous failure of three independent unit processes on the same day would require ~49 million days or ~133,000 Monte Carlo simulations.

However, the failure duration and ingestion frequency also factor into this discussion. If the ingestion frequency is every 15 minutes and the failure duration is 24 hours, then the estimates above would likely be sufficient to observe at least one simultaneous failure. But if the failure duration is only 15 minutes, then the failures might occur on the same day but not during the same 15-minute time interval. The probability of a treatment process failing in a given 15-minute time interval would be 2.85×10^{-5} (i.e., 1/35,040), and the probability of two independent treatment processes failing in the same 15-min time interval would be 8.14×10^{-10} (i.e., $2.85\times10^{-5} \times 2.85\times10^{-5}$), or approximately once every 1.2 billion time intervals. Considering that each simulation includes 35,040 time intervals, a

simultaneous failure of two independent treatment processes in the same 15-minute time interval would require ~35,040 simulations—and a significant amount of computer processing time.

An important question then arises: How important/realistic is this type of extreme low probability event, particularly when considering that surrogate monitoring would be required at critical control points in DPR systems? As noted in the following table, 100 failure simulations **captures greater than 99.99% of the variability** within a given scenario and can also capture rare failures that might occur once every 36,500 days (24-hr failure duration) or once every 3 million time intervals (15-min failure duration and 96 ingestions per day).

No. of Failure Simulations	Max Percentile for Daily Risk	Max Percentile for Annual Risk	Min. Failure Frequency Captured		Min. Daily Failure Probability to Observe a Single Failure[b,c]
			24-hr Duration	15-min Duration[b]	
1	99.7%	N/A	~1 failure per 365 days	~30 failures per million intervals	2.7×10^{-3}
10	99.97%	90%	~1 failure per 3,650 days	~3 failures per million intervals	2.7×10^{-4}
100[a]	**99.997%**	**99%**	**~1 failure per 36,500 days**	**~0.3 failures per million intervals**	**2.7×10^{-5}**
1,000	99.9997%	99.9%	~1 failure per 365,000 days	~0.03 failures per million intervals	2.7×10^{-6}

[a]Recommended setting to achieve adequate risk characterization (>99.99%) within reasonable computer processing time
[b]Assumes 96 ingestions per day (i.e., every 15 minutes) to ensure failure and ingestion event are aligned
[c]Daily failure probability that should be entered into the tool to achieve the specified conditions

Deterministic failures are a more efficient way of observing risk results for a specific numbers of failures rather than relying on probabilistic frequencies that may or may not occur in a given simulation. Coupling deterministic failures with high failure frequencies (e.g., 3 failures per treatment process per year) artificially increases the probability of observing rare compound/simultaneous events in the tool output, which artificially increases the frequency of high-risk scenarios. This deterministic approach could be the first step in characterizing the risk implications of a compound failure. If the risk is deemed to be potentially significant, then a probabilistic assessment with a greater number of failure simulations might be warranted. That final assessment might provide a more reasonable characterization of how the rare event actually affects the overall distribution of risk, rather than forcing it to occur in every simulation.

Even if compound failures are assumed to be unlikely, it is still important to understand the implications of coupling single-process failures with extreme values for other model parameters, such as raw wastewater pathogen concentration. For example, a failure that occurs in conjunction with a very low pathogen concentration may not be as impactful as a failure that occurs with a very high pathogen concentration. In the earlier example, each model simulation would likely result in a single failure per treatment process. By increasing the failure setting to 1,000 Monte Carlo simulations, each treatment process would experience ~1,000 failures, thereby reflecting a much broader range of parameter combinations and perhaps even coupling more extreme parameter values with compound failures. This may require a substantial increase in computer processing requirements and may not be warranted in many instances.

As noted earlier, the default for the DPRisk failure framework is set at 100 Monte Carlo simulations to expedite computer processing and to allow for a preliminary evaluation of failure significance. This is likely adequate for most modeling scenarios, but it is recommended that the user assess model sensitivity to the number of Monte Carlo simulations by changing the setting in the Configure section of the tool. With the examples above as a guide, a probabilistic approach can be used to evaluate whether a sufficient number of simulations has been selected to (1) adequately capture rare events and (2) adequately sample the various combinations that might result from the parameter distributions.

B.14 Final Tool Considerations

B.14.1 Tool Output

After establishing all of the inputs for a particular scenario, the user initiates the calculations by clicking on the PATTP Output section of the tool interface. The tool will then display the following treatment performance plots and statistical summaries:

- Combined plot of benchmark and simulated treatment train performances;
- Plot of benchmark treatment train performance and statistical summary of raw data;
- Plot of simulated treatment train performance with failures considered;
- Plot of simulated treatment train performance in the absence of failures;
- Summary table of raw data and related statistics for non-failure LRVs;
- Summary table of raw data and related statistics for failure LRVs.

After clicking the QMRA Output section of the interface, the tool will initiate Monte Carlo simulations for the risk and failure calculations. A status bar should appear to show the tool's progress on the (1) risk calculations and then the (2) the failure analysis calculations. The tool will then display the following output:

- Plot of annual risk (shows 10^{-4} benchmark) and statistical summary of raw data;
  - Differentiates non-failure and failure data (when applicable);
- Raw data for non-failure and failure annual risks (.csv available for download);
  - Used for Comparison of Risk Curves feature with failures considered;
  - Parameter set for first 5 failure simulations (.csv available for download);
- Plot of daily risk (shows 2.7×10^{-7} benchmark) and statistical summary of raw data;
  - Differentiates non-failure and failure data (when applicable);
- Raw data for non-failure and failure daily risks (.csv available for download);
  - Used for Comparison of Risk Curves feature with failures considered;
- Hazard identification summary;
- Plot of raw wastewater pathogen concentrations and statistical summary of raw data;
- Exposure assessment summary;
- Plot of ingestion volumes and statistical summary of raw data;
- Dose response summary;
- Plot of pathogen doses and statistical summary of raw data;
- Plot of 15-min risk estimates;
- Parameter set for the 10,000 Monte Carlo simulations (.csv available for download);
  - Used for Comparison of Risk Curves feature with failures omitted.

After clicking the Summary of PATTP and QMRA Output section of the interface, the tool will display the following output:

- Combined plot of benchmark and simulated treatment train performances;
- Plot of annual risk (shows 10^{-4} benchmark) with and without failures (when applicable);
- Plot of daily risk (shows 2.7×10^{-7} benchmark) with and without failures (when applicable).

Each downloadable .csv file includes a number of data columns with unique column headers. Definitions and descriptions are provided in Section B.19.

After clicking the Comparison of Risk Curves section of the dashboard, the user can upload up to three .csv files to generate combined plots of (1) daily and annual risk for a *no-failure* scenario, (2) annual risk for a *failure* scenario, or (3) daily risk for a failure scenario. The user can click the upload button and navigate to the directory containing each file or drag and drop each file into one of the "Browse" bars. For (1), the required input files can be downloaded from the QMRA Output page by clicking on Download Parameter Set Data at the bottom of the page. For (2), the required input files can be downloaded from the QMRA Output page by clicking on Download Failure Analysis Pannual Data. For (3), the required input files can be downloaded from the QMRA Output page by clicking on Download Failure Analysis Pdaily Data. When conducting a failure analysis, the no-failure data are extracted from the first file uploaded into the comparison feature. Therefore, the annual or daily comparison can show up to four plots simultaneously (no-failure scenario 1, failure scenario 1, failure scenario 2, failure scenario 3). ***If the tool returns an error when using the Comparison of Risk Curves feature, the user should first verify that the .csv files are uploaded to the correct section of this feature (i.e., no failure vs. annual risk with failures vs. daily risk with failures).***

B.14.2 Tool Precision

For some PATTP/QMRA scenarios, the resulting risks will be incredibly low, particularly for the default 15-minute time intervals in DPRisk. Similar to other software platforms, R has a default limit on precision that prevents it from reporting extremely low values (i.e., when the response computed from the dose-response function is $<10^{-16}$). At that point, R replaces the value with 0. This issue has been observed for highly conservative treatment scenarios in other QMRAs (Amoueyan et al. 2019). However, because this issue is specific to very low risk scenarios, it will not impact decision making, which typically focuses on scenarios in which the modeled risk approaches regulatory benchmarks. Moreover, this precision issue was found to have no appreciable impact on daily and annual risk estimates for DPRisk. Therefore, the increase in computing time that would be required for implementation of high precision computing was found to be unwarranted.

B.14.3 Random Number Seed

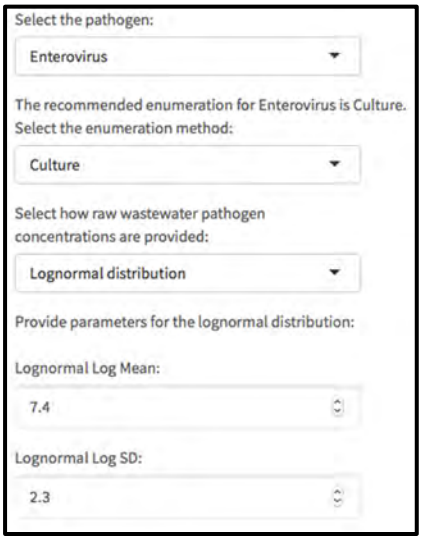
Another important setting in the Configure section of the tool is the random *seed* input. This is a model input that 'seeds' the random number generator involved in developing distributions for the various model inputs. The default setting for the seed is 1, although there is no single 'correct' value to use. With sufficient Monte Carlo simulations, the seed setting should not impact the overall results and conclusions drawn from the PATTP/QMRA. When the default seed setting is used in conjunction with a consistent set of model inputs, the output should be identical every time the tool is reloaded and used, even though the underlying data are randomly determined to account for the variability of model inputs. In other words, two users simulating the exact same model scenario should obtain the same tool output when they initially launch the tool and use the same seed. This is also important for the case studies described in the following sections (i.e., the default seed of 1 should be used to generate the exact same output shown in the case studies). If the user purposefully wants to generate different random number sequences, the user can specify a different random number seed (usually set to a large integer). By modifying the seed, the output will change because of the change in the random number algorithm, but this should have no impact on the overall results assuming a sufficient number of Monte

Carlo simulations are performed. This is irrelevant for the 'no failure' scenarios because of the default setting of 10,000 Monte Carlo simulations, but this could theoretically be an issue for failure scenarios when only a small number of simulations is specified in the Configure section. For more information on random number generation in R, please see: https://stat.ethz.ch/R-manual/R-devel/library/base/html/Random.html.

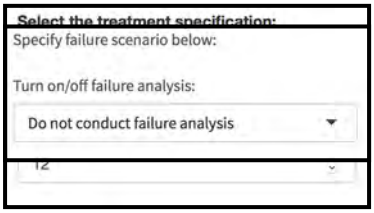
B.15 Case Study 1: QMRA for Enterovirus in a Default DPR Scenario

Case Study 1 demonstrates use of the tool to model enterovirus and *Cryptosporidium* risk using recommended default settings, including the raw wastewater pathogen data from DPR-2. This case study also demonstrates how settings can be changed to evaluate sensitivity on the dose response model and also differential performance between AWPFs. For example, this case study considers differences in overall redundancy and also evaluates tight tolerances on critical control points vs. situations with less stringent monitoring of operational performance.

1. Access the tool via the DPRisk website link. The code can also be downloaded and run locally using R. Input files are available for download under the How to use this tool option in the menu bar.
2. Select Raw Wastewater Pathogen Concentrations on the left menu bar. This will bring the user to an input screen where (1) the target pathogen can be selected, (2) additional information related to the pathogen enumeration method can be identified, and (3) the distribution of raw wastewater concentrations can be characterized. The concentrations can be described by a **lognormal distribution with user-defined parameters (current scenario)**, a user-provided data file that follows a lognormal fit (tool will use MLE to identify lognormal parameters), or a user-provided data file that has already been curated with 10,000 data points. Note that the information for enumeration method does not impact the QMRA and is only stored for user reference. Based on the data from DPR-2, the raw wastewater concentration for **enterovirus** can be described with a **lognormal mean of 7.4** and **lognormal standard deviation of 2.3** based on **culture methods**. This lognormal mean equates to a concentration of $e^{7.4} = 1.6 \times 10^3$ most probable number (MPN) per L of raw sewage.

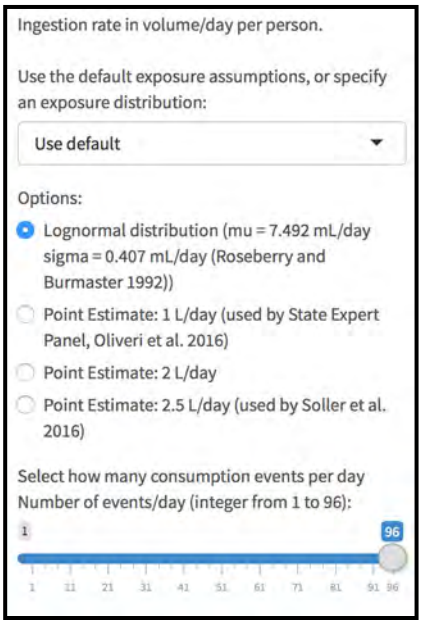


3. Select Treatment Train on the left menu bar. This will bring the user to an input screen where the treatment train can be selected and characterized. Treatment can be characterized as (1) **a single LRV point estimate for the entire treatment train (current scenario)**, (2) a user-provided data file that has already been curated with 10,000 LRVs for the overall treatment train, or (3) individual log removals for each process. This case study will initially assume a **point estimate LRV of 12**, which is consistent with the California potable reuse regulatory framework for groundwater augmentation when targeting viruses. When specifying the point estimate LRV, the user can select an integer by adjusting the arrows up/down or by directly typing a value (including decimals) into the entry box.

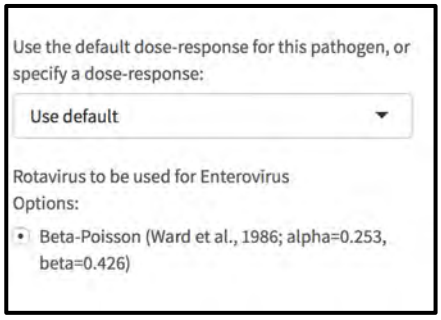


4. Select Treatment Failure on the left menu bar. This case study does not incorporate treatment failures so **"Do not conduct failure analysis"** should be selected.

5. Select Management Barriers on the left menu bar. This case study does not incorporate blending, dilution, or die-off so the **default LRV of 0** can remain unchanged.
6. Select Exposure on the left menu bar. This will bring the user to an input screen where the daily ingestion rate and frequency can be specified and characterized. The ingestion rate can be described by one of the default distributions/point estimates or specified by the user. The user-specified option allows for (1) an input file with 10,000 data points, (2) a point estimate, or (3) a lognormal distribution with user-defined mean and standard deviation. For the user-specified options, ingestion volume should be based on units of ***mL/day***. For this case study, the **default lognormal distribution from Roseberry and Burmaster (1992)** should be selected: lognormal mean of 7.492 and lognormal standard deviation of 0.407. This lognormal mean equates to a daily ingestion volume of $e^{7.492}$ = 1,794 mL/day. In DPRisk, the daily ingestion volume can be divided across any number of aliquots ranging from 1 to 96. For this case study, the **default setting of 96 consumption events per day** (i.e., every 15 minutes) is selected.

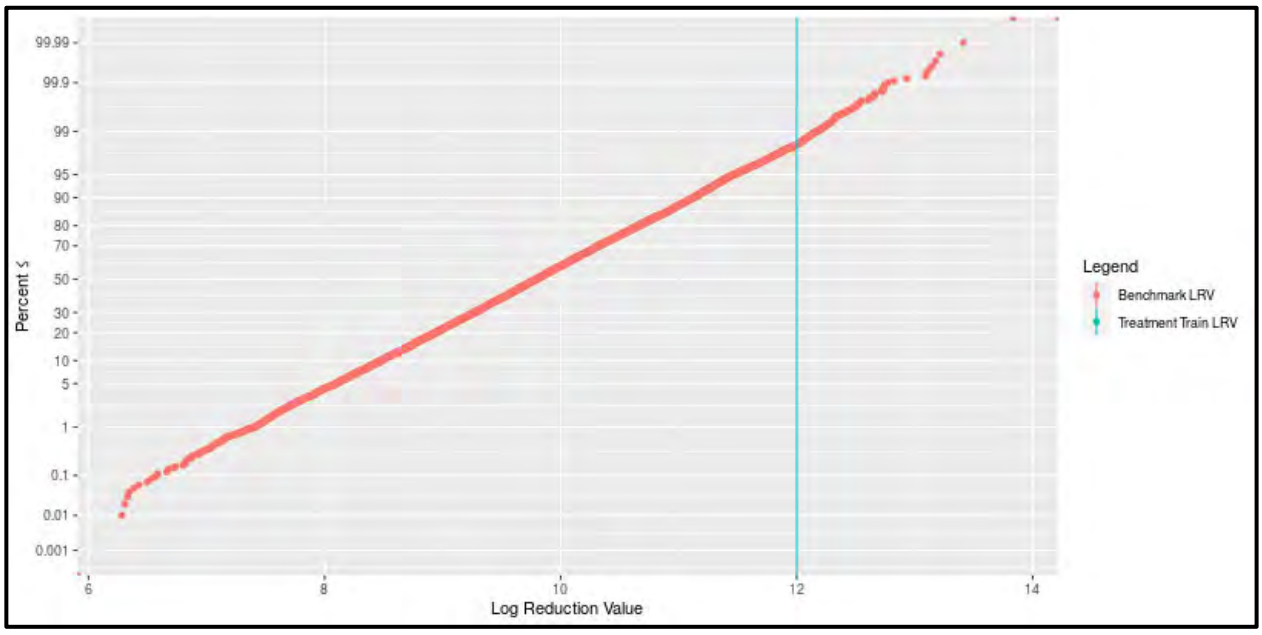


7. Select Dose-Response on the left menu bar. This will bring the user to an input screen where the pathogen dose-response equation can be identified and characterized. The user can **(1) select one of the default dose-response models specific to the target pathogen** (enterovirus in this scenario) or (2) select and characterize one of several dose-response models commonly used in QMRAs. For this case study, the **default** dose response model is used (**Beta-Poisson with alpha = 0.253 and beta = 0.426**).

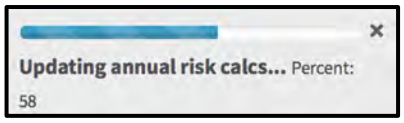


8. Select PATTP Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulations and calculations related to treatment train performance. The following series of figures summarizes the PATTP output for Case Study 1. Assuming the 'seed' for random number generation under the Configure tab is set at 1, some of the output may appear exactly as shown.

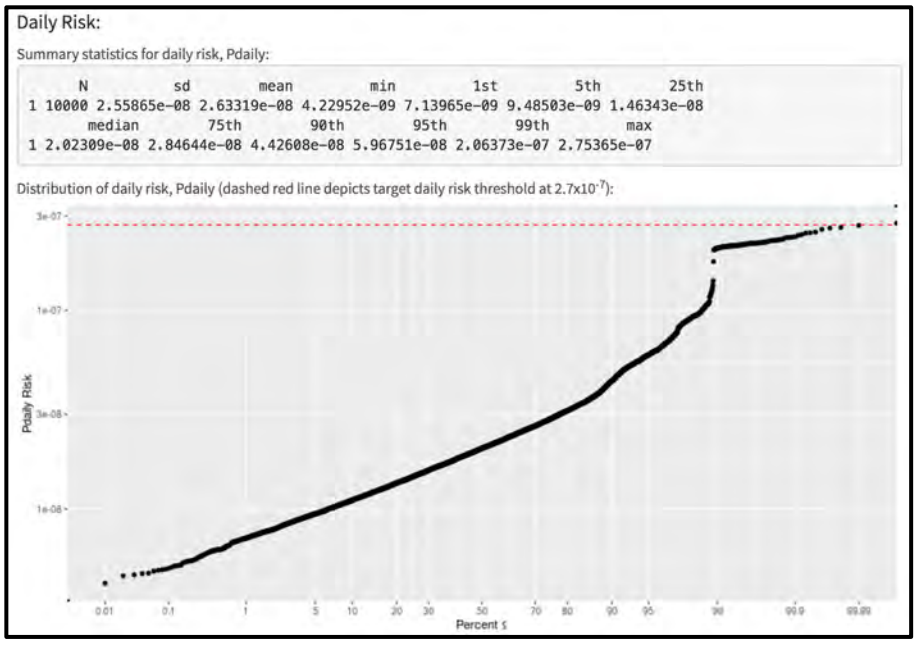
   The first plot shown is the comparison of the 'observed' treatment train performance, which in this scenario is a point estimate of 12, and the benchmark treatment train performance required to achieve an annual risk of infection of 10^{-4}. By cross-referencing with the summary statistics shown below the plots in the tool output, the benchmark LRVs exceed the 12-log point estimate (blue vertical line) beyond the 99th percentile. This apparent discrepancy with California's IPR regulations occurs because the enterovirus concentrations from the DPR-2 distribution exceed the 10^5 MPN/L point estimate beyond the 95th percentile, reaching a maximum of 1.0×10^7 MPN/L (available in QMRA Output). The use of the lognormal distribution for ingestion volume—rather than a 2 L/day point estimate—may also contribute to the apparent discrepancy.

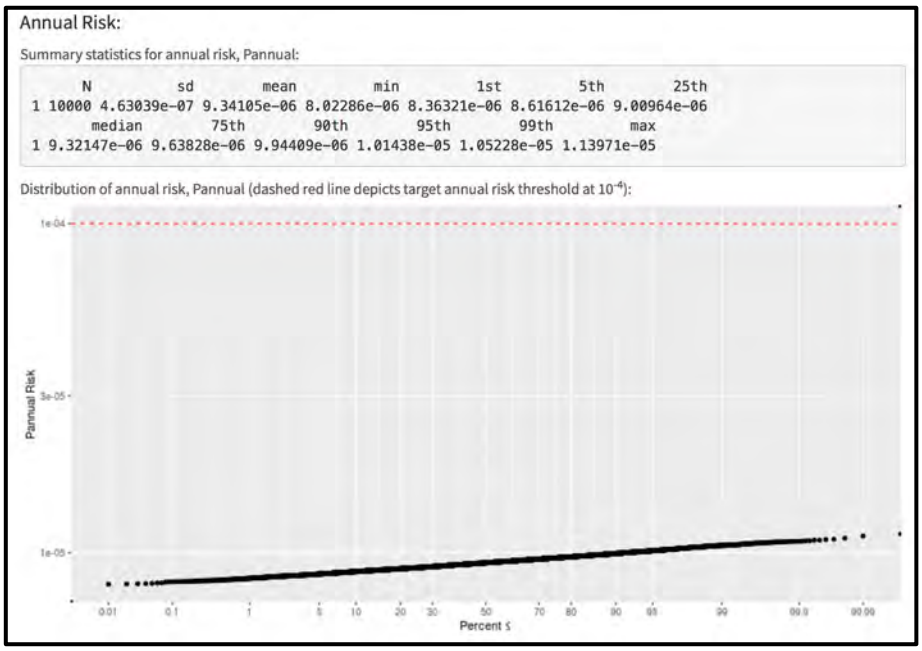


9. Select QMRA Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulation and calculations related to daily and annual risk. A box will likely appear in the bottom right corner of the screen to indicate the tool's progress.



The resulting output includes figures and summary statistics for raw wastewater pathogen concentration, ingestion volume, pathogen dose, 15-min risk of infection, and also the raw data available for download by the user. The output should also include the annual and daily risk statistics and cumulative distribution plots (shown in the following figures).





Interestingly, only the maximum daily risk exceeds the benchmark, despite the fact that the benchmark LRVs exceed 12 at the 99th percentile. The 96 ingestions per day likely attenuate the daily risk so that only the maximum value surpasses the benchmark. This 'averaging effect' is even more apparent in the annual risk distribution, which falls well below 10^{-4} and exhibits ~1 log of buffer relative to the benchmark even at the upper percentiles. This occurs because the high daily risks that occur ~1% of the time are coupled with lower daily risks that occur ~99% of the time, thereby resulting in a relatively flat annual risk curve. Repeating this scenario with the DPR-2 enterovirus distribution, an ingestion volume of 2 L, and an ingestion frequency of once per day—consistent with California's original deterministic approach for IPR—results in a risk distribution that exceeds the daily benchmark at the 99th percentile, but the maximum annual risk (3.8×10^{-5}) still falls well below the 10^{-4} annual risk benchmark.

At the bottom of the QMRA Output screen, there is a table of raw data and a link to download the raw data (Download Parameter Set Data). Click on the link and note where the .csv file is saved. This file will be used in the subsequent sensitivity analysis.

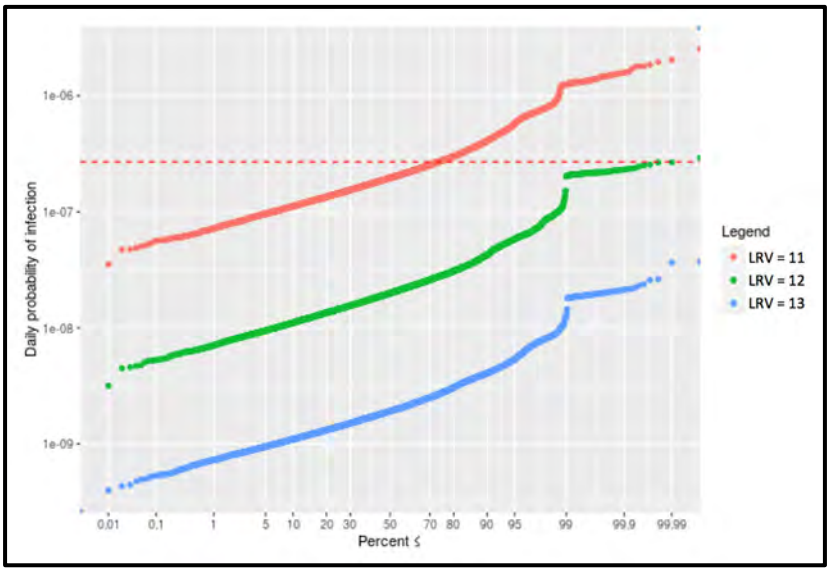
10. Select Summary of PATTP and QMRA Output on the left menu bar, which will bring the user to a screen summarizing only the critical outputs from the tool, specifically the LRV comparison and the daily and annual risks. The supporting data excluded from this summary are still accessible in the other tabs.

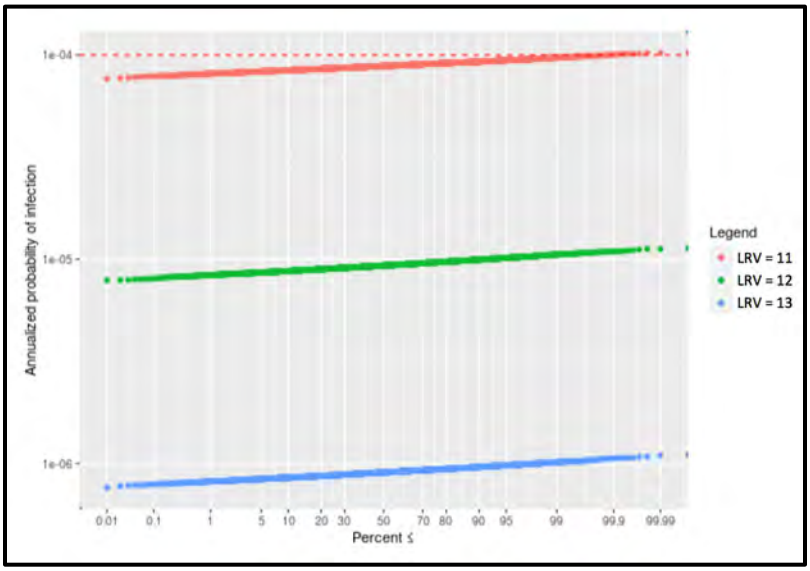
B.15.1 Sensitivity Analysis on LRV Point Estimate

To allow for a straightforward sensitivity analysis on treatment train performance, the preceding case study can be modified in the Treatment Train portion of the model. Instead of assuming a single point estimate of 12, this portion of the case study illustrates the impact of varying the point estimate from 11 to 13. The user should follow the same step-by-step procedure outlined earlier in the case study, but in the Treatment Train tab, the user should select **a single LRV point estimate for the entire treatment train** and run additional scenarios with **LRVs of 11 and 13**. For each model run, the user should navigate to the QMRA Output screen and click the link at the bottom of the page to download the raw data (Download Parameter Set Data). Those .csv files can then be uploaded to the tool using the Comparison of Risk Curves option in the left menu bar. Up to three .csv files can be compared simultaneously by

clicking the upload button and navigating to the directory containing each file or by dragging and dropping each file into one of the “Browse” bars. The files should be uploaded to the **Non-Failure Analyses** section.

The resulting comparisons for daily and annual risk are shown in the following figures. With a point estimate LRV of 13, the daily and annual risk distributions fall well below their respective benchmarks. As mentioned in the previous section, the point estimate LRV of 12 exceeds the daily risk benchmark at the maximum value, but the annual risk distribution satisfies the 10^{-4} benchmark at all times. However, with a point estimate LRV of 11, the daily risk benchmark is surpassed at the 70th percentile, and even the annual risk benchmark is surpassed near the 99.9th percentile. This comparison also illustrates how each additional LRV provides added redundancy that is ultimately reflected as an upward/downward shift in the risk curves. For example, the daily risks for the 50th percentiles are 1.9×10^{-7}, 1.9×10^{-8}, and 1.9×10^{-9} for overall LRVs of 11, 12, and 13, respectively. When modeling more complex scenarios, these types of vertical shifts may not always provide straightforward estimates of LRV redundancy because the risk curves may exhibit unique profiles at the tails of the distributions, particularly when rare failures are simulated.



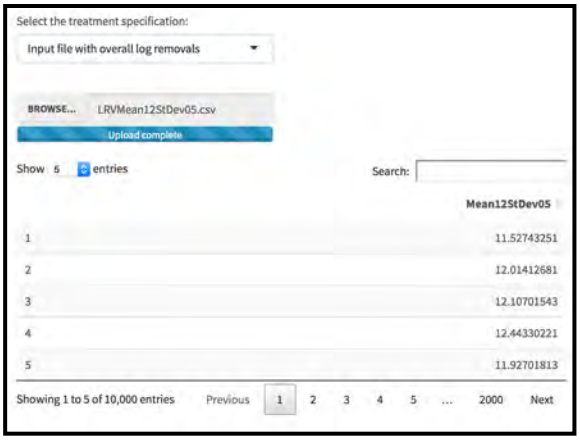


B.15.2 Sensitivity Analysis on Treatment Variability

Instead of assuming point estimates for the LRV, this portion of the case study illustrates the impact of allowing the overall treatment train LRV to follow a normal distribution with a mean of 12 but standard deviations of 0.5, 1.0, or 1.5. From the definition of a normal distribution, this means the LRV would fall between +/- 1 standard deviation of the mean (11.5-12.5, 11.0-13.0, and 10.5-13.5, respectively) for approximately 68% of all simulations or +/- 2 standard deviations of the mean (11.0-13.0, 10.0-14.0, and 9.0-15.0, respectively) for approximately 95% of all simulations.

This option for the overall treatment train LRV is not explicitly available in DPRisk, but due to the flexibility in the tool, there are actually two 'workarounds' that can be exploited to build this scenario. This Guidance Document previously explained that the unit processes under the Treatment Train section of the user interface are capped at 6 logs (e.g., when defining a zero-truncated normal distribution), and the only exceptions include input files and point estimates. This would be a viable option for understanding process-specific tolerances for variability when the individual unit process is not expected to exceed 6 logs, but this would not work for the current scenario evaluating an overall treatment train LRV with a mean of 12 logs. However, the user could define the **overall treatment train LRV** with a **point estimate of 0** and any of the Management Barrier LRVs with a **zero-truncated normal distribution** with a **mean of 12** and **standard deviations of 0.5, 1.0, or 1.5**. Management barrier LRVs are not limited by the 6-log cap so this would allow the user to achieve the desired conditions.

Another approach is for the user to generate unique datasets outside of DPRisk (e.g., in Microsoft Excel) that can be incorporated into the QMRA/PATTP. As an example, three user input files are available for use in this scenario (LRVMean12StDevXX.csv). The input files are single-column .csv files with a column header and are curated with 10,000 data points that follow the aforementioned normal distributions. The user should follow the same step-by-step procedure outlined for the baseline Case Study 1 scenario, but in the Treatment Train tab, the user should select **Input file with overall log removals** and upload the files in separate model runs. For each model run, the user should navigate to the QMRA Output screen to download the raw data (Download Parameter Set Data). Similar to the previous sensitivity analyses, those .csv files can be uploaded to the tool using the Comparison of Risk Curves option in the left menu bar (*Non-Failure Analyses* section).



This table summarizes the log removal values simulated by the tool for each scenario. As noted earlier, the definition of a normal distribution provides some insight into the expected output (e.g., 68% of all data falling within +/- 1 standard deviation of the mean). The LRVs at the lower percentiles drive the daily and annual risks, so although the treatment train LRV increases to >17.5

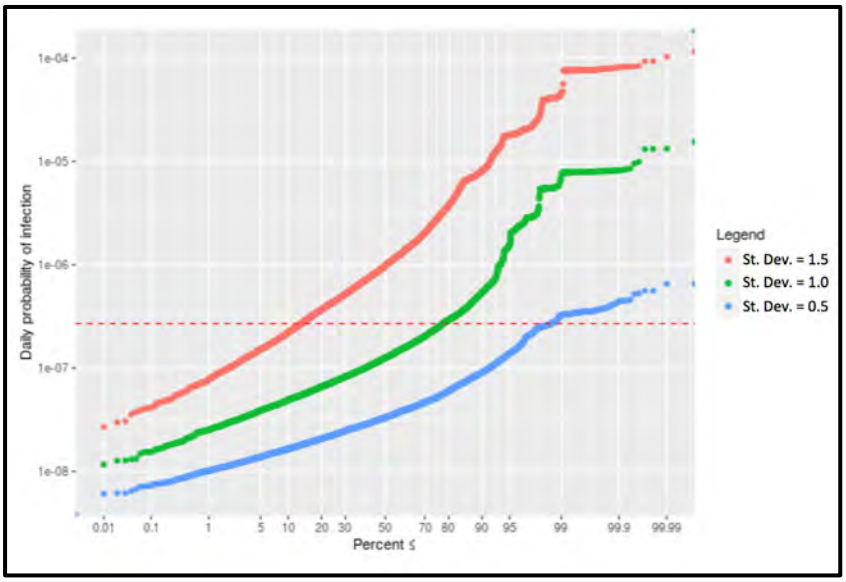
Treatment specification: Overall log removal point estimate

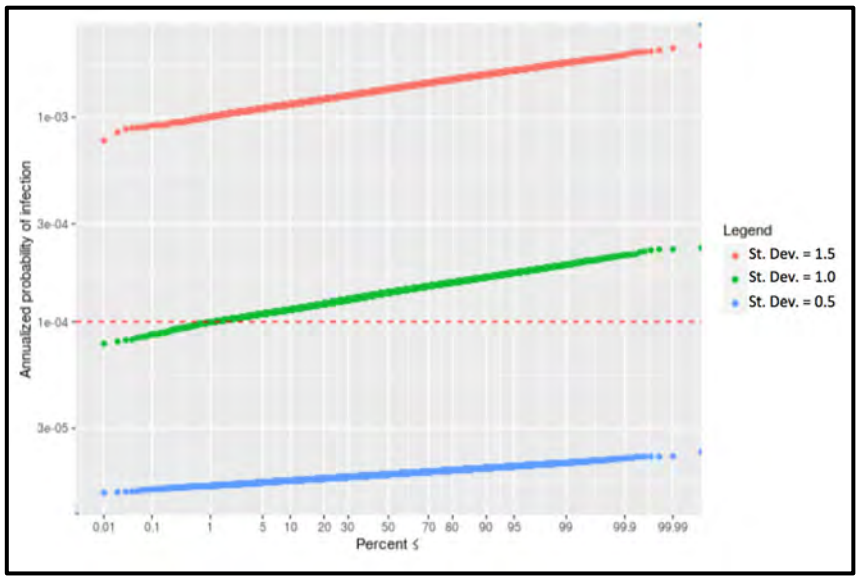
Treatment Process Summary of overall log removal:

Min	25th	50th	75th	Max	Mean		
12	12	12	12	12	12	$\mu = 12.0$	$\sigma = 0.0$
10.19	11.65	11.99	12.33	13.80	11.99	$\mu = 12.0$	$\sigma = 0.5$
8.38	11.31	11.98	12.65	15.59	11.98	$\mu = 12.0$	$\sigma = 1.0$
6.72	11.03	12.00	13.02	17.53	12.02	$\mu = 12.0$	$\sigma = 1.5$

for σ = 1.5, those low risk data points are overshadowed by the minimum LRVs and corresponding high risk data points.

The following plots summarize the daily and annual risks, respectively, for each standard deviation scenario. Recall that the point estimate LRV of 12 (i.e., standard deviation = 0) reached the daily risk benchmark at the far end of the distribution. With greater variability in treatment train performance, the daily risk benchmark was surpassed earlier—at the 15th, 75th, and 98th percentiles for standard deviations of 1.5, 1.0, and 0.5, respectively. In fact, the standard deviations of 1.0 and 1.5 reached *daily* risks of 10^{-5} and 10^{-4}, respectively, at the upper percentiles. The standard deviation of 0.5 still complied with the 10^{-4} annual risk benchmark at all times. However, the standard deviation of 1.0 surpassed the annual risk benchmark at the 1st percentile, and the standard deviation of 1.5 reached an annual risk of nearly 10^{-3} or higher across the entire distribution.





For scenarios with steep daily risk curves at the upper percentiles, the annual risk can be similar in magnitude to the highest daily risks, and for scenarios with flatter daily risk curves, the annual risk is

generally more than 2 orders of magnitude higher than the daily risk. Therefore, when the daily risk curve is steep only at the upper percentiles, indicating events with greater severity but low frequency, evaluating compliance using daily versus annual risk benchmarks may lead to differing regulatory conclusions. This is the case for the preceding scenarios with standard deviations of 0 (baseline) or 0.5, both of which exceeded the daily risk benchmark but always satisfied the 10^{-4} annual risk benchmark. This feature will also be discussed in Section B.16, where failure conditions cause significant increases in daily risk at the upper percentiles.

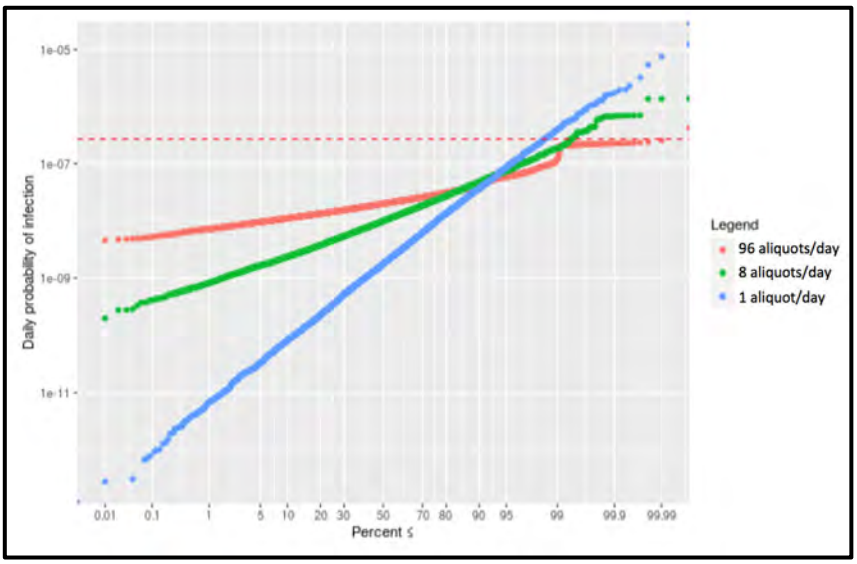
These sensitivity analyses provide a general framework for evaluating the effects of treatment redundancy and assessing the tolerance of a given treatment train (or individual treatment process) to variability in performance. A system with adequate treatment (i.e., high mean LRV) and tight tolerances (i.e., low standard deviations) should consistently comply with acceptable risk thresholds. However, as variability in treatment train performance increases, deviations from nominal performance coupled with high raw wastewater pathogen concentrations may result in regulatory compliance issues. Sensitivity analyses can help identify the level of variability that can be tolerated before public health is potentially compromised.

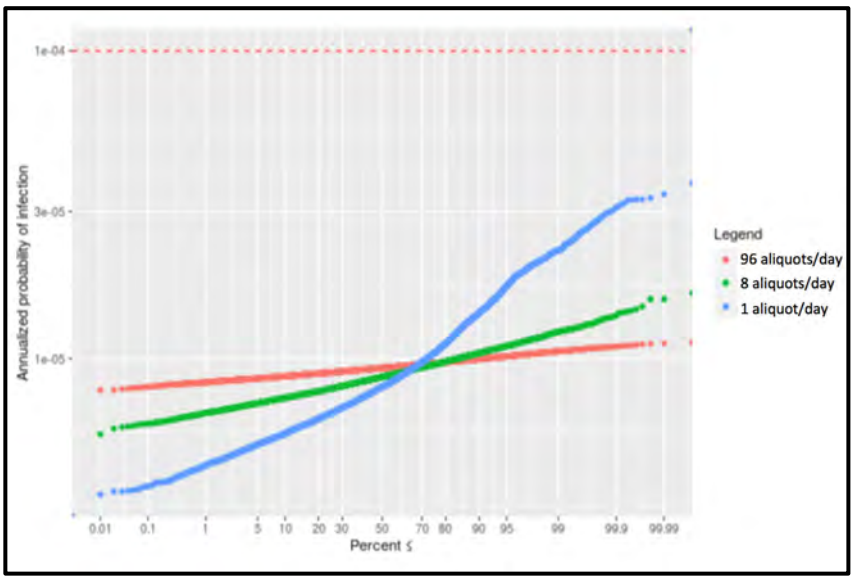
B.15.3 Sensitivity Analysis on Ingestion Frequency

For consistency with some online monitoring approaches, the default ingestion frequency in DPRisk is 96 consumption events per day (i.e., every 15 minutes). Although this may aid in capturing the range in water quality delivered throughout the day, it may not accurately reflect a typical daily exposure, as people are unlikely to fill up a glass of water 96 different times in a given day. Therefore, the tool also provides flexibility to allow any number of consumption events per day, ranging from 1 to 96. The daily ingestion volume for a given day remains the same, but that volume is divided into the specified number of aliquots, with each aliquot potentially being linked to a different pathogen concentration and treatment train LRV (when applicable).

This sensitivity analysis illustrates the potential implications of selecting different ingestion frequencies—a topic that is also addressed later in Section B.17. Many of the baseline settings described earlier remain the same, including the DPR-2 distribution for raw wastewater enterovirus concentrations, the treatment train LRV point estimate of 12, and the distribution on ingestion volume, but instead of using the default setting of 96 consumption events per day in the Exposure tab, additional scenarios with **8 consumption events per day** and **1 consumption event per day** are simulated. The following figure shows the resulting QMRA Output after uploading the .csv files (Download Parameter Set Data) to the Comparison of Risk Curves tab.

Increasing ingestion frequency causes a similar ‘averaging’ effect or curve flattening as when daily risks are converted to annual risks. Assuming the base data distribution is sampled sufficiently to capture the extremes, consuming the entire daily ingestion volume at a single time (i.e., when pathogen concentrations are at a maximum) will result in a higher daily risk than when that maximum pathogen concentration is only present in $1/8^{th}$ or $1/96^{th}$ of the daily ingestion volume. In general, this results in a steeper risk curve. In this comparison, the daily risk benchmark is only exceeded at the far end of the distribution for 96 aliquots per day, but the daily risk benchmark is exceeded at about the 98^{th} percentile when consuming the entire daily volume in a single ingestion event. All scenarios still satisfy the 10^{-4} annual risk benchmark at all times. When using the tool to aid in decision-making, it is therefore important to consider the scenario’s sensitivity to ingestion frequency, in addition to other critical model inputs and assumptions.



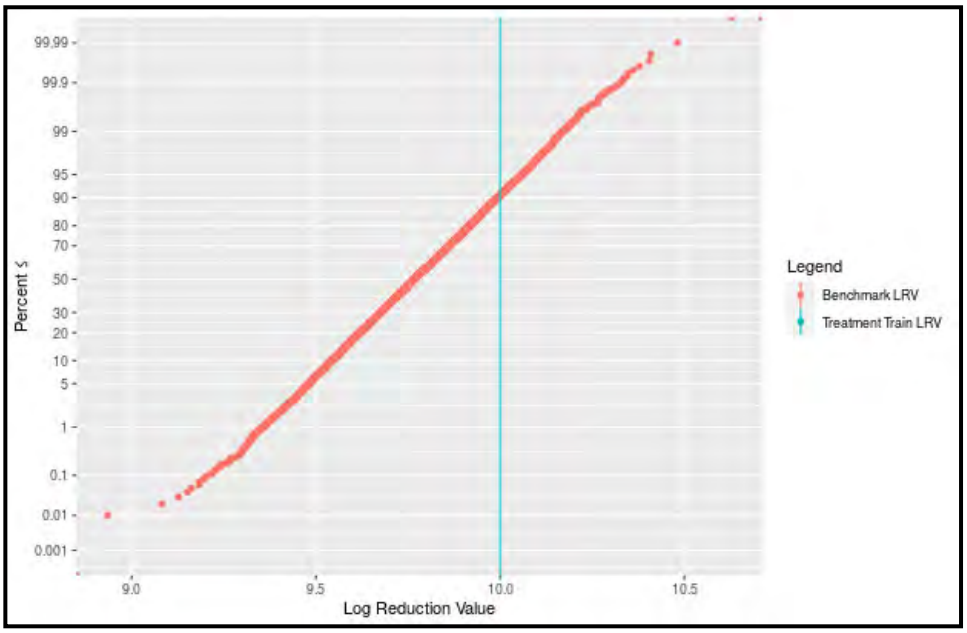


B.15.4 Alternative LRV Point Estimate Analysis on *Cryptosporidium*

Another potential use of the overall treatment train LRV point estimate is an assessment of California's 10-log treatment requirement for *Cryptosporidium* in groundwater augmentation applications. For this sensitivity analysis, a user input file for raw wastewater *Cryptosporidium* concentration (point estimate of 10^4 oocysts/L) is available for download under How to use this tool in the left menu bar (CryptoRawWW.csv). This file can be uploaded in the Raw Wastewater Pathogen Concentrations tab with the **Data file, use as is** option. Alternatively, a lognormal distribution with $\mu = 9.21$ (i.e., $e^{9.21} \approx$ 10,000 oocysts/L) and $\sigma = 0$ can also be used, although output will differ slightly due to precision differences. This portion of the case study initially assumes a **point estimate of 10 for the overall treatment train LRV** and an **exponential dose response function with r = 0.09**. If a point estimate of 2 L/day is selected under the Exposure tab, then there will be no distribution of risks because all critical inputs are point estimates, similar to the original approach used to develop the 12-10-10 framework. The corresponding daily and annual risks would be 1.8×10^{-7} and 6.6×10^{-5}, respectively. Instead, this portion of the case study assumes the **default lognormally distributed ingestion volumes** (**lognormal mean = 7.492** and **lognormal standard deviation = 0.407**) from Roseberry and Burmaster (1992) and the

default setting of 96 consumption events per day (i.e., every 15 minutes). For each model run, the user should navigate to the QMRA Output screen and click the link at the bottom of the page to download the raw data (Download Parameter Set Data). Similar to the previous sensitivity analyses, those .csv files can be uploaded to the tool using the Comparison of Risk Curves option in the left menu bar (*Non-Failure Analyses* section).

The first figures illustrates the point estimate LRV of 10 and the benchmark LRVs needed to achieve an annual risk of 10^{-4} exactly. The benchmark LRVs are only a function of the raw wastewater pathogen concentration and ingestion volume. Because the raw wastewater *Cryptosporidium* concentration was assumed to be constant at 10^4 oocysts/L, the observed distribution is driven entirely by the variability in ingestion volume.

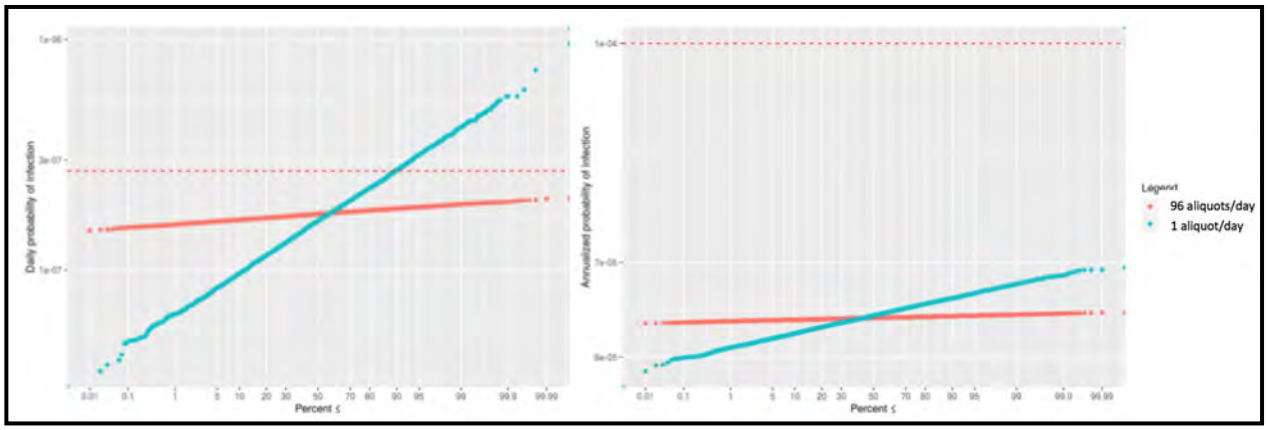


Because the ingestion volume from the default distribution sometimes exceeds 2 L/day, the benchmark LRV also exceeds 10 in approximately 10% of the simulations. However, this does not necessarily mean the corresponding daily and annual risks will exceed their respective benchmarks. The benchmark LRVs are actually calculated based on P_n, which is a function of the ingestion frequency. Specifically, the tool assumes the benchmark annual risk of 10^{-4} is divided equally across the number of intervals spanning one year, and each data point in the underlying distribution is forced to comply with this interval-specific risk target. For example, an ingestion frequency of once per day corresponds with a P_{daily} of 2.7×10^{-7} [i.e., $10^{-4}/(365\times1)$], and an ingestion frequency of 96 per day corresponds with a P_{15min} of 2.9×10^{-9} [i.e., $10^{-4}/(365\times96)$]. As noted earlier, the change in P_n does not actually impact the benchmark LRVs—just the way they are calculated in the tool. But the fact that P_n is assumed to be constant across every interval may affect interpretation of the benchmark LRVs.

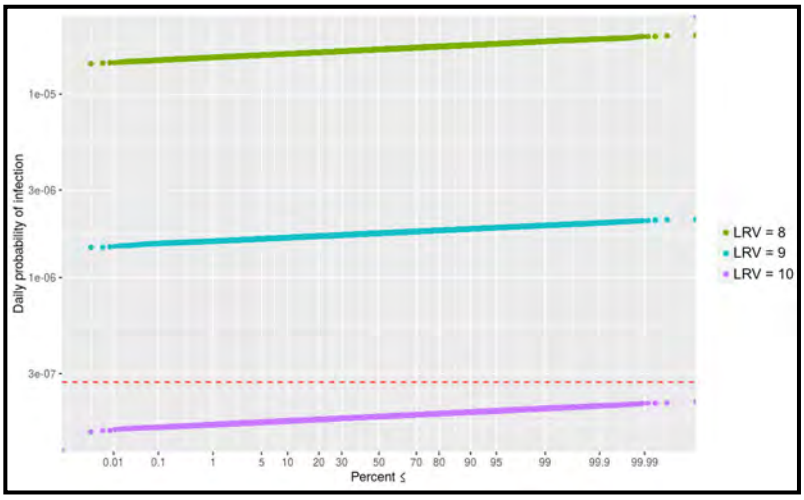
In calculating the *actual* daily and annual risks from the simulations, a small number of P_n values from larger volumes of drinking water (i.e., higher risks) may be mitigated by many P_n values from smaller volumes of drinking water (i.e., lower risks). This is demonstrated in the daily risk plot below, in which increasing ingestion frequency provides additional 'buffering capacity' for when the benchmark LRV exceeds the treatment train LRV. The scenario with one ingestion per day does not provide this 'buffering capacity' so the daily risk exceeds the daily risk benchmark 10% of the time, consistent with

the previous benchmark LRV curve. However, both ingestion frequencies comply with the annual risk benchmark because of the additional 'averaging' effect over 365 days.

Therefore, the various outputs from the tool should be evaluated collectively before drawing broad conclusions. Stated a different way, one should not rely exclusively on compliance with the benchmark LRV when drawing broad conclusions or making policy decisions. Also, it is always advisable to review the outputs for each of the critical model parameters to better understand what might be driving risk and whether some of the more extreme scenarios are actually reasonable. For example, the output from the Roseberry and Burmaster (1992) distribution yields a 99th percentile ingestion volume of 4.6 L/day and a maximum ingestion volume of 8.5 L/day (see QMRA Output tab). The 4.6-L volume might be reasonable, but it might not be justifiable to make policy decisions based on a daily ingestion volume of nearly 9 L, even if that value is possible based on the assumed distribution.



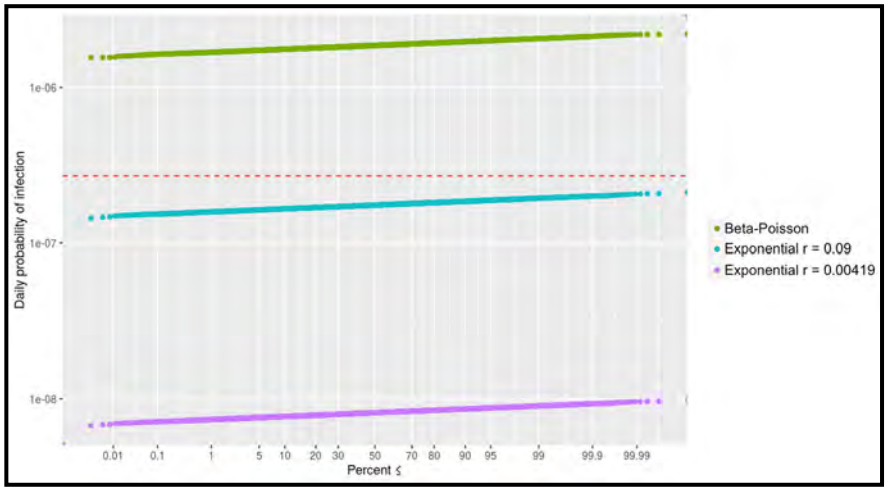
Returning to the sensitivity analysis on treatment train LRV, California's **10-log** treatment requirement for *Cryptosporidium* is sufficient to satisfy the daily benchmark in all simulations (assuming **96 ingestions per day**). However, reductions in treatment redundancy cause significant vertical shifts in the daily risk curve, and these LRV reductions (i.e., down to **8 or 9 logs**) cause the daily risk to exceed the benchmark in all simulations.



B.15.5 Alternative Dose Response Function for *Cryptosporidium*

One final component of Case Study 1 demonstrates the potential impact of the dose response function on risk estimates. As an extension to the *Cryptosporidium* example assuming a **point estimate of 10 logs**

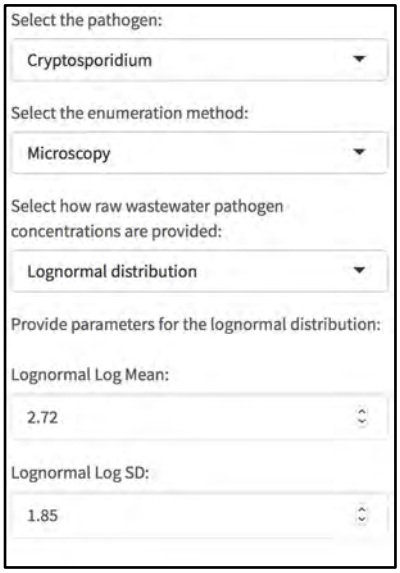
for the overall treatment train LRV and **96 ingestions per day**, the following plot shows the differences in daily risk assuming an **exponential dose response model with r = 0.09**, an alternative **exponential dose response model with r = 0.00419**, and the **Beta-Poisson dose response model from Messner and Berger (2016)**. The alternative exponential model reduces the daily risk by >1 log across all simulations, and the Beta-Poisson model increases the risk by ~1 log across all simulations, thereby exceeding the daily risk benchmark. This example shows that even the selection of the dose response model can have significant implications for policy decisions and should be evaluated as part of a sensitivity analysis.



B.16 Case Study 2: QMRA for *Cryptosporidium* in a FAT-Based DPR Scenario

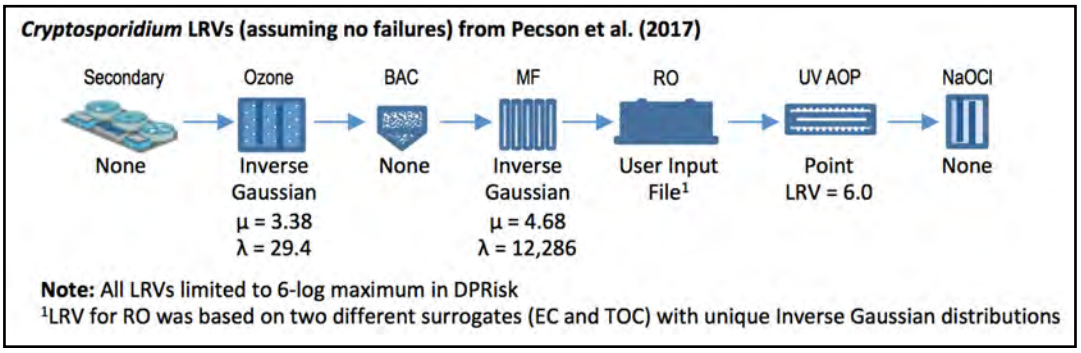
Pecson et al. (2017) evaluated the reliability of pathogen control at the North City Demonstration Pure Water Facility. The QMRA used actual performance data collected over one year of operation of the AWPF to generate annual risk estimates for *Cryptosporidium* and enterovirus. The data summarized in that QMRA are incorporated into the case study below as a demonstration of the use of the DPRisk tool. The user can follow the specified approach to recreate the QMRA for *Cryptosporidium* in Pecson et al. (2017) or incorporate any desired changes to evaluate impacts on the results.

1. Access the tool via the DPRisk website link. The code can also be downloaded and run locally using R. Input files are available for download under How to use this tool in the left menu bar.
2. Select Raw Wastewater Pathogen Concentrations on the left menu bar. This will bring the user to an input screen where (1) the target pathogen can be selected, (2) additional information related to the pathogen enumeration method can be identified, and (3) the distribution of raw wastewater concentrations can be characterized. The concentrations can be described by a **lognormal distribution with user-defined parameters (current scenario)**, a user-provided data file that follows a lognormal fit (tool will use MLE to identify lognormal parameters), or a user-provided data file that has already been curated with 10,000 data points. Note that the information for enumeration method does not impact the QMRA and is only stored for user reference. The raw wastewater concentration for ***Cryptosporidium*** oocysts was defined in Pecson et al. (2017) as having a **lognormal mean of**



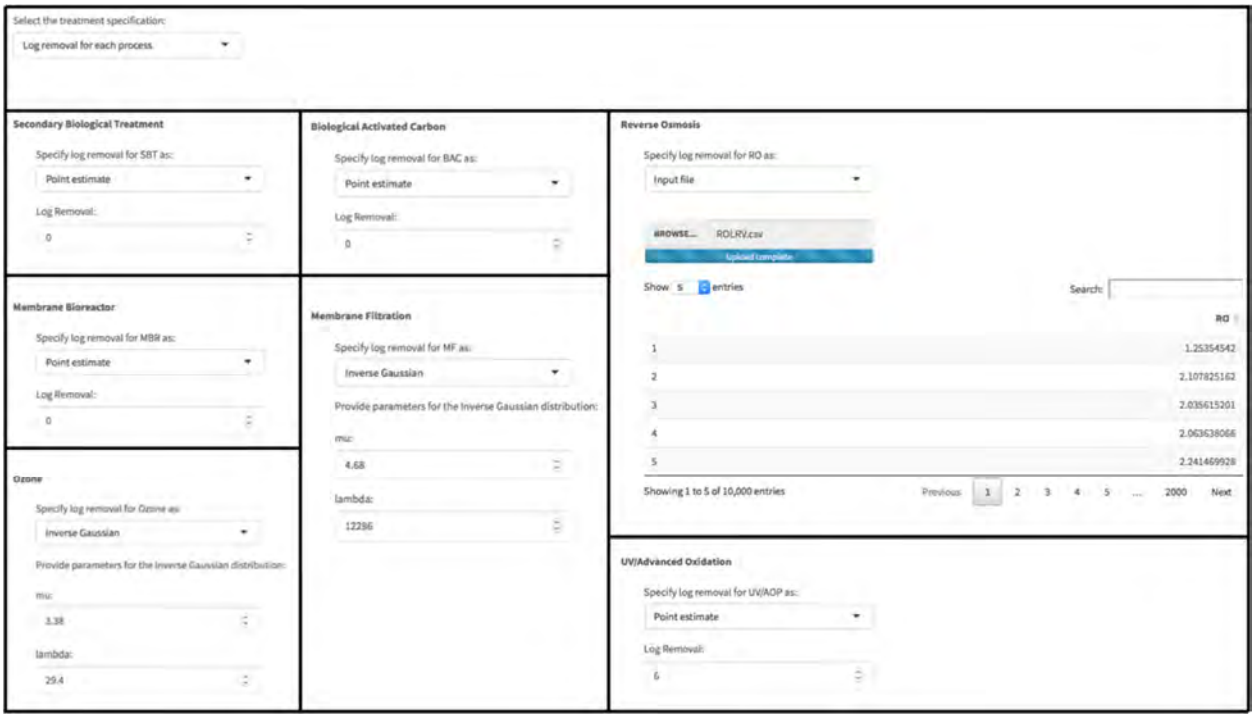
2.72 and **lognormal standard deviation of 1.85** based on **microscopy** (see figure). In developing inputs or datasets, concentrations should be based on units of target pathogen *per liter*, and all lognormal parameters are base *e* (natural logarithm).

3. Select Treatment Train on the left menu bar. This will bring the user to an input screen where the treatment train can be selected and characterized. Treatment can be characterized as (1) a single LRV point estimate for the entire treatment train, (2) a user-provided data file that has already been curated with 10,000 LRVs for the overall treatment train, or (3) **individual log removals for each process (current scenario)**. The treatment train and corresponding **assumptions to be used as DPRisk inputs are shown in the following figure**. All LRV estimates should be base 10 (i.e., $\log_{10}$ reductions) and not base *e* (i.e., natural logarithm).



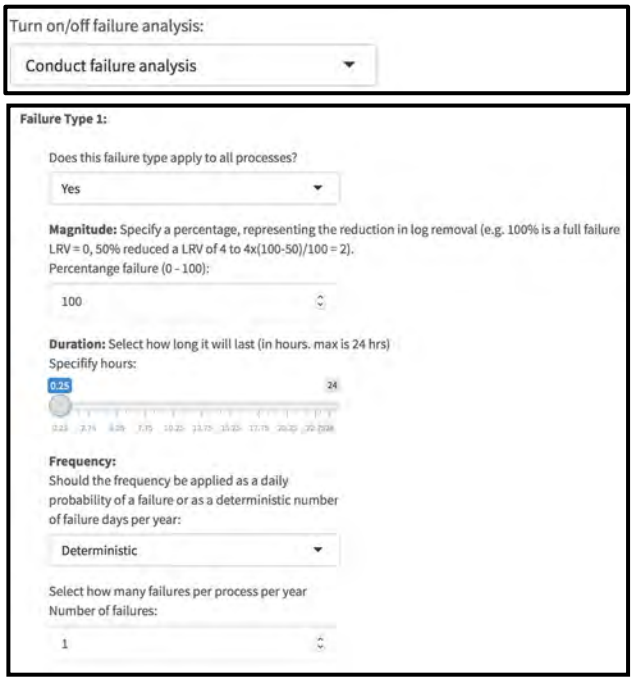
Source: Data from Pecson et al. 2017.

By default, DPRisk includes a number of unit processes that are common to advanced treatment for potable reuse but also provides flexibility to allow for user-defined processes (e.g., "Custom Process #1"). For any process that is not included in a particular treatment scenario, the corresponding LRV should be described as a point estimate of 0; the remaining processes should be characterized by the user. The inputs for Pecson et al. (2017) are shown in the following figure, including examples for processes that are not included in the treatment train (e.g., "Secondary Biological Treatment" and "Membrane Bioreactor"). The user input file for RO is available for download under How to use this tool in the left menu bar (ROLRV.csv).

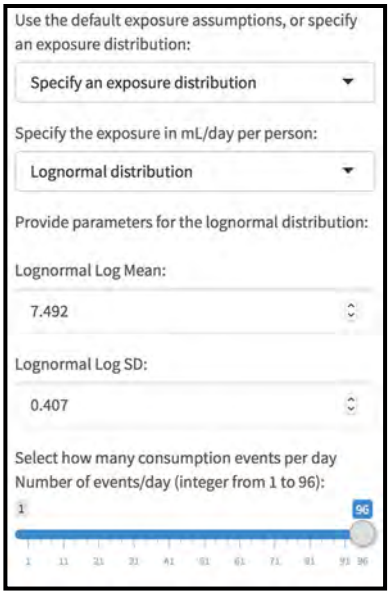


In Pecson et al. (2017), pathogen reduction by secondary biological treatment was omitted from the analysis because an accepted surrogate had not been identified at that time. The Inverse Gaussian distribution for ozone was based on the T_{10} approach for determining CT at the City of San Diego's demonstration-scale facility coupled with the U.S. EPA's ozone CT equation for *Cryptosporidium* (shown previously in the discussion of Step 5 – Assigning Treatment Process Log Reduction Values). The Inverse Gaussian distribution for MF was based on the standard LRV crediting approach with pressure decay testing (shown previously in Step 5). The LRV assigned to RO was primarily based on online TOC analyzer data as a surrogate for pathogen removal (85% of the time), but EC was also used as a monitoring backup (15% of the time). Each RO surrogate was characterized by a unique inverse Gaussian distribution, resulting in a bimodal overall LRV distribution. Because the bimodal LRV distribution for RO represents a unique modeling scenario, this cannot be simulated directly with DPRisk. Instead, a corresponding LRV dataset that followed the assumptions above was generated independent of the tool. The user may encounter other situations in which a particular input is not available. Sufficient flexibility has been integrated into the tool to allow for data entry alternatives that still accurately represent the scenario in question. The user input file for RO includes 10,000 data points representing the bimodal LRV scenario. Finally, the point estimate for UV AOP assumed high-dose UV conditions consistent with California's AOP framework for potable reuse, which would consistently achieve the maximum allowable 6-log inactivation of *Cryptosporidium*.

4. Select Treatment Failure on the left menu bar. This will bring the user to an input screen where **"Conduct failure analysis"** can be selected. Over 12 months of monitoring at the City of San Diego's demonstration-scale facility, there were no observed failures affecting pathogen removal/inactivation performance, but for added conservatism, Pecson et al. (2017) assumed a global frequency, magnitude, and duration for hypothetical failures. For each engineered treatment process credited with a *Cryptosporidium* LRV (i.e., ozone, MF, RO, and UV AOP), the following assumptions were used: **deterministic frequency = 1 failure per process per year**, **magnitude = 100%** (i.e., LRV = 0 during failure), **duration = 0.25 hours**. Pecson et al. (2017) actually evaluated durations of 15 minutes, 1 hour, 8 hours, and 24 hours, but only 15-minute failures are considered for this initial phase of the case study.

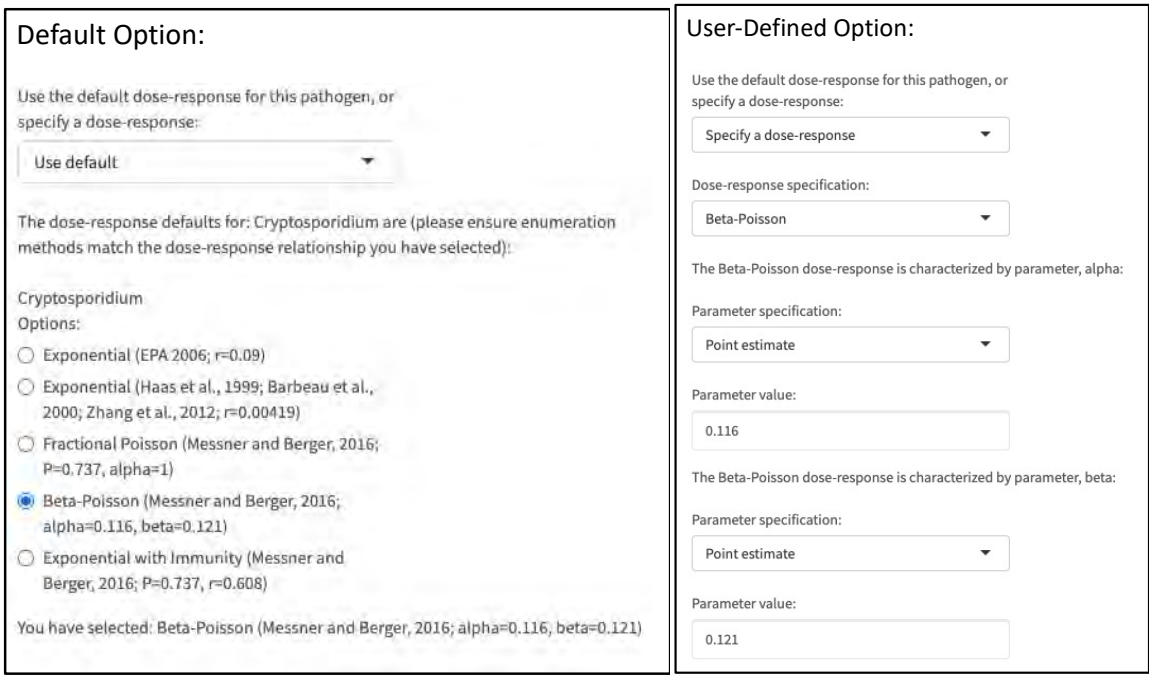


5. Select Management Barriers on the left menu bar. This portion of the case study does not incorporate blending, dilution, or die-off so the **default LRV of 0** can remain unchanged.
6. Select Exposure on the left menu bar. This will bring the user to an input screen where the daily ingestion rate can be specified and characterized. The ingestion rate in *mL/day* can be described by one of the default distributions/point estimates or specified by the user. The user-specified option allows for (1) an input file with 10,000 data points, (2) a point estimate, or (3) a lognormal distribution with user-defined mean and standard deviation. This case study uses the **default lognormal distribution from Roseberry and Burmaster (1992)** and the **default setting of 96 consumption events per day** (i.e., every 15 minutes). The figure to the right shows how this same **lognormal distribution can be specified manually with a lognormal mean of 7.492 and lognormal standard deviation of 0.407.** This lognormal mean equates to a daily ingestion rate of $e^{7.492}$ = 1,794 mL/day.



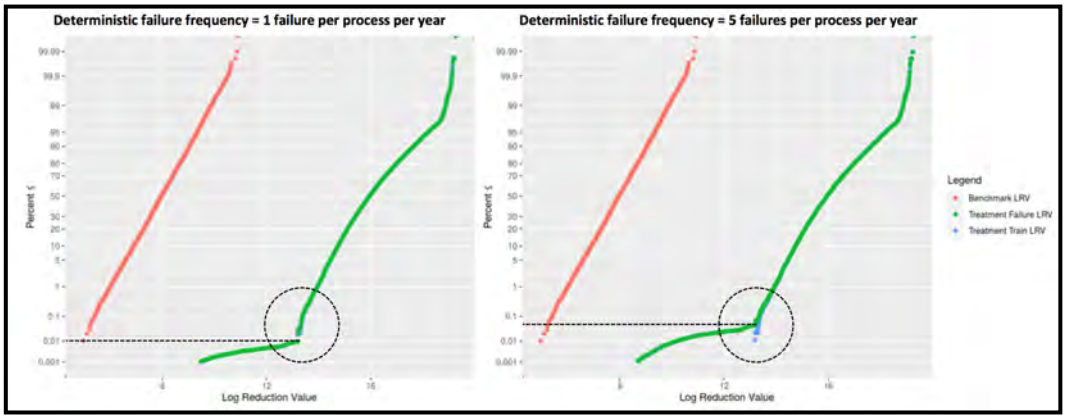
7. Select Dose-Response on the left menu bar. This will bring the user to an input screen where the pathogen dose-response equation can be identified and characterized. The user can (1) select one of the default dose-response models specific to the target pathogen (*Cryptosporidium* in this scenario) or (2) select and characterize one of several dose-response models commonly used in QMRAs. Both approaches are shown in the figure below based on the assumptions in Pecson et al. (2017). For the user-defined dose-response models, the parameters can be described as (1) **point estimates** or (2) based on an input file with 10,000 data points for that particular parameter. Based on Pecson et al. (2017), the **Beta-Poisson dose-response model** (**α = 0.116** and **β = 0.121**) should be selected either with the default setting or with the user-specified option. ***Note: If the user-specified dose-response option is selected, the tool will not be able to***

perform the benchmark LRV calculations in the next step, but the benchmark LRVs can be calculated for the default dose-response option.



8. Select PATTP Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulation and calculations related to treatment train performance. The following series of figures summarizes the PATTP output for Case Study 2. Assuming the 'seed' for random number generation is set at 1 and the number of failure simulations is set to 100 under the Configure tab, some of the output should appear exactly as shown.

   The following plot (left side) shows the comparison of observed treatment train performance with and without failures vs. the benchmark treatment train performance required to achieve an annual risk of infection of 10^{-4}.



   One important note is the distinction between the failure frequency and duration specified in the model (1 failure per process per year and 15 minutes per failure) vs. the percentile in the LRV cumulative distribution plots. On the left side of the plot, the LRVs for the *failure* scenario (green) and *no-failure* scenario (blue) are equivalent down to 0.01%. This is because the *no-failure* scenario

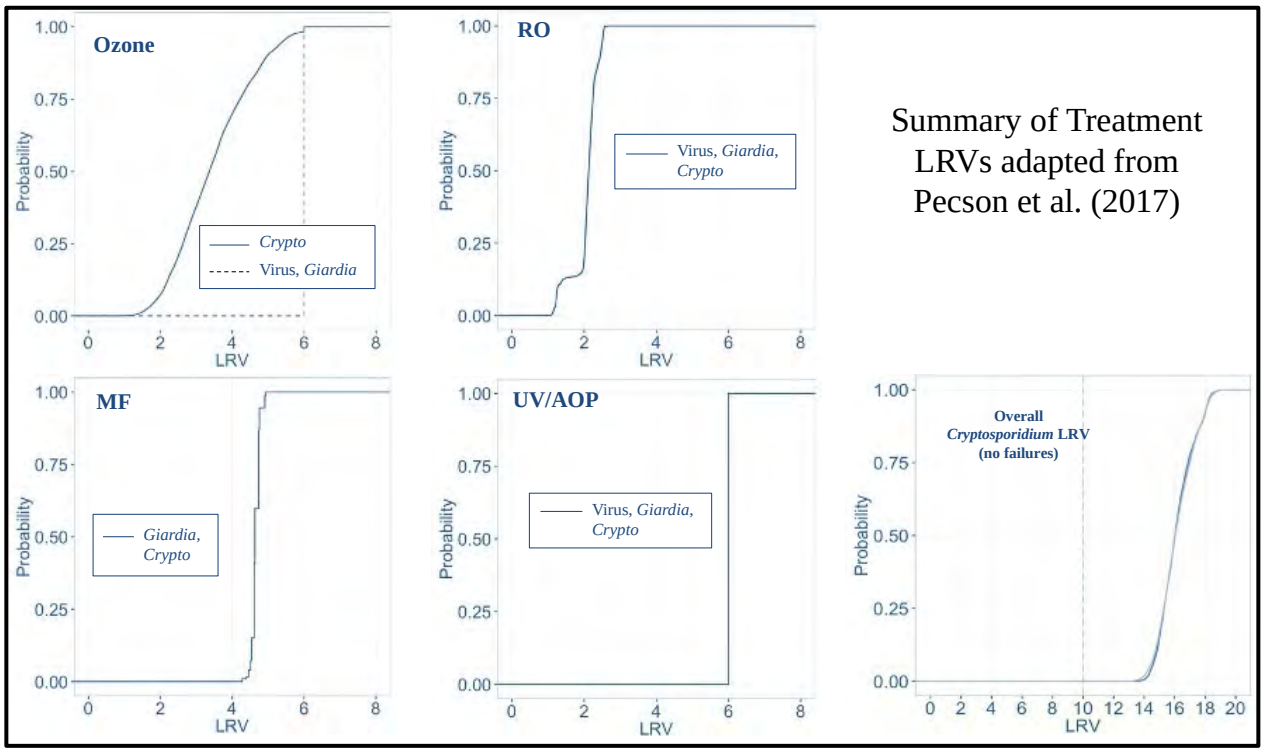
(and the benchmark treatment train) samples from exactly 10,000 LRVs, so the lowest possible percentile in the *no-failure* and benchmark plots is 0.01% (i.e., 1/10,000×100). For the *failure* scenario with 100 failure simulations (each simulation represents one year), the tool actually generates 3,504,000 LRVs [i.e., 35,040 time points per simulation (or year) × 100 simulations (or years)]. For this case study, there was exactly 1 failure per treatment process per year, 4 total treatment processes, and 100 total simulations, and each failure covered a duration of 15 minutes (or 1 time increment). Therefore, there were up to 400 unique LRVs associated with failures out of 3,504,000 total LRVs, which equates to 0.01%:

$$\left[\frac{1 \text{ failure per process per year} \times 4 \text{ processes} \times 100 \text{ years} \times 1 \text{ time increment per failure}}{3{,}504{,}000 \text{ time increments}}\right] \times 100 = 0.01\%$$

Therefore, the *no-failure* and *failure* LRVs were essentially equivalent above 0.01%, but additional LRVs were generated for the *failure* scenario below 0.01%. This also relates to why the failure percentiles do not directly correspond with the specified daily frequency of failures (i.e., 1/365 = 0.00274 or 2.74%). In order to see a more visually apparent separation between the *no-failure* and *failure* LRVs, the modeling scenario can be repeated with a greater deterministic failure frequency. For example, 5 failures per process per year would result in a deviation at 0.057% (see right side of figure above):

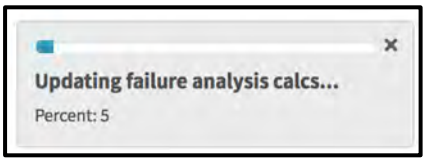
$$\left[\frac{5 \text{ failure per process per year} \times 4 \text{ processes} \times 100 \text{ years} \times 1 \text{ time increment per failure}}{3{,}504{,}000 \text{ time increments}}\right] \times 100 = 0.057\%$$

Although not shown here, the tool output also includes the distribution of LRVs for each treatment process, which should be consistent with the plots from Pecson et al. (2017) (shown below). The format of the plots in DPRisk is slightly different from Pecson et al. (2017), but it is still possible to compare notable features, either in the statistical summary table or cumulative distribution plot, to verify consistency. For example, the median LRV for ozone in DPRisk is 3.22, which is consistent with the Pecson et al. (2017) plot below. Also, the LRV for RO increases abruptly from ~1.4 to ~1.9 around the 15th percentile, which is consistent with the change in surrogate from EC to TOC. Recall that the input file for RO utilized the EC surrogate 15% of the time and the TOC surrogate 85% of the time. Finally, the LRV for the UV AOP should be 6.0 at all times in the absence of treatment process failure. With respect to the overall treatment train, the median observed LRV without failures was 15.9, which is consistent with the plot from Pecson et al. (2017).



Source: Adapted from Pecson et al. 2017.

9. ***Note: Ensure all inputs are returned to their original values (e.g., deterministic failure frequency = 1 per process per year).*** Select QMRA Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulation and calculations related to daily and annual risk. A box should appear in the bottom right corner of the screen to indicate the tool's progress.



Before evaluating the risk plots, one interesting feature to note is the ability to download the 15-min data points for a subset of the failure simulations. The links to download the files are located under the **Pannual Table for Failure Simulations** and are listed as Download 15-min events for failure simulation X. While these files do not provide the entirety of the raw data used to develop the risk distributions, they still provide insight into the factors driving the risk estimates. For example, by using Microsoft Excel to sort the data from smallest to largest based on the "failure_lr" column (top half of following figure), it is possible to see how certain types of failures impact the overall treatment train LRV.

Sorted by column AQ: "failure_lr" (overall log removal with failures)

AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ
failure_ozon	failure_bac_l	failure_mf_lr	failure_ro_lr	failure_uvao	failure_pipel	failure_fsf_lr	failure_ozon	failure_chlor	failure_custc	failure_custc	failure_lr
1.48290028	0	4.75348593	2.02368429	0	0	0	0	0	0	0	8.2600705
3.67246764	0	0	2.10782516	6	0	0	0	0	0	0	11.7802928
0	0	4.80059465	2.10982454	6	0	0	0	0	0	0	12.9104192
1.07695886	0	4.73335119	1.28833637	6	0	0	0	0	0	0	13.0986464
1.07695886	0	4.73335119	1.28833637	6	0	0	0	0	0	0	13.0986464
1.07695886	0	4.73335119	1.28833637	6	0	0	0	0	0	0	13.0986464
1.24145996	0	4.57339161	1.33054705	6	0	0	0	0	0	0	13.1453986
1.24145996	0	4.57339161	1.33054705	6	0	0	0	0	0	0	13.1453986
1.24145996	0	4.57339161	1.33054705	6	0	0	0	0	0	0	13.1453986

Sorted by column AI: "failure_ro_lr" (RO log removal with failures)

AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ
failure_ozon	failure_bac_l	failure_mf_lr	failure_ro_lr	failure_uvao	failure_pipel	failure_fsf_lr	failure_ozon	failure_chlor	failure_custc	failure_custc	failure_lr
3.13469583	0	4.77342845	0	6	0	0	0	0	0	0	13.9081243
3.28114137	0	4.90179086	1.06989948	6	0	0	0	0	0	0	15.2528317
3.28114137	0	4.90179086	1.06989948	6	0	0	0	0	0	0	15.2528317
3.06230521	0	4.88777357	1.10503339	6	0	0	0	0	0	0	15.0551122
3.06230521	0	4.88777357	1.10503339	6	0	0	0	0	0	0	15.0551122
3.06230521	0	4.88777357	1.10503339	6	0	0	0	0	0	0	15.0551122
3.06230521	0	4.88777357	1.10503339	6	0	0	0	0	0	0	15.0551122
4.36311492	0	4.68853363	1.10813797	6	0	0	0	0	0	0	16.1597865
4.36311492	0	4.68853363	1.10813797	6	0	0	0	0	0	0	16.1597865

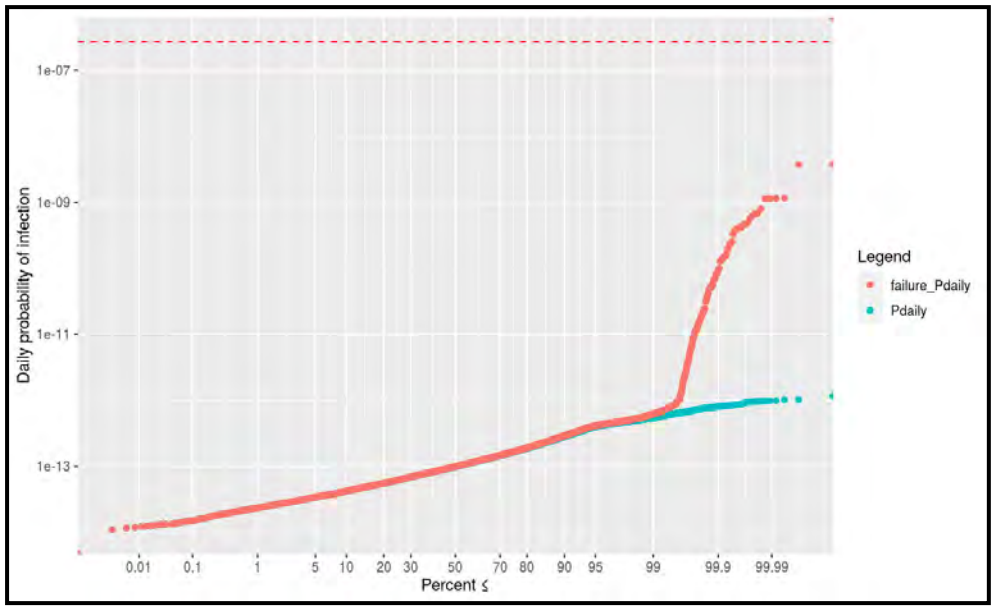
Here are some important notes about this data table example:

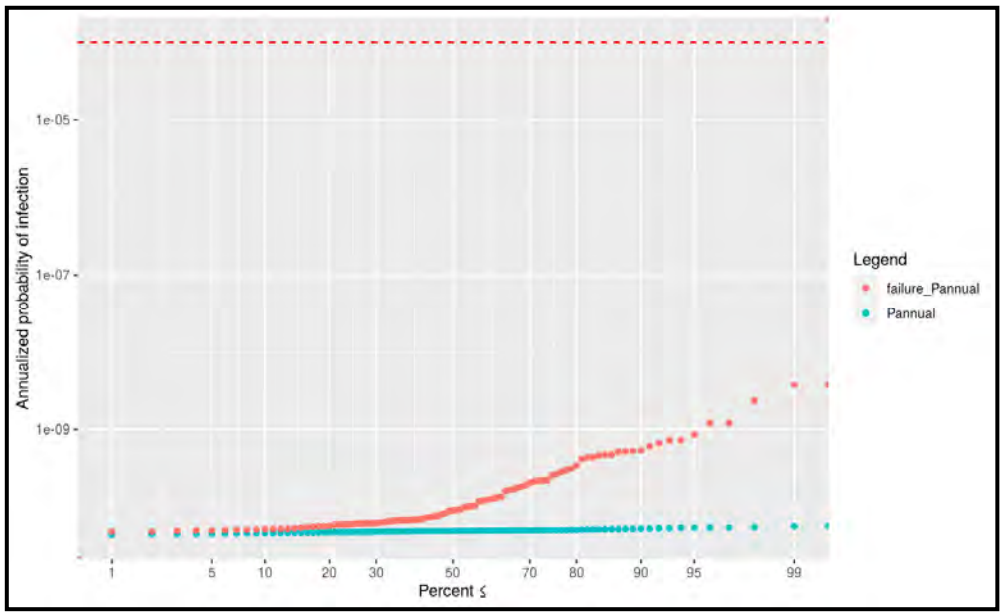
- ***UV Failure:*** As might be expected, the reduction in LRV during a UV AOP failure (i.e., from 6 to 0) resulted in the lowest overall treatment train LRV of 8.3. It should be noted that the PATTP Output (bottom summary table in tool output) indicated that the lowest overall treatment train LRV across the 100 failure simulations was 7.8. This means that at least one other simulation combined a UV AOP failure with lower LRVs for the remaining treatment processes.
- ***MF Failure:*** MF failure resulted in the second-lowest treatment train LRV (11.8).
- ***Ozone Failure:*** Ozone failure resulted in the third-lowest treatment train LRV (12.9).
- ***RO Failure:*** By looking only at the data sorted by the "failure_lr" column (i.e., top half of figure), it might appear as if the tool failed to simulate an RO failure. However, by resorting by "failure_ro_lr," the RO failure can be seen. Because RO is awarded a relatively low LRV compared to the other treatment processes, even a complete RO failure is sometimes overshadowed by the general variability in other treatment processes. With greater failure frequencies, or perhaps in one of the other 99 simulations not shown, an RO failure might be coupled with low LRVs for other treatment processes, thereby having a more significant impact on the overall treatment train LRV and the final risk estimates. In this simulation, however, the RO failure was relatively inconsequential.
- ***Simultaneous Failures:*** Because of the low failure frequency (i.e., one failure per treatment process per year) coupled with the short failure duration (i.e., 15 min), there were no simultaneous failures observed in this particular simulation. In other words, each treatment process failed on a different day and/or a different 15-min time interval. Capturing a simultaneous failure of two independent unit processes assuming a 15-min failure duration would require ~6,000 simulations (i.e., 1/6th of the 35,040 simulations noted in Step 10: Risk Characterization). This is because there are 4 independent treatment processes yielding 6 possible combinations of dual-process failures, instead of the 2 independent treatment processes in the earlier example. In order to observe the effects of a simultaneous failure, the number of failure simulations could theoretically be increased to ~6,000, which would significantly increase processing time, or the **failure duration could be increased to 24 hr** with the **number of failure simulations remaining unchanged at 100** (theoretically 61 simulations or 365/6; see Step 10: Risk Characterization). With this change, the revised PATTP Output indicates a minimum overall LRV of 7.2 (actual value might differ due to random number generator), although it is not clear which combination of treatment process failures resulted in that LRV. To

increase the probability of capturing a simultaneous failure of UV AOP with some other treatment process (3 possible combinations), the **failure duration could remain at 24 hr** with the **number of failure simulations increasing to ~150** (theoretically 122 simulations or 365/3). With that change, the minimum observed LRV is 3.4, which most likely represents a combined failure of UV AOP and ozone or MF, or the less likely combination of three simultaneous failures. Regardless, this represents an exceptionally rare event considering that the 1st percentile LRV increases to 13.4. Therefore, it is important to understand whether the failure specifications for a given scenario capture the full range of potential outcomes desired by the user (e.g., 'black swan' events), but it is also important to keep these events in context in terms of their likelihood of occurrence.

If any changes have been made to the model inputs, it might be beneficial at this point to reload the baseline inputs for Case Study 2 before proceeding. The two plots on the following page illustrate the daily and annual risks, respectively, for the baseline model inputs under normal operational conditions and when accounting for at least one failure per treatment process per year. The effects of failures are readily apparent in both plots, although the treatment train still satisfies both the daily and annual benchmarks across the entire distribution. Because of the way daily risks are converted to annual risks, this failure scenario is a prime example of where the maximum daily and annual risks are nearly equivalent (1×10^{-7}) because of the steep daily risk curve. So, depending on the regulatory benchmark, a treatment scenario might nearly exceed the target (i.e., daily risk benchmark) or actually provide a ~1,000-fold safety factor (i.e., annual risk benchmark).

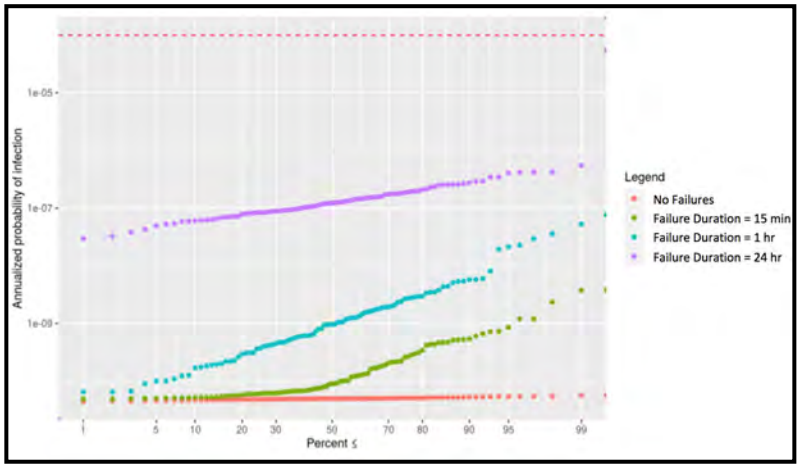
10. Select Summary of PATTP and QMRA Output on the left menu bar, which will bring the user to a screen summarizing only the critical outputs from the tool, specifically the LRV comparison and the daily and annual risks. The supporting data excluded from this summary are still accessible in the other tabs.

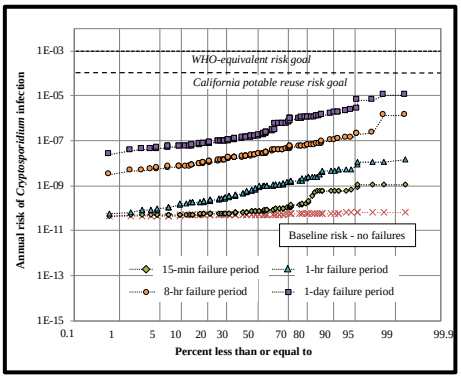




B.16.1 Sensitivity Analysis on Failure Duration

The following plot was generated using the Comparison of Risk Curves functionality (*Comparison of Pdaily Risk Curves – Failure Analyses section*) in conjunction with the raw data generated from multiple failure scenarios. Each failure scenario assumed a **magnitude of 100%** and a **deterministic frequency of 1 failure per process per year**, but the **failure duration varied: green = 0.25 hr, blue = 1 hr, and purple = 24 hr**. By default, the tool automatically loads and plots the *no-failure* data from the first file uploaded. The required input files can be downloaded for each scenario from the QMRA Output page by clicking on Download Failure Analysis Pannual Data. This allows for a direct comparison with the summary data from Pecson et al. (2017) (right side of figure).

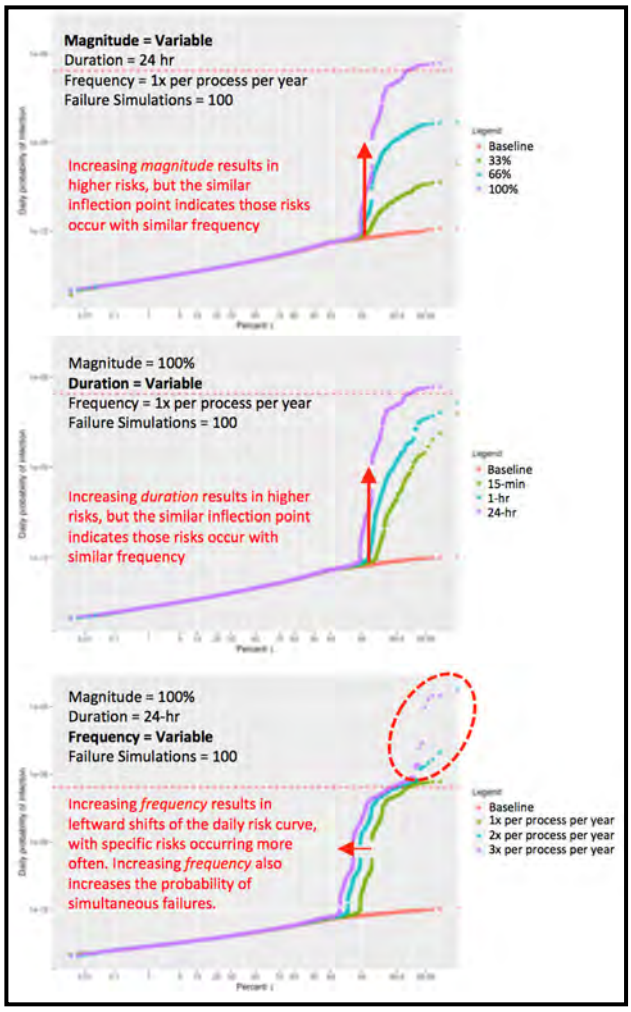




Source: Adapted from Pecson et al. 2017.

The following plots were also developed using the Comparison of Risk Curves functionality (*Comparison of Pdaily Risk Curves – Failure Analyses section*), but these plots illustrate how daily risk curves change in a general sense when evaluating changes in (top) failure magnitude, (middle) failure duration, and (bottom) failure frequency.

In Case Study 1, the sensitivity analysis on overall treatment train LRV demonstrated that changes in treatment redundancy cause vertical shifts in the risk plots across all percentiles. Changes in *failure magnitude* also cause vertical shifts in the risk plots, but these shifts are isolated to the 'tail' of the distribution that represents the low probability failure events. The shape of each daily risk curve is also dependent on which processes are failing because a 33% reduction in UV AOP (2-log change) will have a more significant effect on daily risk than a 33% reduction in RO (<1-log change). These nuances are often reflected as inflection points in the daily risk curves.



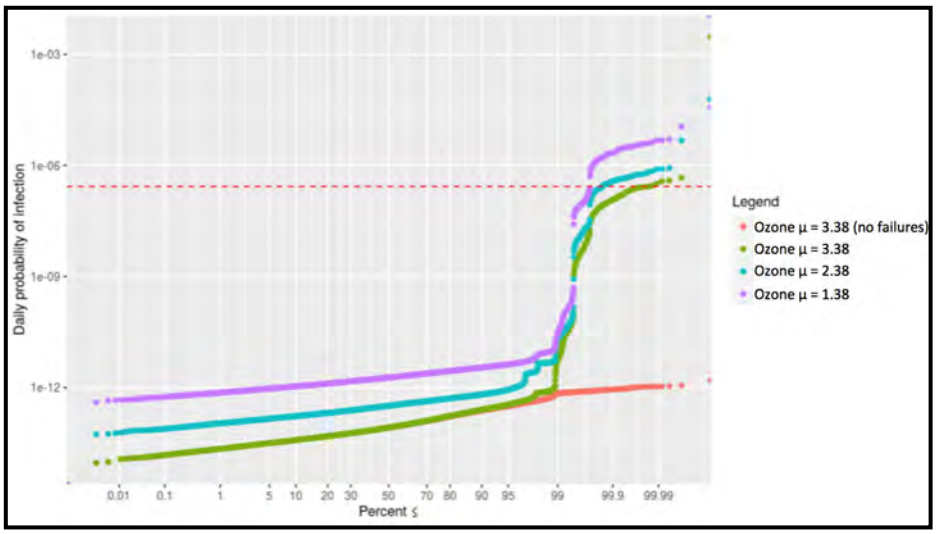
Changes in *failure duration* have similar impacts as changes in failure magnitude. Specifically, these changes result in daily risk curves that 'bend' in the same general percentile range, but risk increases as the duration of failure increases. In the example plot shown with a probit scale, the inflection points seem to occur at different locations, but they actually occur within ±0.5% of each other.

Increasing *failure frequency* causes leftward shifts in the daily risk curve, which means higher risks will occur more frequently. Moreover, increasing failure frequency also increases the probability of simultaneous failures, including more severe simultaneous failures, as illustrated by the secondary inflection point in the 3x curve (purple data in bottom figure).

B.16.2 Sensitivity Analysis on Treatment Redundancy

The following plot was generated using the Comparison of Risk Curves functionality (*Comparison of Pdaily Risk Curves – Failure Analyses section*) using the baseline inputs for Case Study 2 but with a **failure duration of 24 hr** instead of 15 min. The three input files represent changes to the **Inverse Gaussian parameters for ozone treatment**, which were meant to simulate changes in treatment redundancy. The baseline daily risk (red data) represents the no-failure condition for μ = 3.38 for the ozone LRV. The other data include the effects of failure with **μ = 3.38 (green)**, **μ = 2.38 (blue)**, and **μ = 1.38 (purple)** for the ozone LRV. With the reduction in treatment redundancy caused by the stepwise reduction in ozone LRV, the daily risk curve shifted vertically, which also caused the daily risk to exceed the 2.7×10^{-7} benchmark at different percentiles:

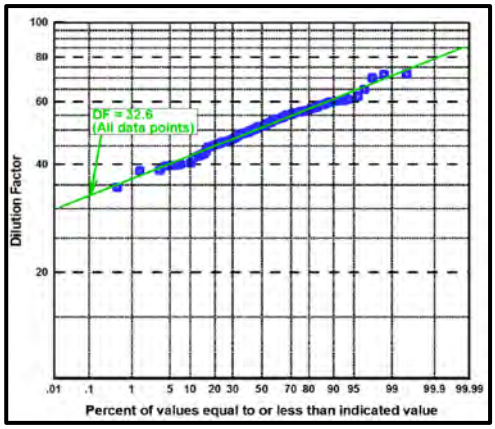
- μ for ozone LRV = 3.38 → exceeds daily risk benchmark at ~99.95%
- μ for ozone LRV = 2.38 → exceeds daily risk benchmark at ~99.7%
- μ for ozone LRV = 1.38 → exceeds daily risk benchmark at ~99.5%



B.16.3 Sensitivity Analysis on Management Barriers

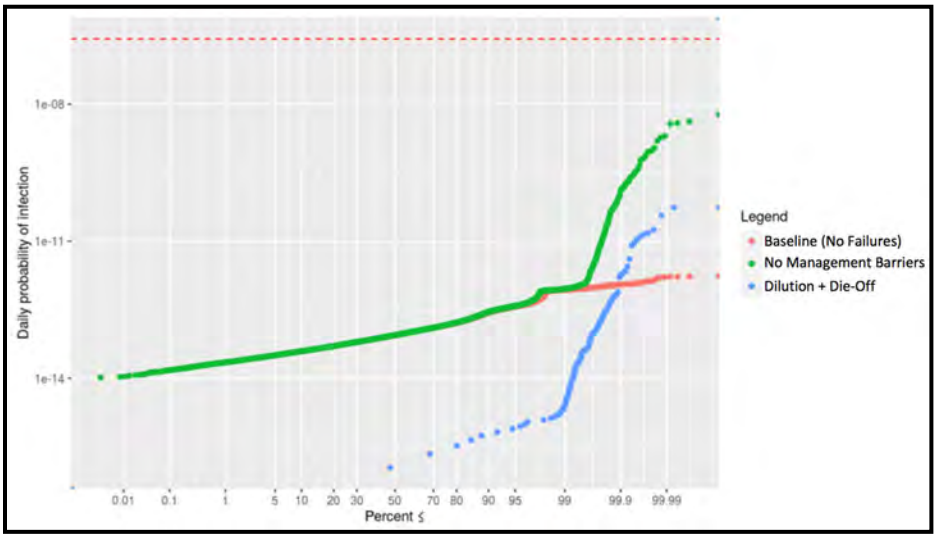
The City of San Diego's Pure Water Program will ultimately involve augmentation of local reservoirs with purified water. For Phase 1, the current plan is to pump purified water from the North City AWPF to Miramar Reservoir, which will have a theoretical hydraulic retention time (HRT) of approximately 60 days. In accordance with California's Surface Water Augmentation regulations, the reservoir will achieve significant dilution, and although it is not considered in the regulatory framework, this approach would theoretically achieve pathogen die-off as well over the 60-day storage period. As such, this case study was expanded to evaluate the significance of dilution and die-off relative to the LRVs achieved by the engineered treatment train. In particular, this evaluation demonstrates how the reservoir—even with a relatively short retention time of 60 days—can potentially buffer off-specification or failure conditions.

For this sensitivity analysis, all baseline inputs remain the same except for the Management Barriers. **Blending should remain set with an LRV of 0**, **pathogen die-off should be set to a point estimate of 1.07** (i.e., 0.041 d^{-1} × 60 d / 2.303; see earlier section on Step 7: Management Barriers), and **dilution should be modeled as a user-input file**, which is available for download under How to use this tool in the left menu bar (MiramarDilution.csv). Because the user-input file for dilution only includes 104 LRVs, DPRisk samples with replacement to generate 10,000 data points for the underlying parameter set. The user-input file is based on hydrodynamic modeling for Miramar Reservoir (i.e., dilution estimates) for a 24-hr tracer pulse, which could represent a 24-hr (or 1-day) pulse of off-specification recycled water. The original dilution data from the tracer study (see figure) approximately follow a normal distribution with a mean X-fold dilution of 51 and standard deviation of 7.35. The ideal CSTR approach described earlier would result in a comparable 61-fold dilution [i.e., 1/(1-exp(-1/60)) = 61]. LRVs were calculated from the dilution data as the $-\log_{10}$ of (1/X). The mean 51-fold dilution equates to an LRV of 1.71, although the use of the input file allows the entire range of dilutions to be sampled by DPRisk.



This sensitivity analysis provides another practical example of redundancy. In other words, the management barriers supplement the engineered treatment processes by increasing the overall LRV, which causes a vertical downward shift in the daily risk curve. In a scenario in

which the daily risk approaches the 2.7×10^{-7} benchmark, inclusion of management barriers might demonstrate sufficient redundancy to mitigate public health concerns.

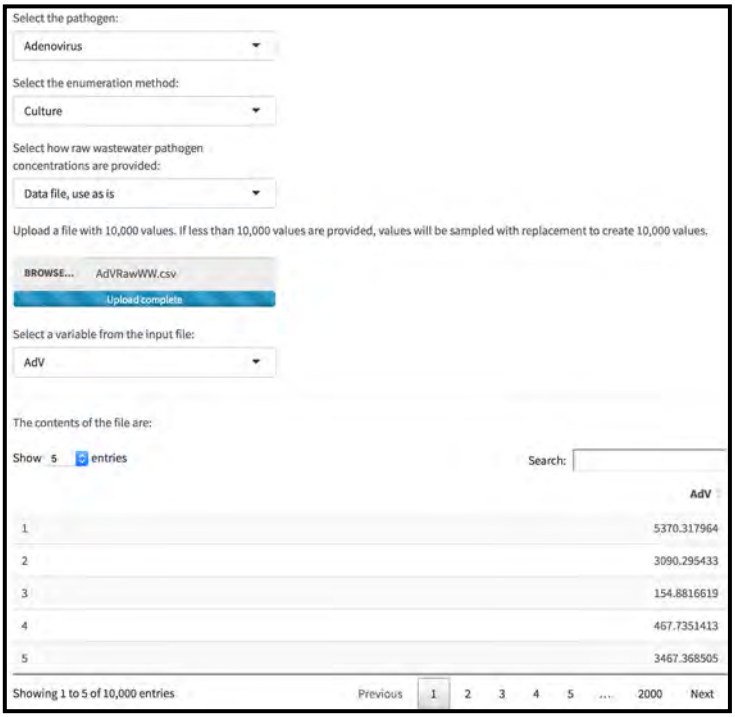


B.17 Case Study 3: QMRA for Adenovirus in an FAT-Based DPR Scenario

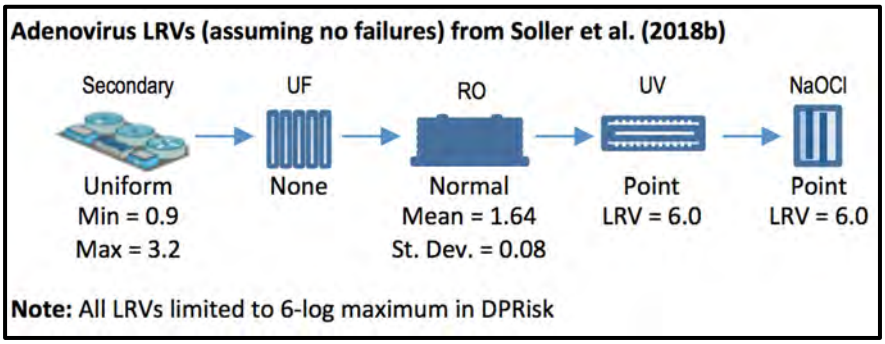
Soller et al. (2018b) evaluated the reliability of pathogen control in hypothetical potable reuse treatment trains experiencing short-duration, off-specification conditions. The QMRA primarily relied on literature data for pathogen concentrations and project-specific data (e.g., operational performance and industry surveys) for treatment performance and estimating probabilities of off-specification conditions. The data summarized in that QMRA are incorporated into this case study as a demonstration of the use of the DPRisk tool. The user can follow the specified approach to recreate the QMRA for adenovirus in Soller et al. (2018b) or incorporate any desired changes to evaluate impacts on the results.

1. Access the tool via the DPRisk website link. The code can also be downloaded and run locally using R. Input files are available for download under the How to use this tool option in the menu bar.
2. Select Raw Wastewater Pathogen Concentrations on the left menu bar. This will bring the user to an input screen where (1) the target pathogen can be selected, (2) additional information related to the pathogen enumeration method can be identified, and (3) the distribution of raw wastewater concentrations can be characterized. Note that the information for enumeration method does not impact the QMRA and is only stored for user reference. The concentrations can be described by a lognormal distribution with user-defined parameters, a user-provided data file that follows a lognormal fit (tool will use MLE to identify lognormal parameters), or **a user-provided data file that has already been curated with 10,000 data points (current scenario)**.

Soller et al. (2018b) uses a $\log_{10}$uniform distribution to describe raw wastewater pathogen concentrations. For a $\log_{10}$uniform distribution, the concentrations are uniformly distributed between the $\log_{10}$ of the minimum concentration and the $\log_{10}$ of the maximum concentration. The final concentrations are then calculated as the base 10 antilogarithm of each data point. This allows the data to be weighted evenly across multiple orders of magnitude. Because $\log_{10}$uniform distributions are less common in the literature, this option was not integrated into DPRisk. Instead, a corresponding dataset was generated independent of the tool and is available for download under How to use this tool in the left menu bar (AdVRawWW.csv). The provided data file includes 10,000 data points representing the raw wastewater concentration of **adenovirus** according to a $\log_{10}$uniform distribution. The distribution was developed assuming a minimum of 1.8 $\log_{10}$ and a maximum of 3.8 $\log_{10}$ infectious viruses per liter based on **cell culture** data (see preceding figure).



3. Select Treatment Train on the left menu bar. This will bring the user to an input screen where the treatment train can be selected and characterized. Treatment can be characterized as (1) a single LRV point estimate for the entire treatment train, (2) a user-provided data file that has already been curated with 10,000 LRVs for the overall treatment train, or (3) **individual log removals for each process (current scenario)**. All LRV estimates should be base 10 (i.e., $\log_{10}$ reductions) and not base *e* (i.e., ln). The figure above summarizes the LRV inputs for **secondary biological treatment (uniform distribution), RO (zero-truncated normal distribution), UV (point estimate), and pipeline chlorine (point estimate)**.

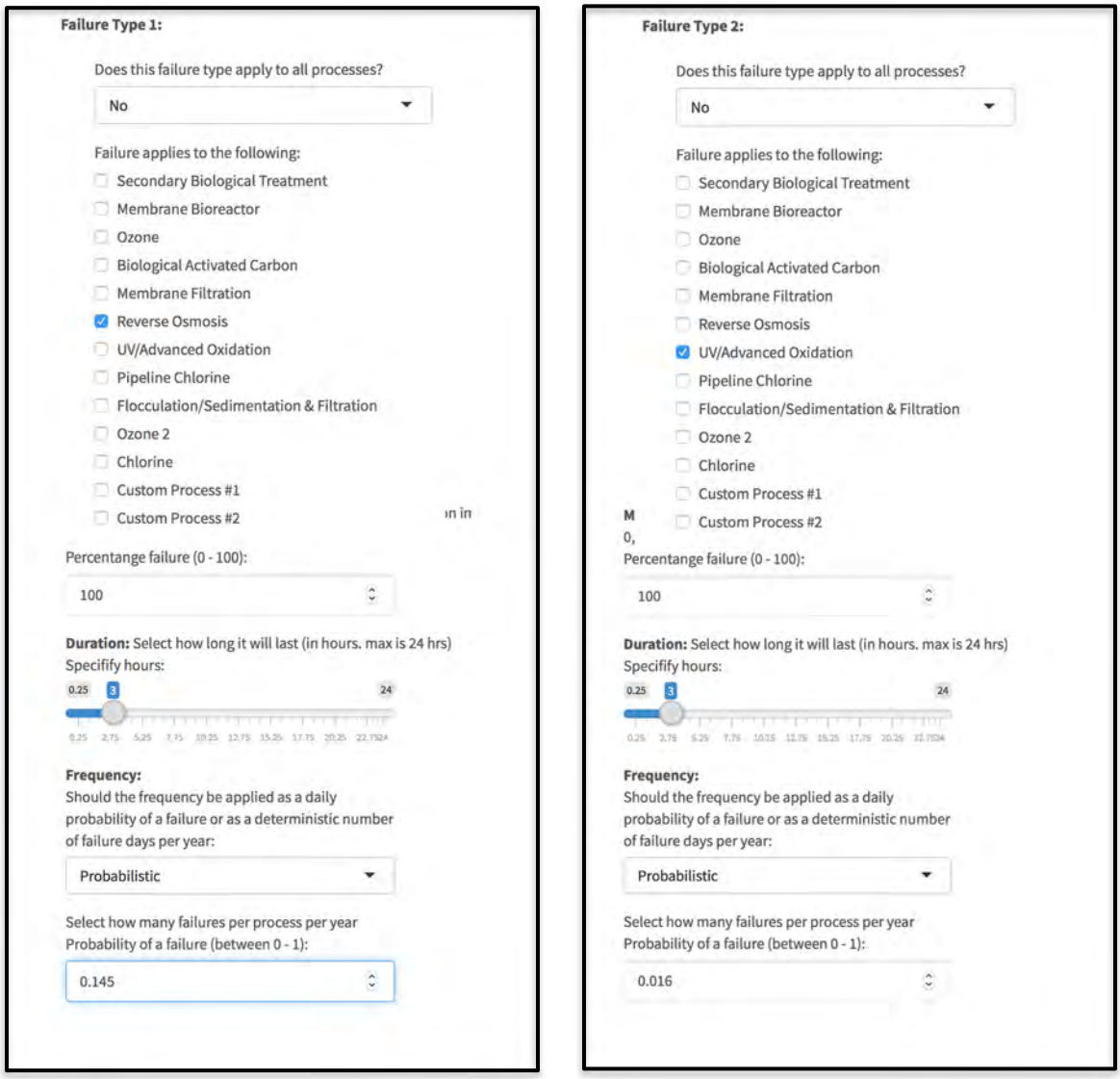


4. Select Treatment Failure on the left menu bar. This will bring the user to an input screen where **"Conduct failure analysis"** can be selected. In contrast with Case Study 2, different failure settings will be applied to the four treatment processes in Section B.17. Specifically, two treatment processes (secondary biological treatment and pipeline chlorine) will be excluded from the failure analysis, and two treatment processes (RO and UV AOP) will be characterized with process-specific failure types. Note that selecting "No" in the dropdown box for "Does this failure type apply to all processes?" allows the user to apply failure types to individual processes.

Based on operational performance and industry surveys, Soller et al. (2018b) assumed process-specific probabilities of off-specification performance for any random 15-min time period. This requires reconciliation with the daily failure probability in DPRisk; specifically, the 15-minute failure probabilities reported in Soller et al. (2018b) require adjustments to achieve similar frequencies in the tool output. For example, Soller et al. (2018b) reported a 15-minute probability of 0.018 for an off-specification condition for RO. With 8 samplings of the performance distribution each day (i.e., every 3 hours and 2,920 samplings per year), an off-specification condition would be expected for RO approximately 53 times in a year (i.e., 0.018×2,920 = 53). DPRisk's framework does not allow for multiple failures of a single process within a given day. Assuming a similar off-specification frequency in DPRisk (i.e., 53 failures per year), that would equate to a daily probability of 0.145 (i.e., 53/365). The **process-specific daily failure probabilities** are summarized in the far right column of the following table. In order to increase the probability of a failure in DPRisk aligning with an ingestion event, the **failure duration** should be consistent with the ingestion frequency in Soller et al. (2018b) (i.e., **3 hours**). Finally, all **failure magnitudes** are assumed to be **100%** for this scenario.

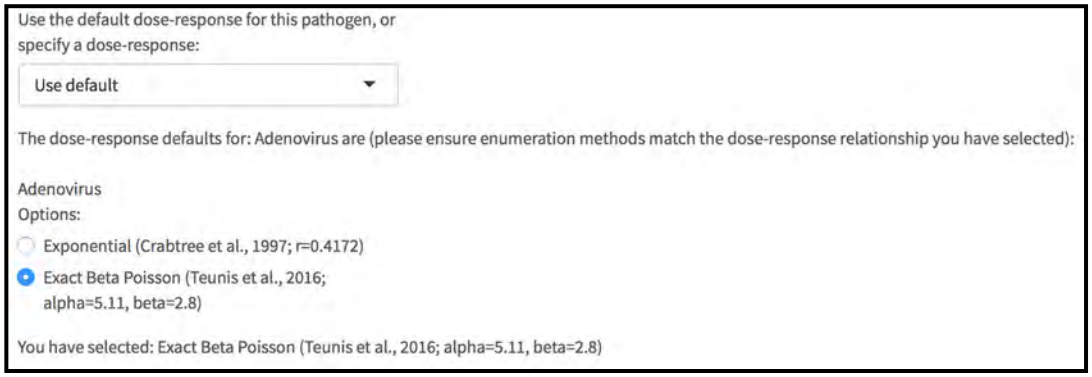
Unit Process	15-min Off-Spec Probability[1]	No. of 3-hr Time Increments per Year	Expected Off-Spec Events per Year	No. of Days per Year	Adjusted Daily Off-Spec Probability[3]
Secondary	0.000	2,920	0.0	365	0.000
UF	0.021	2,920	61	365	0.167[2]
RO	0.018	2,920	53	365	0.145
UV	0.002	2,920	6.0	365	0.016
NaOCl	0.000	2,920	0.0	365	0.000

[1]Soller et al. (2018b); [2]Adenovirus LRV for UF is assumed to be 0 so failures need not be applied; [3]Failure magnitude = 100% and failure duration = 3 hours



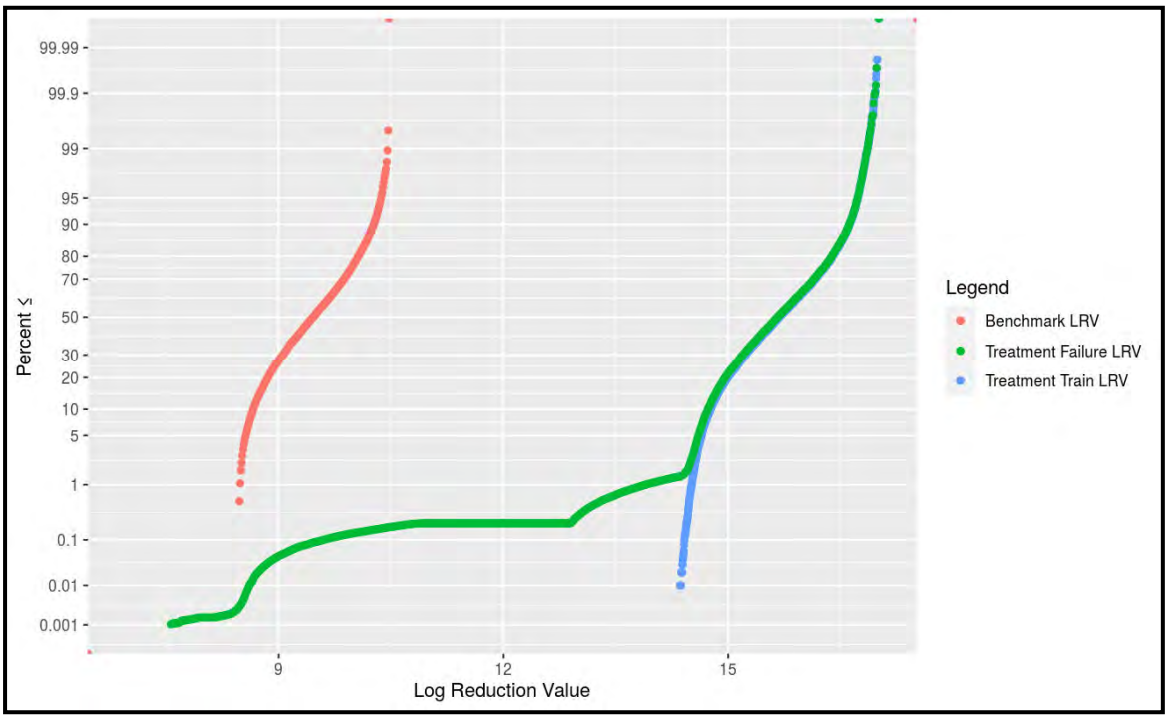
5. Select Management Barriers on the left menu bar. This portion of the case study does not incorporate blending, dilution, or die-off so the **default LRV of 0** can remain unchanged.
6. Select Exposure on the left menu bar. This will bring the user to an input screen where the daily ingestion rate can be specified and characterized. The ingestion rate in *mL/day* can be described by one of the default distributions/point estimates or specified by the user. The user-specified option allows for (1) an input file with 10,000 data points, **(2) a point estimate (current scenario)**, or (3) a lognormal distribution with user-defined mean and standard deviation. The ingestion frequency in Soller et al. (2018b) was assumed to be eight 250-mL aliquots (i.e., 2 L total) spread randomly throughout the day. This should be described in DPRisk as a point estimate of **2 L/day** distributed evenly across **8 ingestion events per day**.
7. Select Dose-Response on the left menu bar. This will bring the user to an input screen where the pathogen dose-response equation can be identified and characterized. The user can (1) select one of the default dose-response models specific to the target pathogen (adenovirus in this scenario) or (2) select and characterize one of several dose-response models commonly used in QMRAs. Soller et al. (2018b) used a hypergeometric dose response model for adenovirus, which is also described as an Exact Beta Poisson dose response model. For this case study, the user can either select the **Exact**

Beta Poisson default (see figure on next page) or **specify a dose response** and select **hypergeometric**. For the user-defined hypergeometric approach, the parameters can then be described as (1) **point estimates** or (2) based on an input file with 10,000 data points for each parameter. Based on Soller et al. (2018b), the **alpha** parameter should be **5.11** and the **beta** parameter should be **2.8**. ***Note that if the user-defined dose response model is selected, it will not be possible to view the benchmark LRVs in the PATTP output tab because the DPRisk algorithm is not equipped to make the benchmark LRV calculations with user-defined dose response models.***

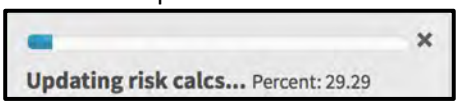


8. Select PATTP Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulation and calculations related to treatment train performance. A box will likely appear in the bottom right corner of the screen to indicate the tool's progress. The following series of figures summarizes the PATTP output for Case Study 1. Assuming the 'seed' for random number generation under the Configure tab is set at 1 and the number of failure simulations is set to 100, some of the output may appear exactly as shown. Recall that the benchmark LRV data are not available when using a user-specified dose response function. These data were generated using the Exact Beta Poisson default for adenovirus.

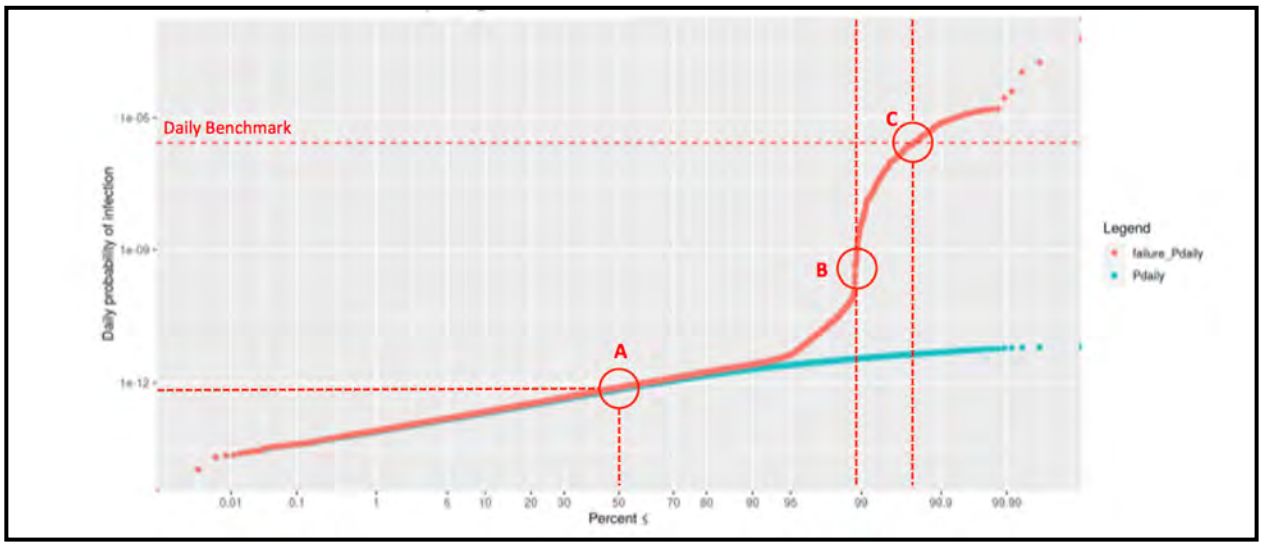
   The following figure shows the distributions for the benchmark LRVs, the observed treatment performance in the absence of failures, and the observed treatment performance when accounting for failures. In the absence of failures, the modeled treatment train includes ~6 logs of redundancy beyond the benchmark LRV curve. For the default setting of 100 failure simulations (i.e., 36,500 simulated days and 3,504,000 total time intervals) and the failure specifications described earlier (i.e., daily failure probabilities of 0.145 for RO and 0.016 for UV), approximately 5,293 RO failures (i.e., 0.145×36,500), 584 UV failures (i.e., 0.016×36,500), and 85 simultaneous failures (i.e., 0.145×0.016×36,500) are expected. For an assumed failure duration of 3 hours (or twelve 15-min time intervals per failure), these failures would span 63,510 (RO), 7,008 (UV), and 1,016 (simultaneous) time intervals, accounting for 1.8%, 0.2%, and 0.03% of the LRVs, which appears to be consistent with the inflection points in the failure LRV curve.



9. Select QMRA Output on the left menu bar, which will trigger the tool to perform the Monte Carlo simulation and calculations related to daily and annual risk. A box will likely appear in the bottom right corner of the screen to indicate the tool's progress.



The following figure shows a comparison of the daily risk estimates from Figure 1 of Soller et al. (2018b) versus the output from DPRisk. Several daily risk points are noted by red circles to highlight direct comparisons between the data. For example, point A represents the median daily risk in all datasets, which was relatively consistent at ~10^{-12}. Point B represents the inflection point in the failure analyses, which occurs immediately before the 99th percentile in the published QMRA and in the output from DPRisk. Finally, point C represents the intersection point with the daily risk benchmark of 2.7×10^{-7}, which occurs between the 99th and 99.9th percentile in the published QMRA and in the output from DPRisk. Based on these similarities, the output from DPRisk appears to be consistent with the output from Soller et al. (2018b).



10. Select Summary of PATTP and QMRA Output on the left menu bar, which will bring the user to a screen summarizing the critical outputs from the tool, specifically the LRV comparison and the daily and annual risks. The supporting data excluded from this summary are still accessible in the other tabs.

B.18 Conclusions

Probabilistic assessment of treatment train performance (PATTP) and quantitative microbial risk assessment (QMRA) are tools that are constantly evolving as the industry develops new datasets and refines its understanding of underlying principles and assumptions. Many of the assumptions incorporated into these tools can have significant implications for final risk calculations and any regulations or policies being considered. This is one of the limitations of trying to apply published QMRAs to a specific application: there may be an assumption built into the published QMRA that significantly deviates from the application being considered. For example, a published QMRA may have considered a long environmental buffer storage time, but the application in question may have a storage time of only a few days. As another example, a past QMRA may have considered an outdated pathogen dataset or dose response model that no longer meets updated standards of practice. This tool was developed to alleviate this problem by providing a relatively simple user interface that provides sufficient flexibility to tailor the model to the potentially unique characteristics of a project under consideration. Moreover, the tool can be configured to allow for relatively rapid risk calculations, which facilitates sensitivity analyses on a wide range of input parameters. The goal of this Guidance Document was to not only provide context about important components of PATTP and QMRA but to also ensure transparency with respect to the underlying structure and calculation methodology of DPRisk. Considering these features, DPRisk provides a robust platform for evaluating a wide range of drinking water applications, particularly in the context of potable reuse, and can be a powerful tool for facilitating the decision-making process.

B.19 Summary of Output File Headers

Parameter Set Data File

Heading	Description
(none)	The first column does not have a heading and is a count of the rows from 1 to 10,000
input	The raw wastewater concentration in pathogen units/L
Lr	Treatment train log removal value if LRVs are not provided for specific unit processes (optional)
sbt_lr	Treatment LRV for secondary biological treatment (optional)
mbr_lr	Treatment LRV for membrane bioreactor (optional)
ozone_lr	Treatment LRV for ozone (optional)
bac_lr	Treatment LRV for biological activated carbon (optional)
mf_lr	Treatment LRV for membrane filtration (optional)
ro_lor	Treatment LRV for reverse osmosis (optional)
uvaop_lr	Treatment LRV for the UV advanced oxidation process (optional)
pipelinechlorine_lr	Treatment LRV for pipeline chlorine (optional)
fsf_lr	Treatment LRV for flocculation/sedimentation/filtration (optional)
ozone2_lr	Treatment LRV for ozone2 (optional)
chlorine_lr	Treatment LRV for chlorine (optional)
custom1_lr	Treatment LRV for custom process 1 (optional)
custom2_lr	Treatment LRV for custom process 2 (optional)
blending_lr	LRV from blending management barrier
dilution_lr	LRV from dilution management barrier
dieoff_lr	LRV from die-off management barrier
lr_with_mb	overall LRV including management barriers
Ceff	final drinking water concentration [i.e., input x 10^(- lr_with_mb)]
exposure	ingestion volume in mL/day
eventsperday	number of exposure/ingestion events per day (from 1 to 96)
dose	dose for given exposure (i.e., Ceff x exposure/1000/eventsperday)
alpha	alpha parameter for dose-response (optional)
beta	beta parameter for dose-response (optional)
r	r parameter for dose-response (optional)
p	p parameter for dose-response (optional)
response	probability of infection from given dose (calculated from the dose-response function)
vc	exposure (i.e., ingestion volume) times raw wastewater concentration, which is used as the input for the benchmark treatment calculation (i.e., input x exposure/1000/eventsperday)
bttp_lrv	LRV solution ot the benchmark treatment calculation

LRVs for Failure Analysis

Heading	Description
(none)	The first column does not have a heading and is a count of the rows from 1 to (35,040 x number of failure simulations)
lr_with_mb	The overal LRV (including treatment and management barriers) without failure for each 15-min time interval
failure_lr_with_mb	The overal LRV (including treatment and management barriers) with failures for each 15-min time interval
Note: The failure_lr_with_mb and lr_with_mb columns are paired. Each row is computed for the same combinations of treatment and management barrier LRV parameters, but the failure_lr_with_mb column includes the effects of a failure if it occurred within that 15-min time interval, whereas the lr_with_mb column omits the effects of the failure.	

Failure Analysis Pannual File

Heading	Description
(none)	The first column does not have a heading and is a count of the rows from 1 to 100 (or the number of failure simulations specified in the tool settings)
failure_Pannual	The annualized risk with failures included
Pannual	The annualized risk with failures omitted
Note: The failure_Pannual and Pannual columns are paired. Each row is computed for the same combinations of input, treatment, and exposure parameters, but failure_Pannual includes the failure, whereas Pannual does not.	

Failure Analysis Pdaily File

Heading	Description
(none)	The first column does not have a heading and is a count of the rows from 1 to 100 (or the number of failure simulations specified in the tool settings)
failure_Pdaily	The daily risk with failures included
Pdaily	The daily risk with failures omitted
Note: The failure_Pdaily and Pdaily columns are paired. Each row is computed for the same combinations of input, treatment, and exposure parameters, but failure_Pdaily includes the failure, whereas Pdaily does not.	

15-min Events for Failure Simulations

Heading	Description
These files should have the same headings as the Parameter Set Data File, as well as:	
(none)	The first column does not have a heading. The value shown indicates which row out of the underlying 10,000-parameter dataset was selected for the given 15-min data point. There should be 35,040 rows in total, corresponding to the number of 15-min periods in a year. Values with a decimal point and number after the decimal point indicate rows in the underlying parameter dataset that were sampled a second time (X.1), a third time (X.2), etc.
failure_sbt_lr	Treatment LRV for secondary biological treatment with failure if a failure occurred within the 15-min time interval (optional)
failure_mbr_lr	Treatment LRV for membrane bioreactor with failure if a failure occurred within the 15-min time interval (optional)

failure_ozone_lr	Treatment LRV for ozone with failure if a failure occurred within the 15-min time interval (optional)
failure_bac_lr	Treatment LRV for biological activated carbon with failure if a failure occurred within the 15-min time interval (optional)
failure_mf_lr	Treatment LRV for membrane filtration with failure if a failure occurred within the 15-min time interval (optional)
failure_ro_lor	Treatment LRV for reverse osmosis with failure if a failure occurred within the 15-min time interval (optional)
failure_uvaop_lr	Treatment LRV for the UV advanced oxidation process with failure if a failure occurred within the 15-min time interval (optional)
failure_pipelinechlorine_lr	Treatment LRV for pipeline chlorine with failure if a failure occurred within the 15-min time interval (optional)
failure_fsf_lr	Treatment LRV for flocculation/sedimentation/filtration with failure if a failure occurred within the 15-min time interval (optional)
failure_ozone2_lr	Treatment LRV for ozone2 with failure if a failure occurred within the 15-min time interval (optional)
failure_chlorine_lr	Treatment LRV for chrlorine with failure if a failure occurred within the 15-min time interval (optional)
failure_custom1_lr	Treatment LRV for custom process 1 with failure if a failure occurred within the 15-min time interval (optional)
failure_custom2_lr	Treatment LRV for custom process 2 with failure if a failure occurred within the 15-min time interval (optional)
lr_with_mb	overall LRV including management barriers
failure_lr	Treatment log removal value with failure if a failure occurred within the 15-min time interval
failure_lr_with_mb	Treatment log removal value with failure and including additional LRVs from management barriers (if applicable) if a failure occurred within the 15-min time interval
failure_dose	15-min dose computed with the failure if a failure occurred within the 15-min time interval
failure_response	15-min probability of infection computed from the dose-response function if a failure occurred within the 15-min time interval
Note: These failure values are paired with their non-failure variables. If a failure was not identified within a given 15-min time interval, then the parameter values will be the same as their non-failure counterpart.	

B.20 References

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APPENDIX C

Training Workshop Materials

Location: Teleconference
Date: July 14, 2020
Time: 1:00pm – 3:00pm PDT

DPR-1 QMRA/PATTP Introduction and Virtual Training Meeting Agenda

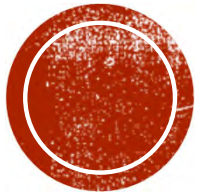
Join the Meeting: Click HERE
Call-in: +1 661-383-2580
Access Code: 329 909 249#

Time	Topic	Speaker(s)
1:00 – 1:05 pm	Welcome	Adam Olivieri & Brian Pecson
1:05 – 1:45 pm	Introduction and Background on PATTP & QMRA	Brian Pecson & TWG
1:45 – 1:55 pm	Questions from State Board	All
1:55 – 2:15 pm	Live Demo of DPRisk Tool	Edmund Seto
2:15 – 2:35 pm	Case Study Live Demo	Daniel Gerrity
2:35 – 2:40 pm	Next Steps	Brian Pecson & Adam Olivieri
2:40 – 3:00 pm	Questions from State Board	All

DPR-1 QMRA/PATTP: STATE BOARD WEBINAR

Part 1: Tool Introduction and Virtual Training

July 14, 2020



WELCOME & INTRODUCTIONS

Adam Olivieri

Brian Pecson

INTRODUCTIONS

- Technical Working Group
  - Brian Pecson, Trussell Technologies (Chair)
  - Nick Ashbolt, University of Alberta
  - Charles Haas, Drexel University
  - Theresa Slifko, Metropolitan Water District
- Research Team
  - Dan Gerrity, Southern Nevada Water Authority
  - Edmund Seto, University of Washington
- Additional Staff
  - Anya Kaufmann, Trussell Technologies
- WRF/State Board Coordination
  - Adam Olivieri
- State Water Board
  - Randy Barnard
  - Mark Bartson
  - Brian Bernados
  - Steven Book
  - Robert Brownwood
  - Jing Chao
  - Asad Faraz
  - Candida Granillo-Doods
  - Saeedreza Hafeznezami
  - Tricia Lee
  - Eugene Leung
  - Laura McLellan
  - Aide Ortiz
  - Sherly Rosilela
  - Kurt Souza
  - Dave Spath
  - Bob Hultquist
- Water Research Foundation
  - Julie Minton
  - Erin Partlan

AGENDA

Time	Topic	Speaker(s)
1:00 – 1:05 pm	Welcome & Introductions	Adam Olivieri & Brian Pecson
1:05 – 1:45 pm	Introduction & Background on PATTP & QMRA	Brian Pecson & TWG
1:45 – 1:55 pm	Q&A	All
1:55 – 2:15 pm	Live Demo of DPRisk Tool	Edmund Seto
2:15 – 2:35 pm	Case Study Live Demo	Daniel Gerrity
2:35 – 2:40 pm	Next Steps	Brian Pecson & Adam Olivieri
2:40 – 3:00 pm	Q&A	All

BACKGROUND ON PATTP/QMRA

Brian Pecson and TWG

PATTP AND QMRA OVERVIEW

- A probabilistic assessment of treatment train performance (PATTP) and QMRA can provide insight on multiple public health aspects
  - Reliability of DPR treatment trains in consistently meeting risk goals
  - Benefit of additional redundancy in treatment in achieving goals
  - Benefit of the *diversity* of treatment barriers (i.e., robustness)
  - Impact of management barriers on system resilience (failure response)
  - Impact of a range of treatment failures on reliability

GOALS OF DPR-1 RESEARCH PROJECT

- Goal #1: Develop guidelines for evaluating DPR facility treatment performance

- Goal #2: Use QMRA to confirm the level of treatment needed to achieve risk-based targets

STEPS IN QMRA

1. Exposure Assessment

Raw wastewater

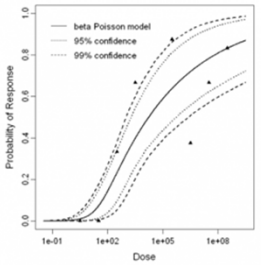
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

3. Risk Characterization

Risk

THERE ARE A LOT OF DECISIONS….

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Drinking water levels

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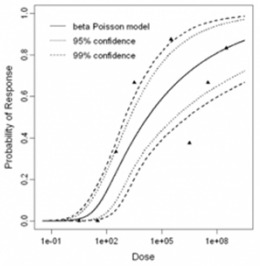

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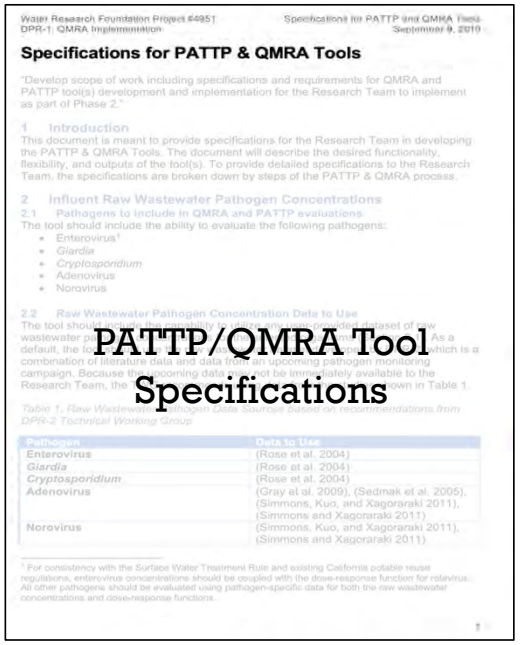
CONSISTENT FRAMEWORK FOR PATTP/QMRA



Water Research Foundation Project #4951 — Specifications for PATTP and QMRA Tools
DPR-1: QMRA Implementation — September 9, 2019

Specifications for PATTP & QMRA Tools

"Develop scope of work including specifications and requirements for QMRA and PATTP tool(s) development and implementation for the Research Team to implement as part of Phase 2."

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This document is meant to provide specifications for the Research Team in developing the PATTP & QMRA Tools. The document will describe the desired functionality, flexibility, and outputs of the tool(s). To provide detailed specifications to the Research Team, the specifications are broken down by steps of the PATTP & QMRA process.

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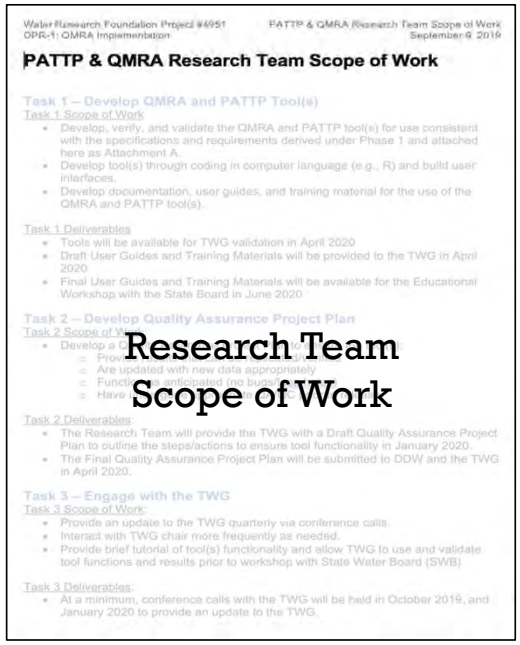
PATTP/QMRA Tool Specifications

July 2019



Water Research Foundation Project #4951 — PATTP & QMRA Research Team Scope of Work
DPR-1: QMRA Implementation — September 9, 2019

PATTP & QMRA Research Team Scope of Work

Task 1 – Develop QMRA and PATTP Tool(s)

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Task 2 – Develop Quality Assurance Project Plan

Task 2 Scope of W…

- Develop a Q…
  - Prov… updated with new data appropriately
  - Are updated as needed
  - Functions anticipated (no bugs/…
  - Have…

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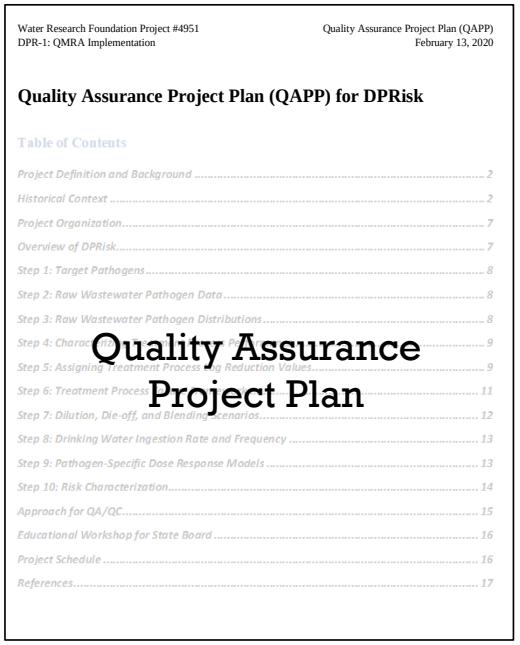
August 2019



Water Research Foundation Project #4951 — Quality Assurance Project Plan (QAPP)
DPR-1: QMRA Implementation — February 13, 2020

Quality Assurance Project Plan (QAPP) for DPRisk

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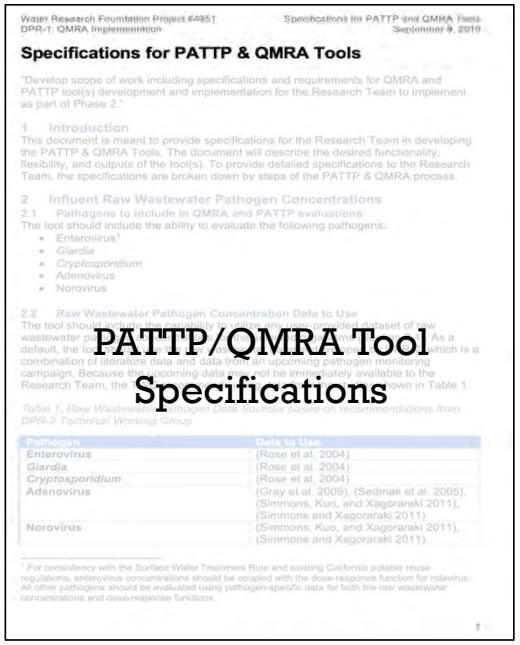
Quality Assurance Project Plan

February 2020

CONSISTENT FRAMEWORK FOR PATTP/QMRA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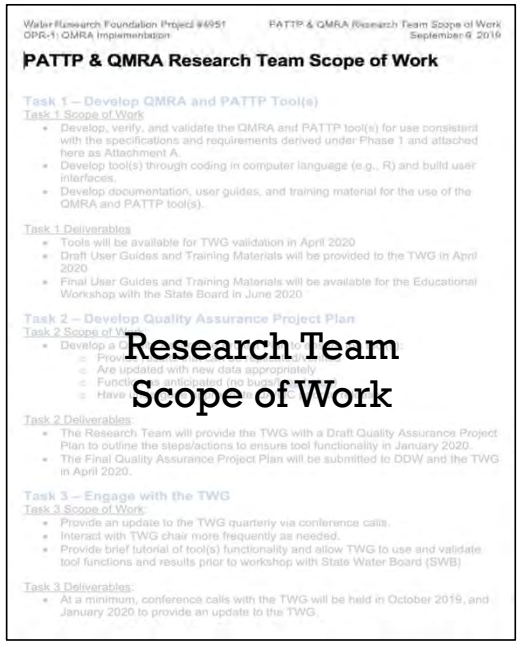
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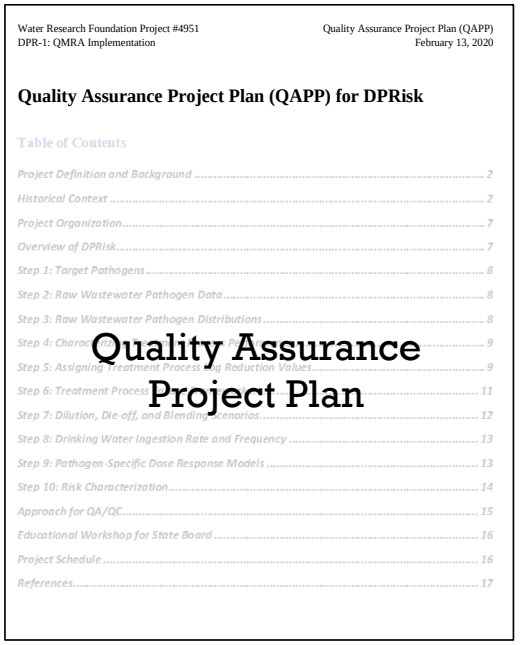
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DPR-1: QMRA Implementation February 13, 2020

Quality Assurance Project Plan (QAPP) for DPRisk

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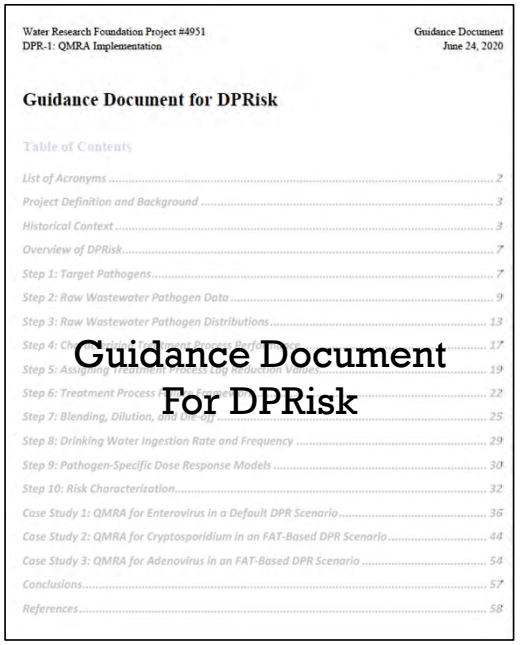
Water Research Foundation Project #4951 Guidance Document
DPR-1: QMRA Implementation June 24, 2020

Guidance Document for DPRisk

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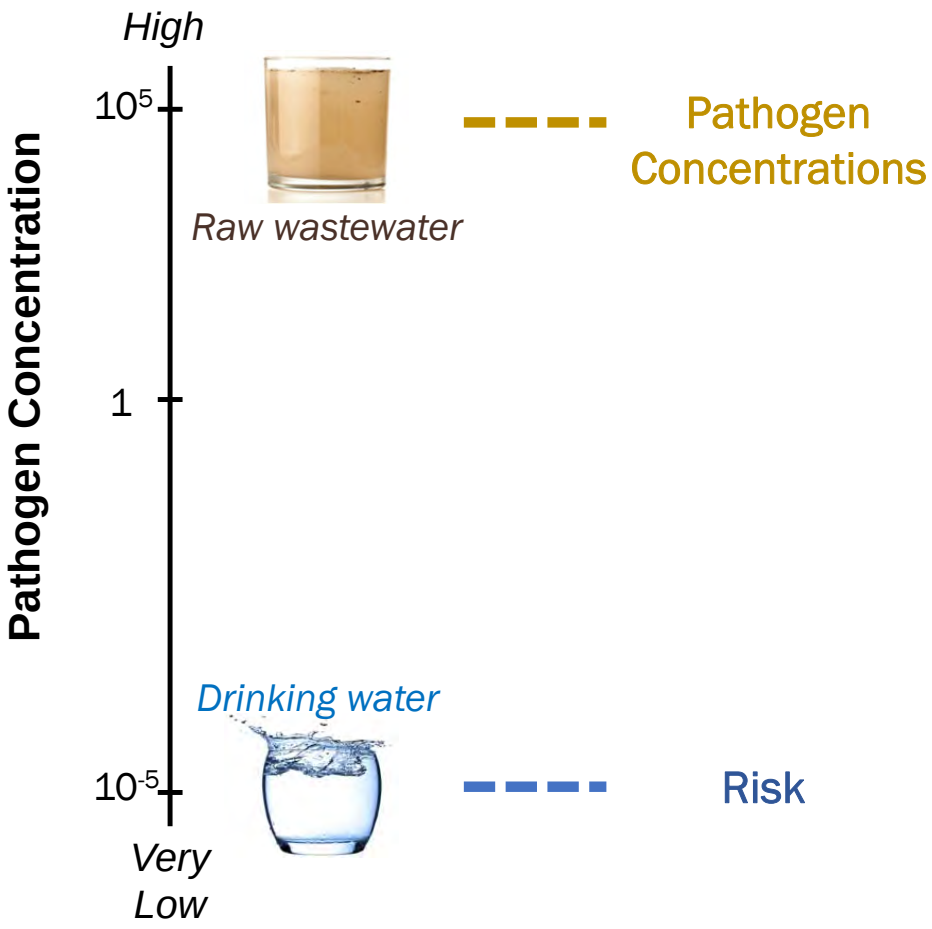
Guidance Document For DPRisk

July 2020

DPR PATHOGEN RISK AND TREATMENT



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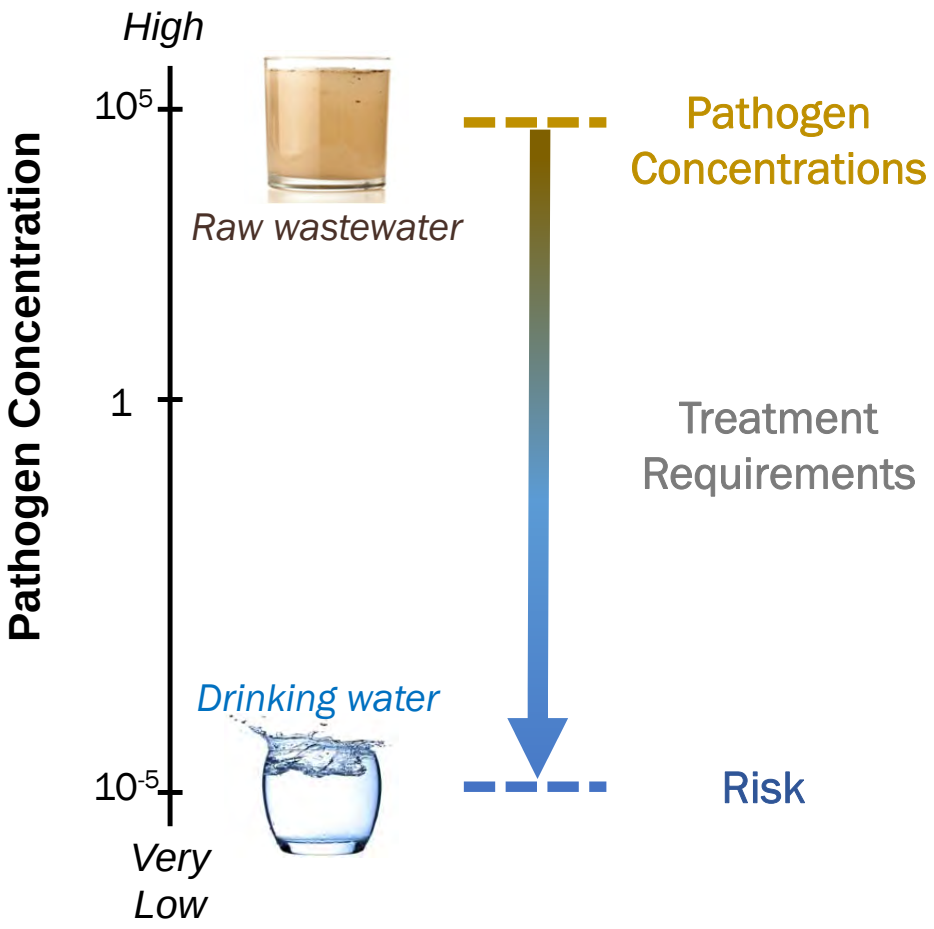

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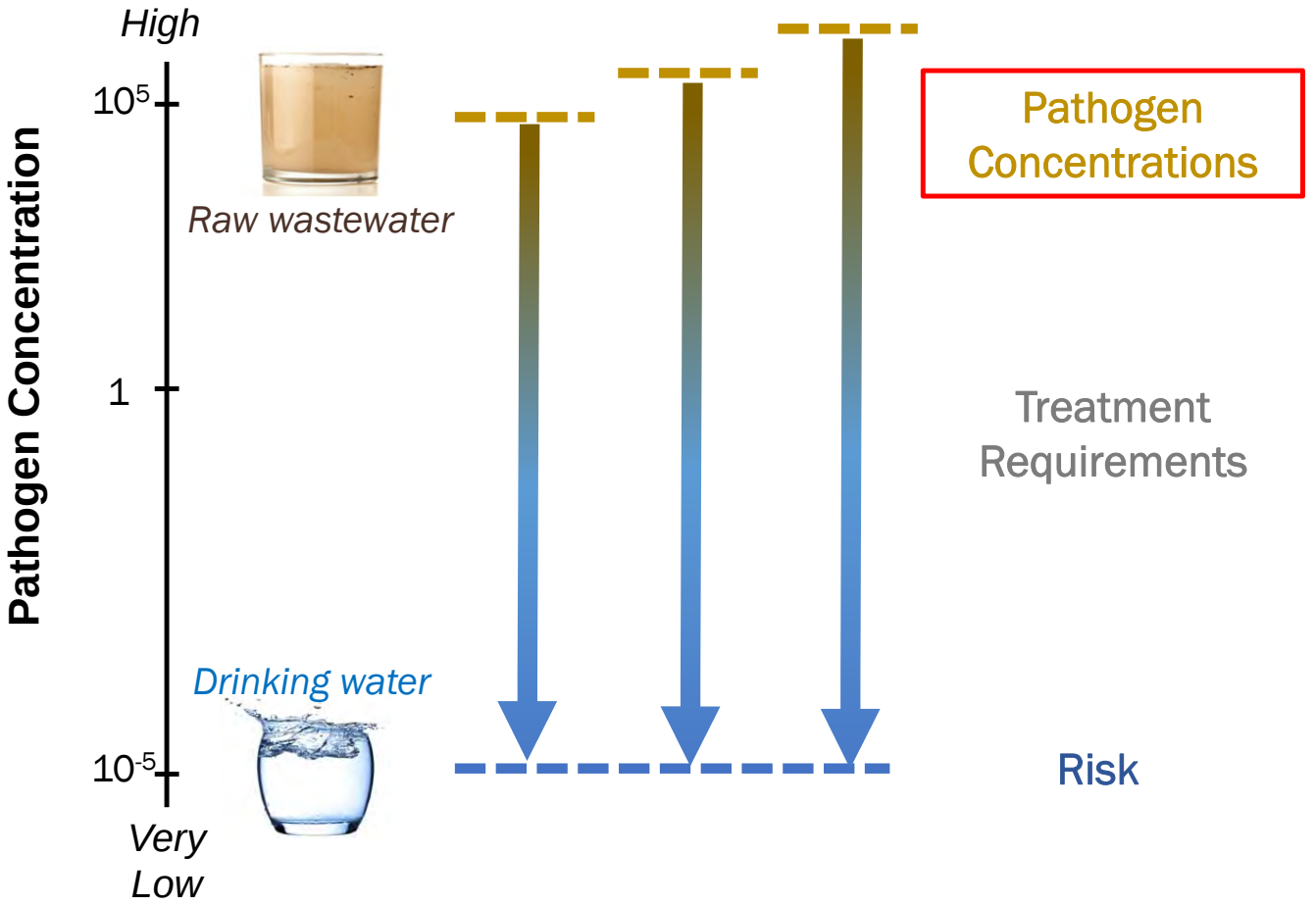
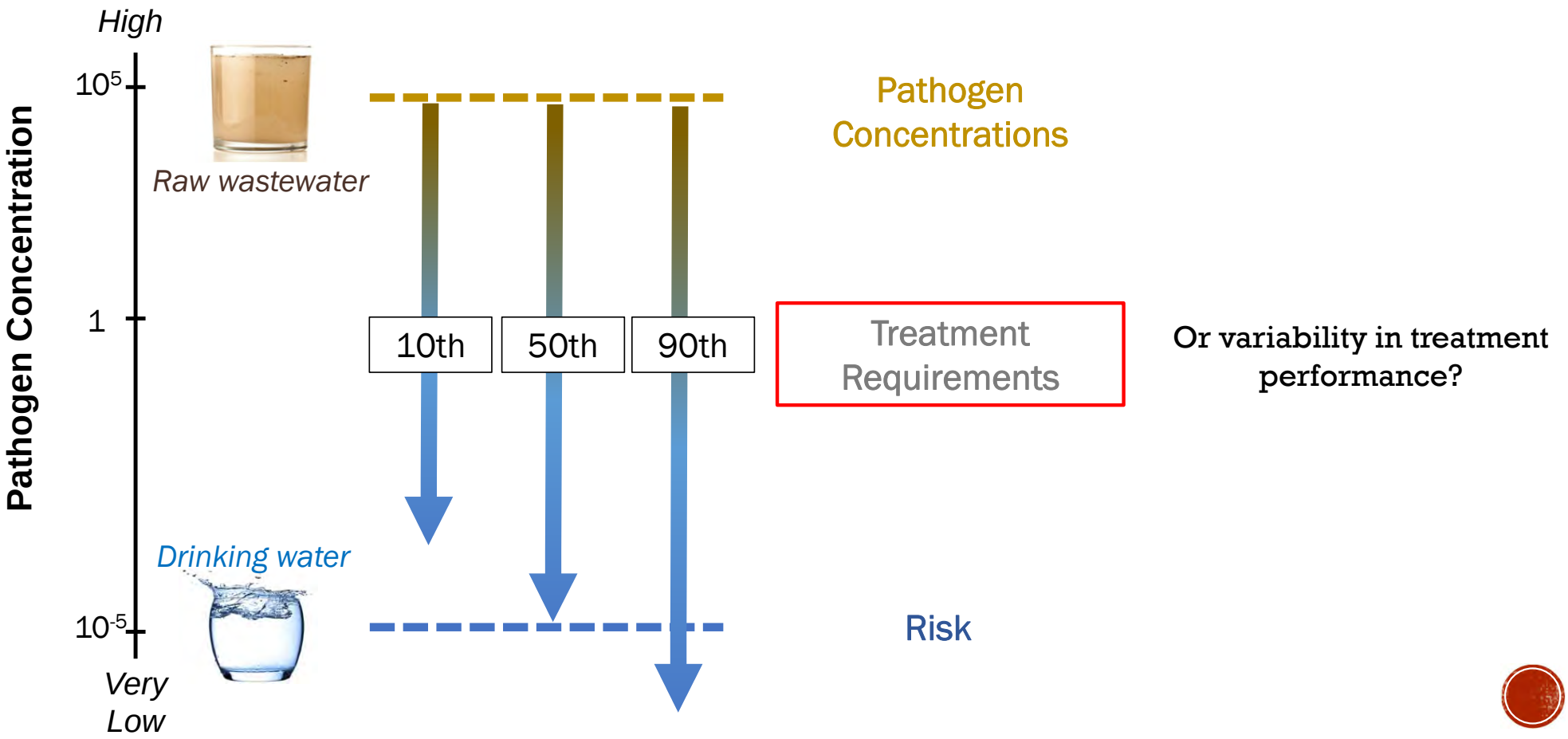


How do we account for variability in pathogen concentrations?

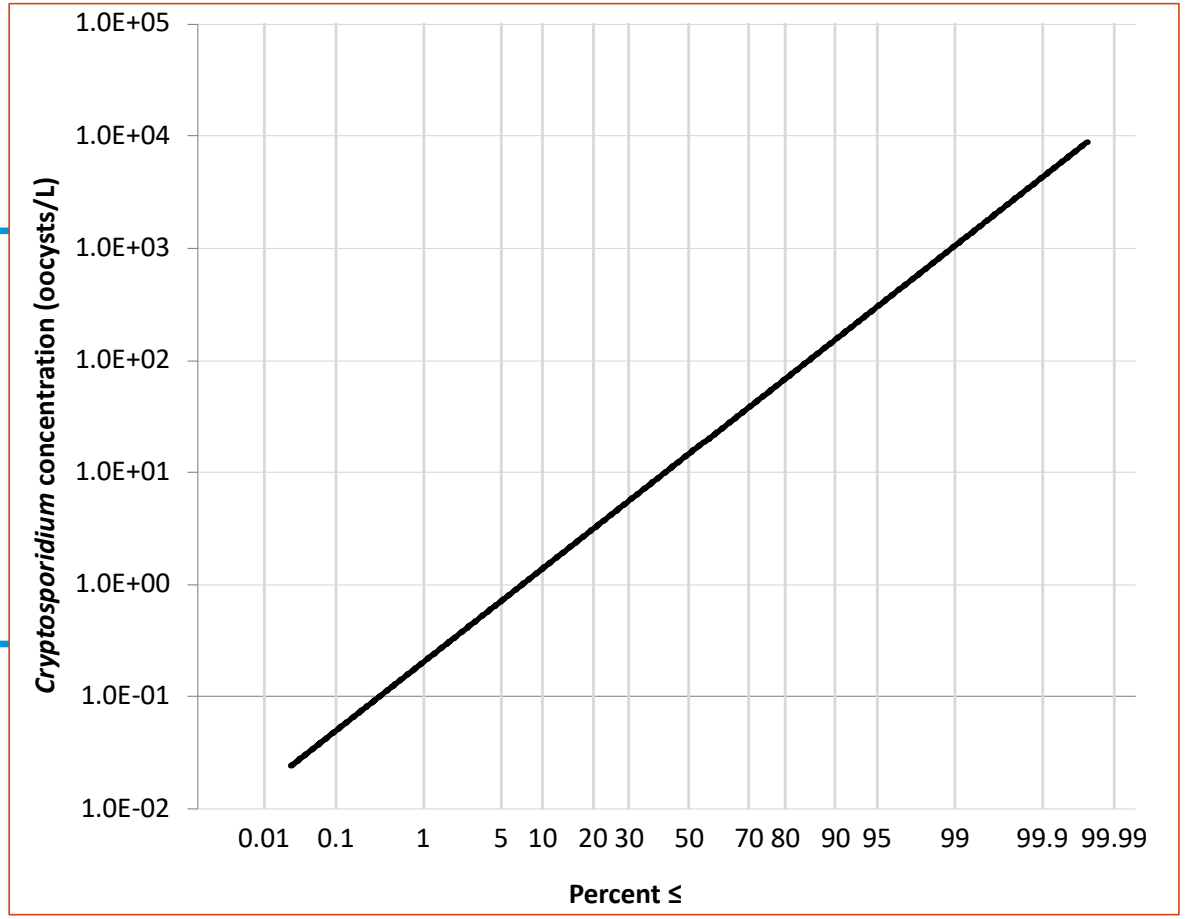
DPR PATHOGEN RISK AND TREATMENT



STEPS IN QMRA

1. Exposure Assessment

Raw wastewater



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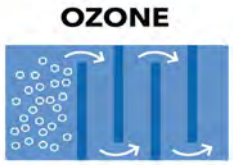
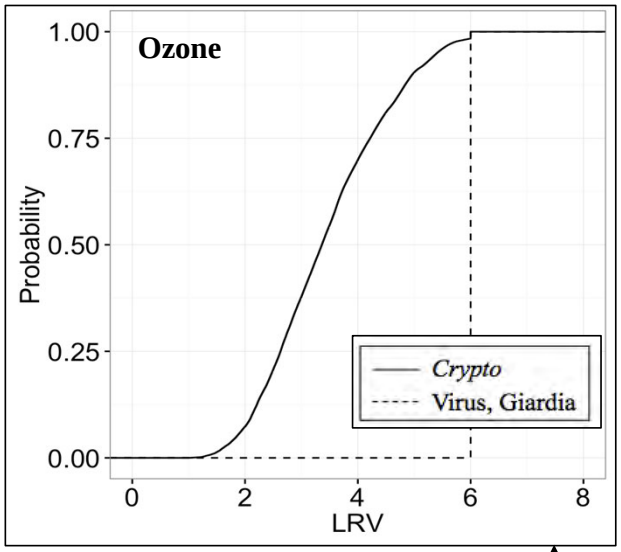
EVALUATING TREATMENT TRAIN PERFORMANCE



Date	Time	Applied O3 Dose	Ozone Demand	CT10	Virus LRV	Giardia LRV	Crypto LRV
6/16/15	0:00:01	10.770	8.688	8.08678188	6	6	3.939
6/16/15	0:00:04	10.571	8.479	8.14627964	6	6	3.968
6/16/15	0:00:14	10.225	8.161	7.87600246	6	6	3.832
6/16/15	0:00:24	10.132	8.107	8.00297707	6	6	3.899
6/16/15	0:00:34	9.982	7.979	8.0756773	6	6	3.926
6/16/15	0:00:44	9.960	7.975	7.94716956	6	6	3.864
6/16/15	0:00:54	10.158	8.138	8.16645995	6	6	3.978
6/16/15	0:01:04	10.510	8.463	8.1376053	6	6	3.969
6/16/1							3.971

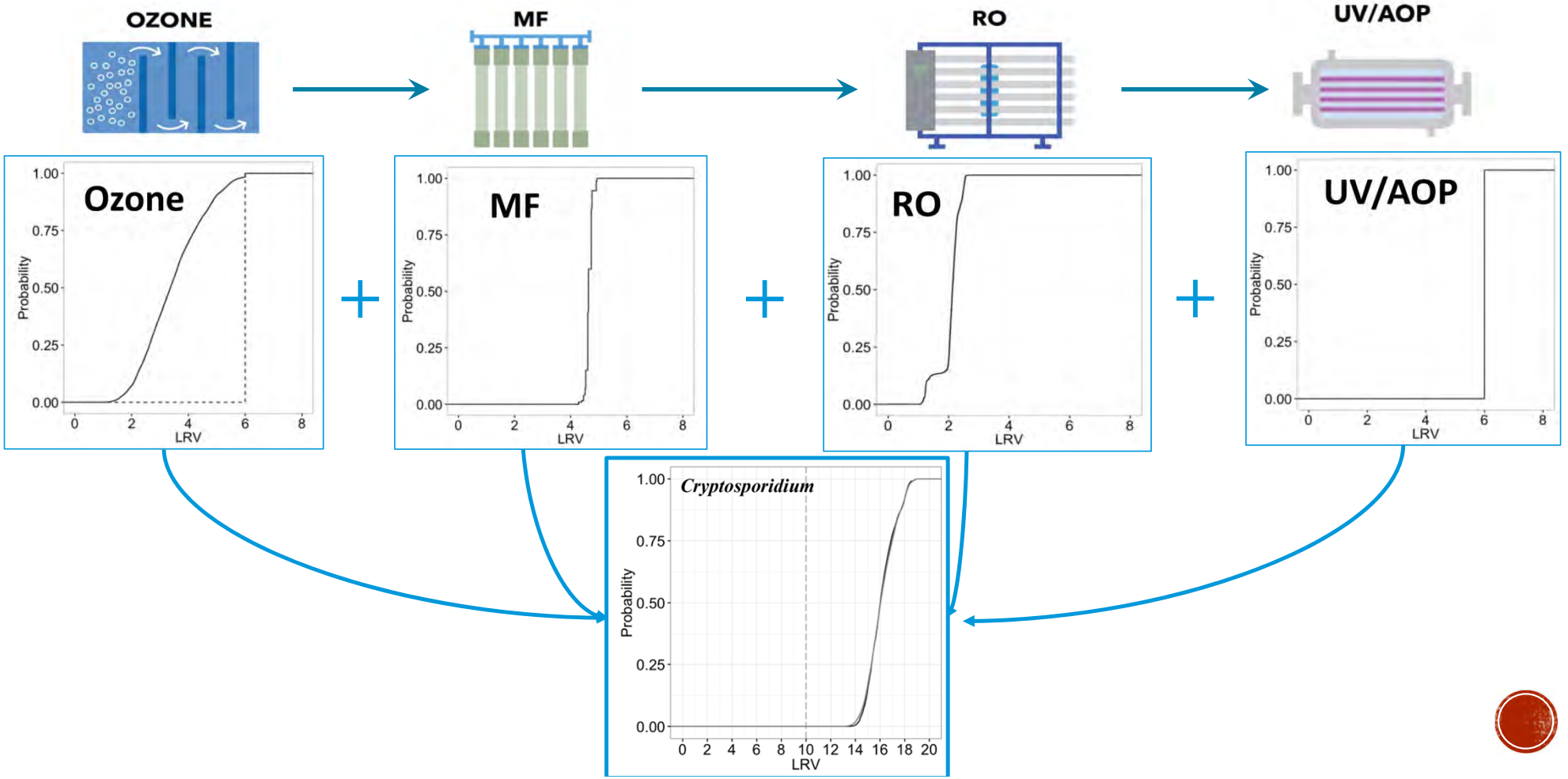
Collect performance data and calculate LRVs



Crypto LRV	"--> Sorted	Ranked	Probability
3.93938786	1.6863	1	0.00034775
3.96837154	1.7362	2	0.00090416
3.83174964	1.7527	3	0.00146056
3.89856325	1.7657	4	0.00201697
3.92635468	1.777	5	0.00257338
3.86387484	1.7882	6	0.00312978
3.97820216	1.8349	7	0.00368619
3.96927378	1.8765	8	0.00424259
3.97			

Rank data and develop distributions

EVALUATING TREATMENT TRAIN PERFORMANCE



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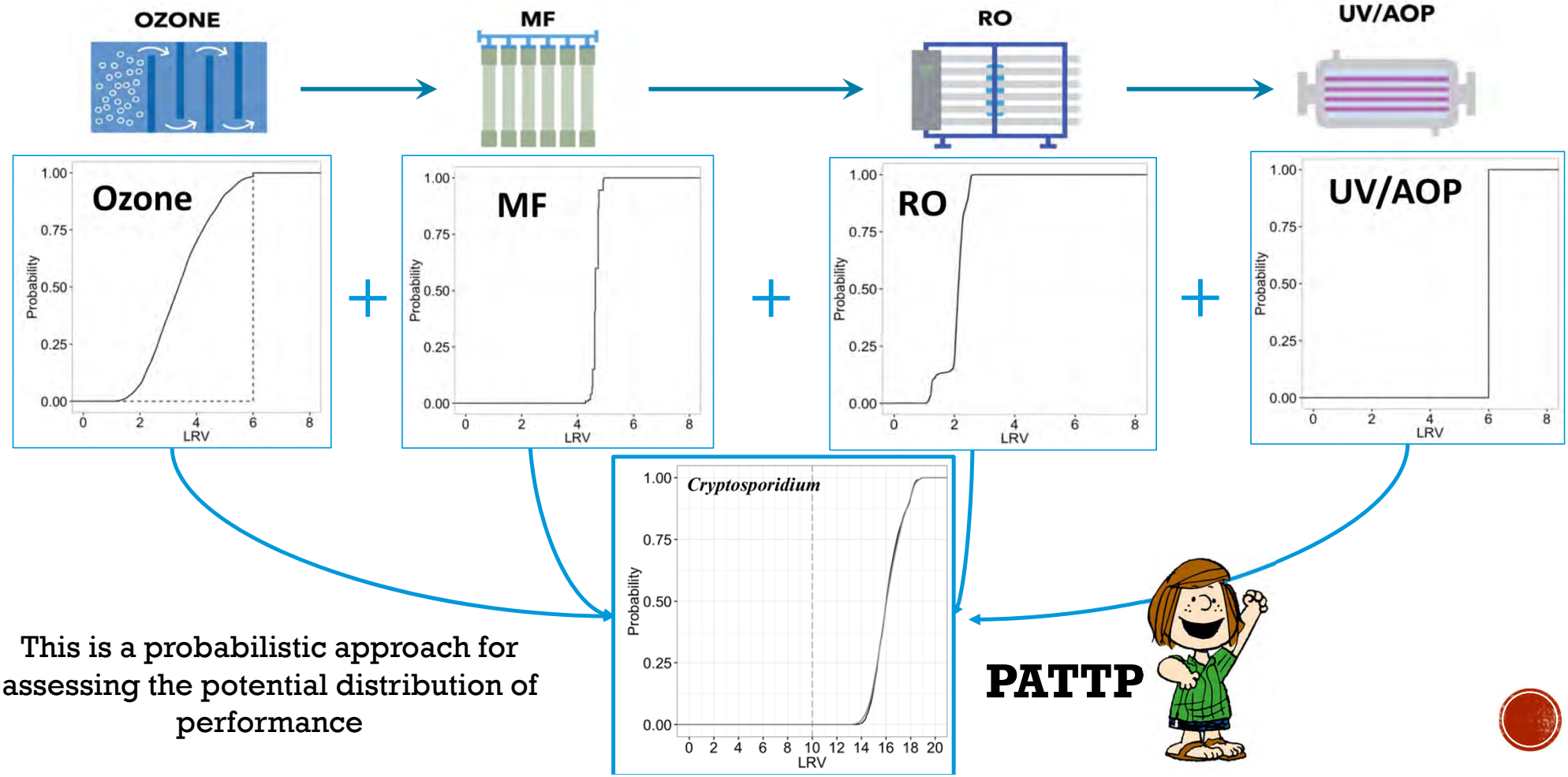

This is a probabilistic approach for assessing the potential distribution of performance

STEPS IN QMRA

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Drinking water levels

Drinking water consumption

Exposure

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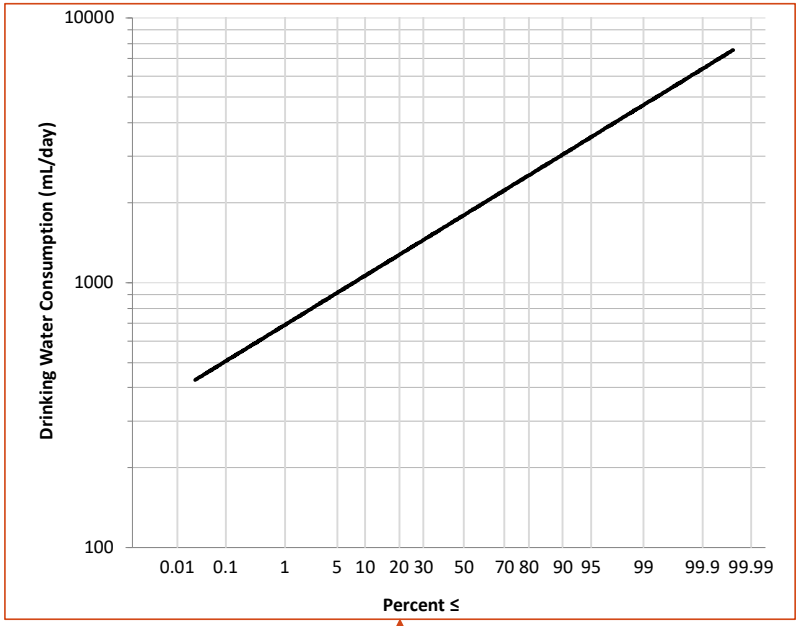

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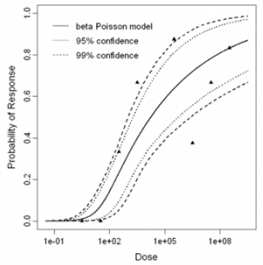

Dose-response

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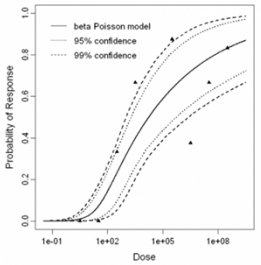


Dose-response

Calculated

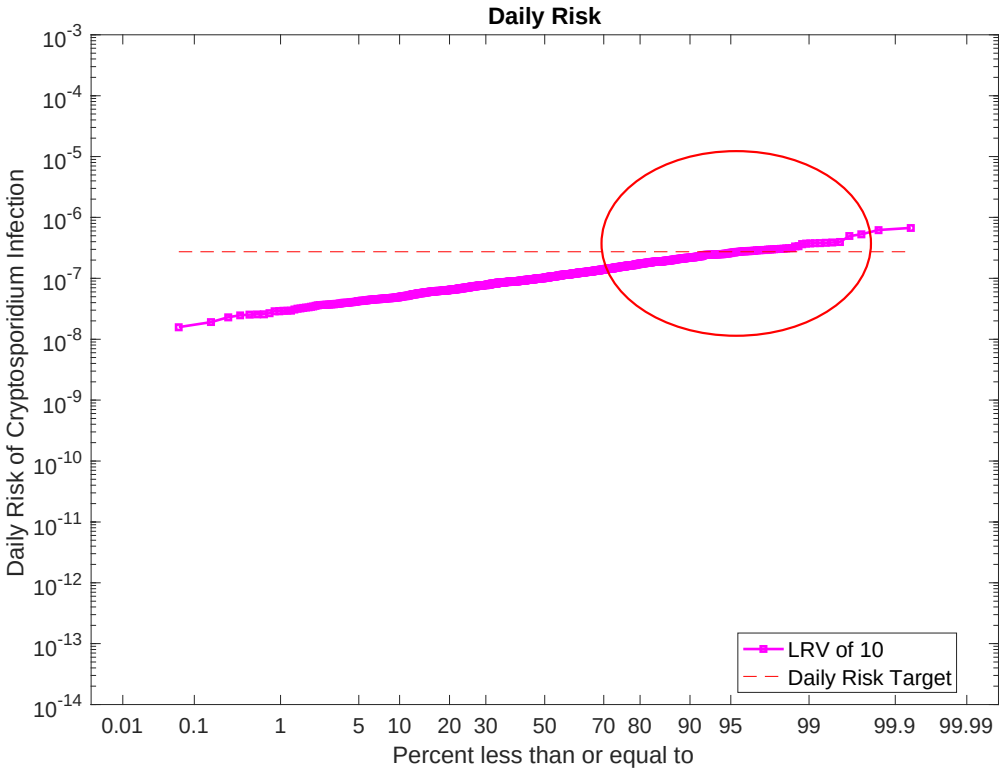
3. Risk Characterization

Risk

Calculated

RISK CURVES PROVIDE INSIGHT ON RELIABILITY

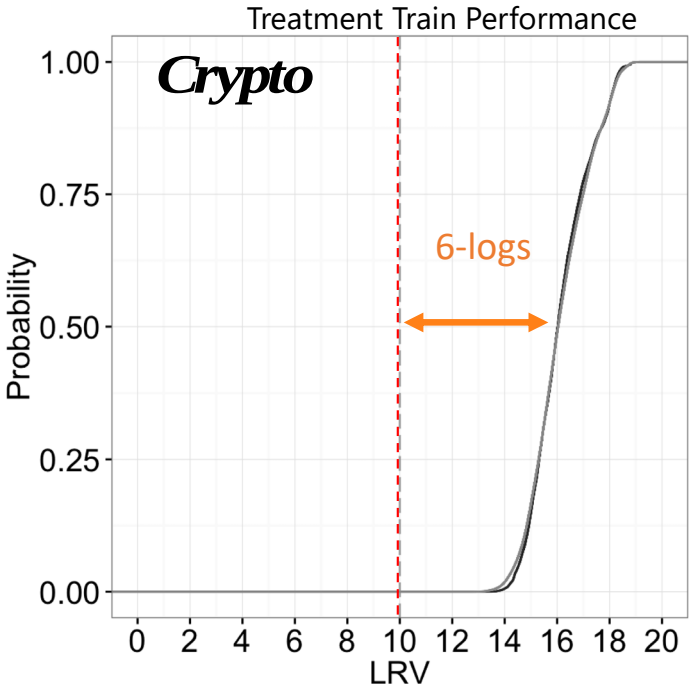
- Intersection of risk curve and health threshold tells what percent of time the system meets the health goal
  - Treatment train providing 10 LRV of Cryptosporidium control meets goal 95% of time



Consistency of public health protection = *Reliability*

WHAT INSIGHT CAN PATTP AND QMRA GIVE?

HOW DOES TREATMENT REDUNDANCY IMPACT RISK?



If our risk-based standards require 10-logs of Crypto reduction, this train provides **6 logs** of redundancy at median performance

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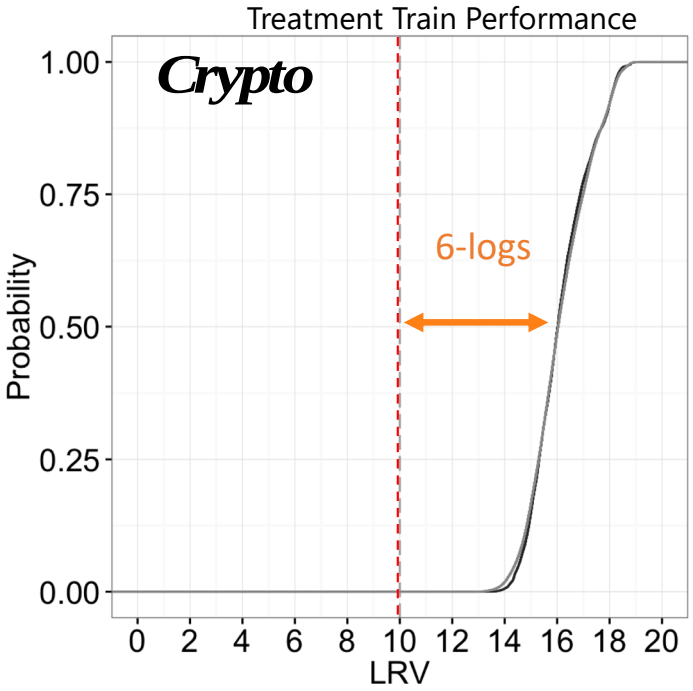
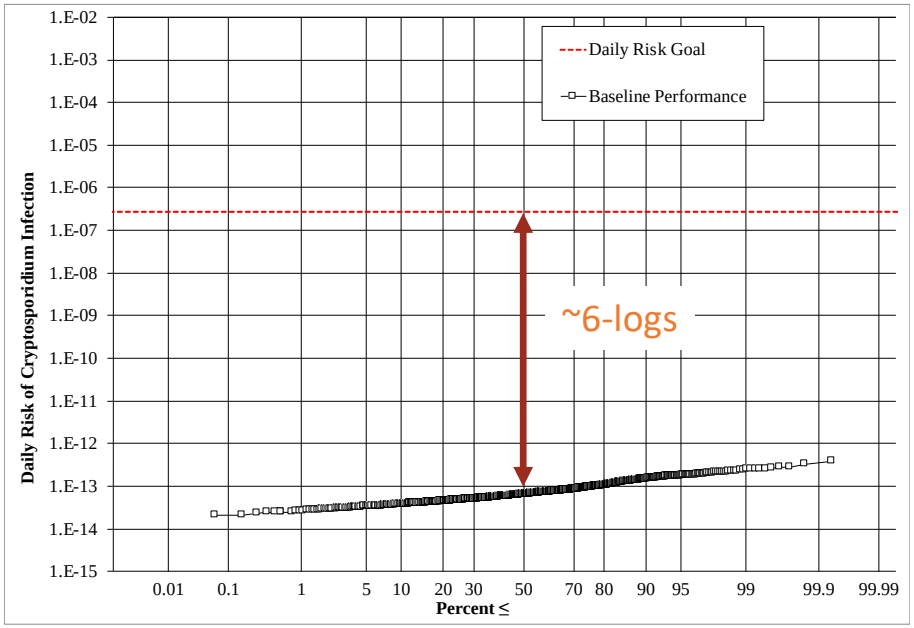


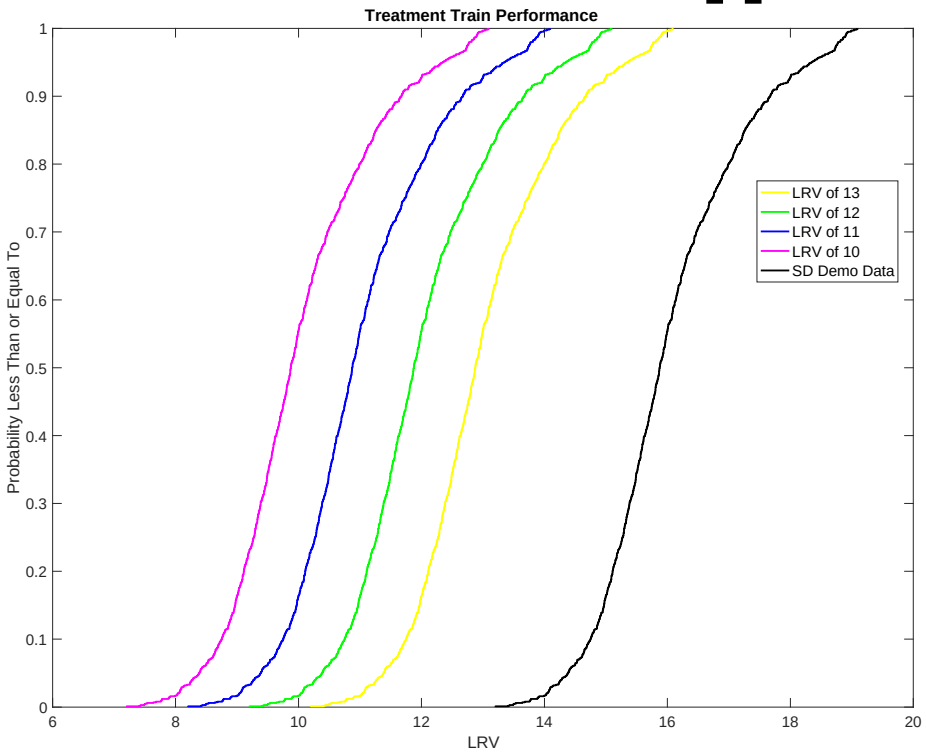
6 logs of redundancy is reflected in the risk curve being ~6-logs below risk threshold



- There is a direct relationship between treatment redundancy and risk

HOW DOES TREATMENT REDUNDANCY IMPACT RISK?

- We can model what happens at different levels of redundancy



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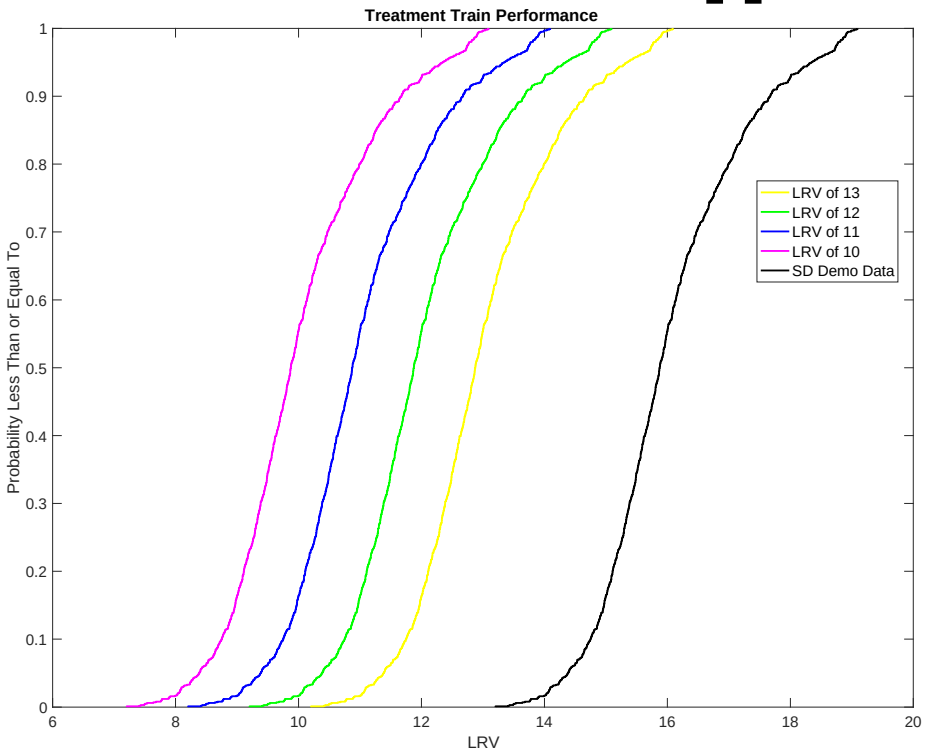
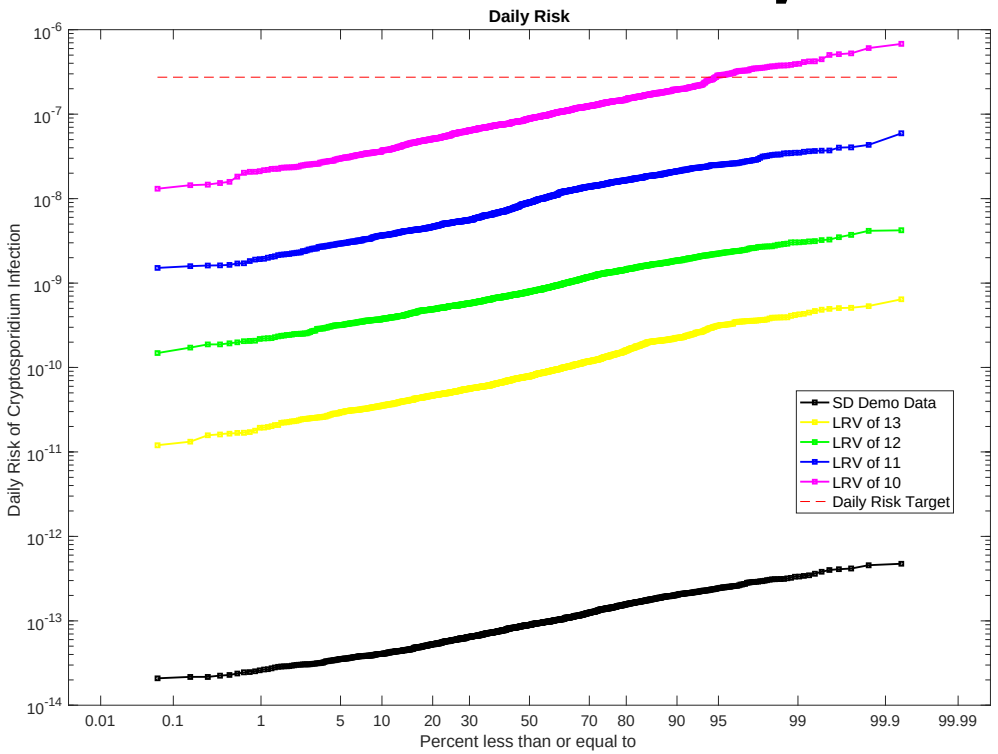
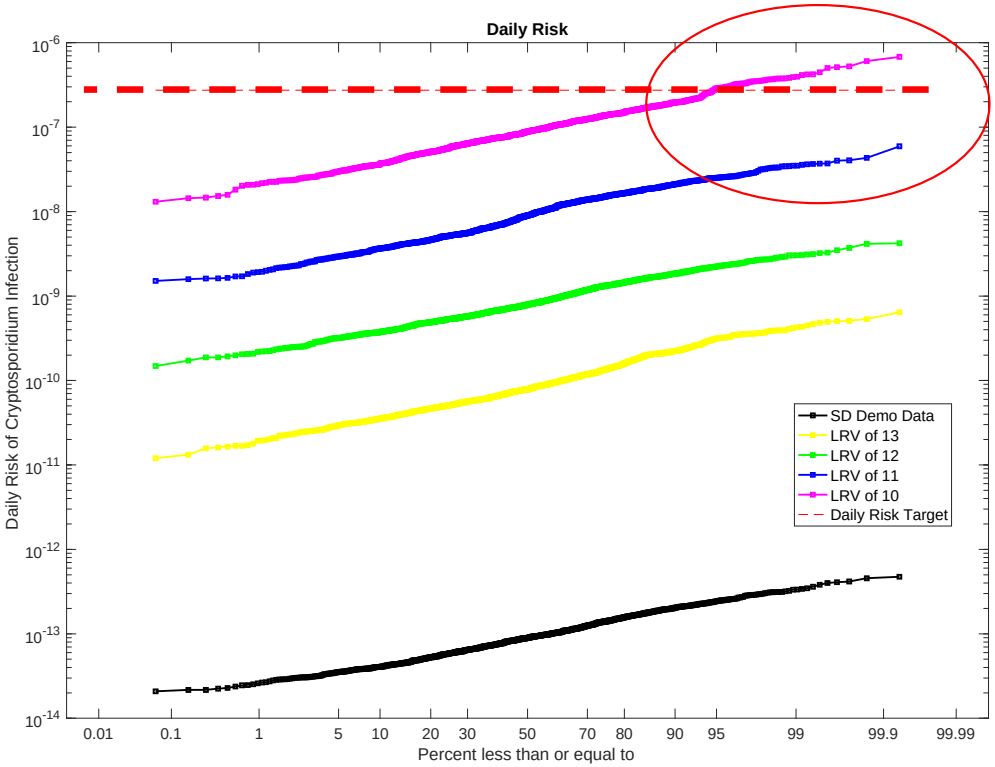




- Lower redundancy causes upward shifts in risk

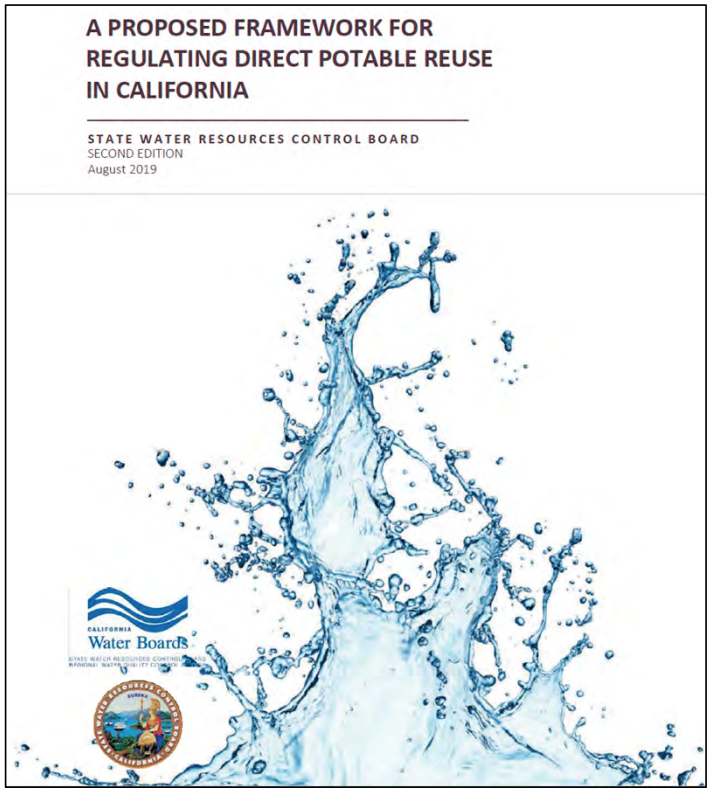
RELIABILITY IMPACTED BY TREATMENT PROVIDED

- Different degrees of compliance can be achieved by shifting the level of treatment provided
  - 10 LRV meets goal 95% of time
  - 11 LRV provides >99.9% compliance

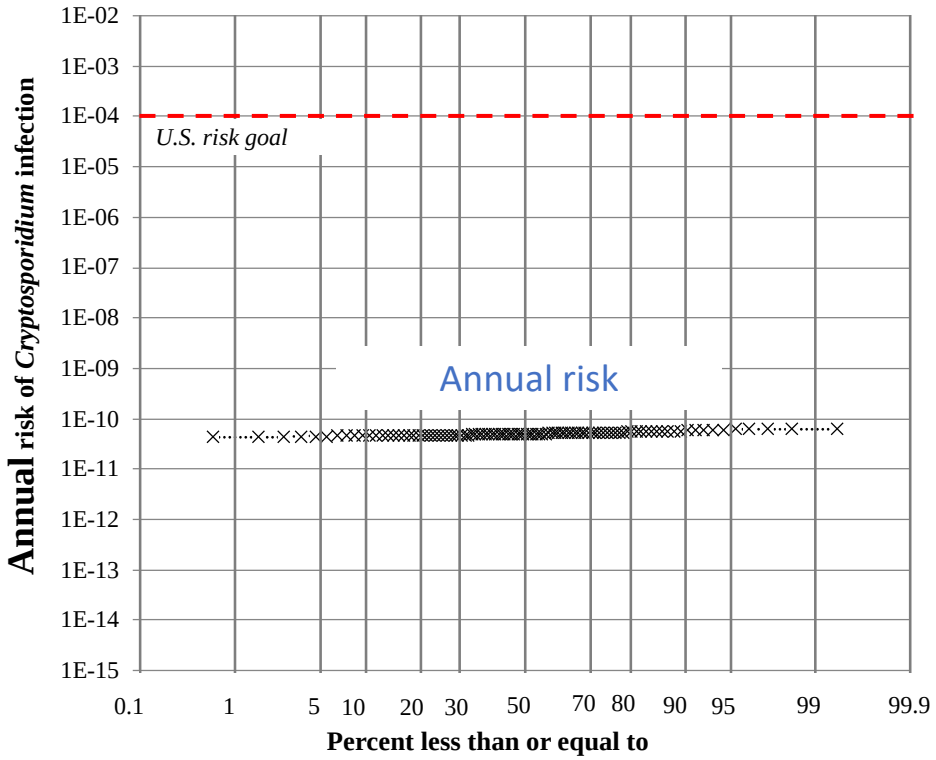


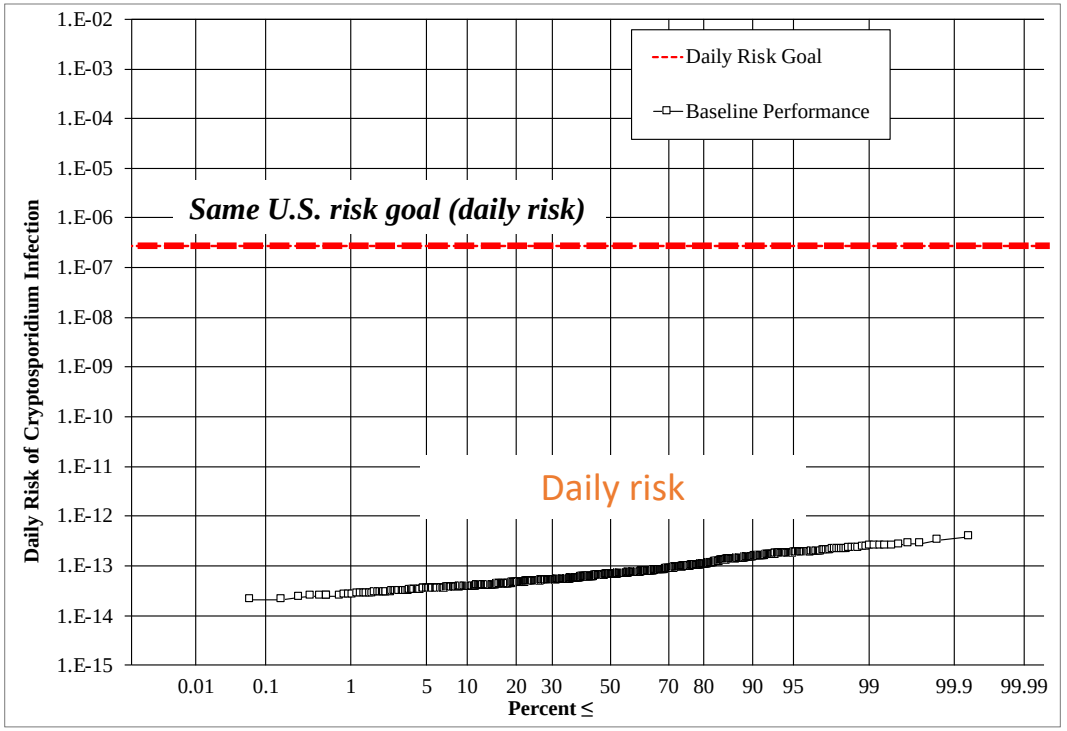
ANNUAL RISK VERSUS DAILY RISK

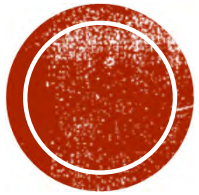
- *Rather than allow water microbial quality and risk of infection to fluctuate significantly and meet the risk objective on an annual average, the treatment scheme is expected to be regulated to provide consistently safe water by imposing a daily risk objective that would not exceed* ***$2.7x10^{-7}$ per day****.*



ANNUAL RISK VERSUS DAILY RISK



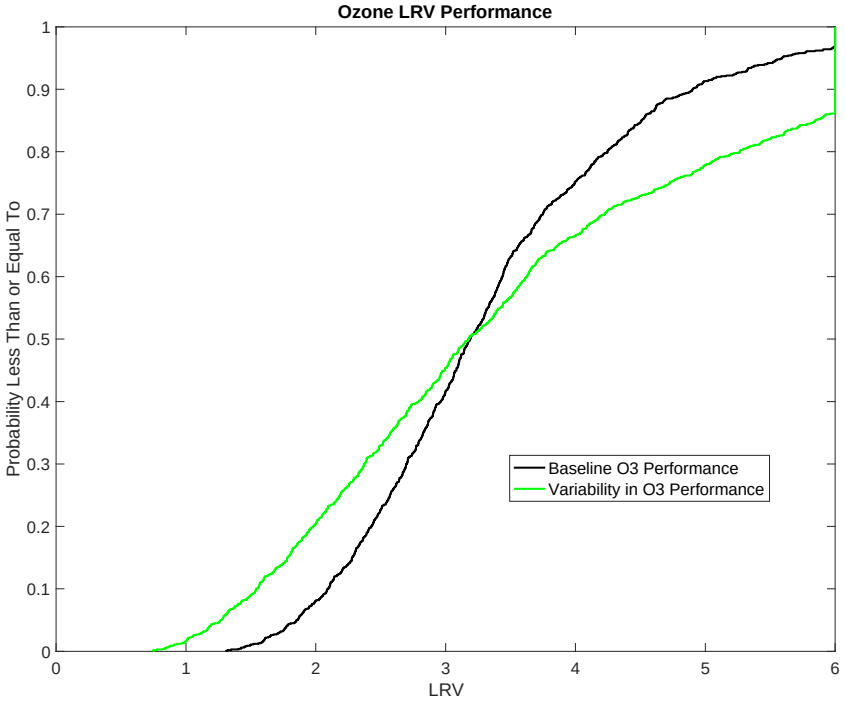




WHAT ELSE INFLUENCES THE RISK CURVES?

PERFORMANCE VARIABILITY IMPACTS RISK CURVES

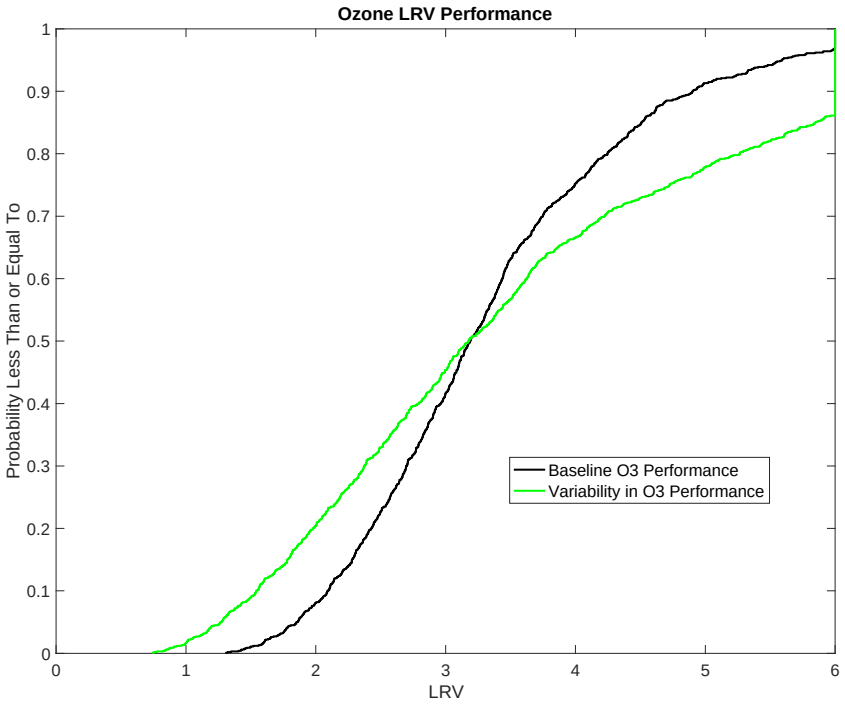
- If ozone performs less consistently…



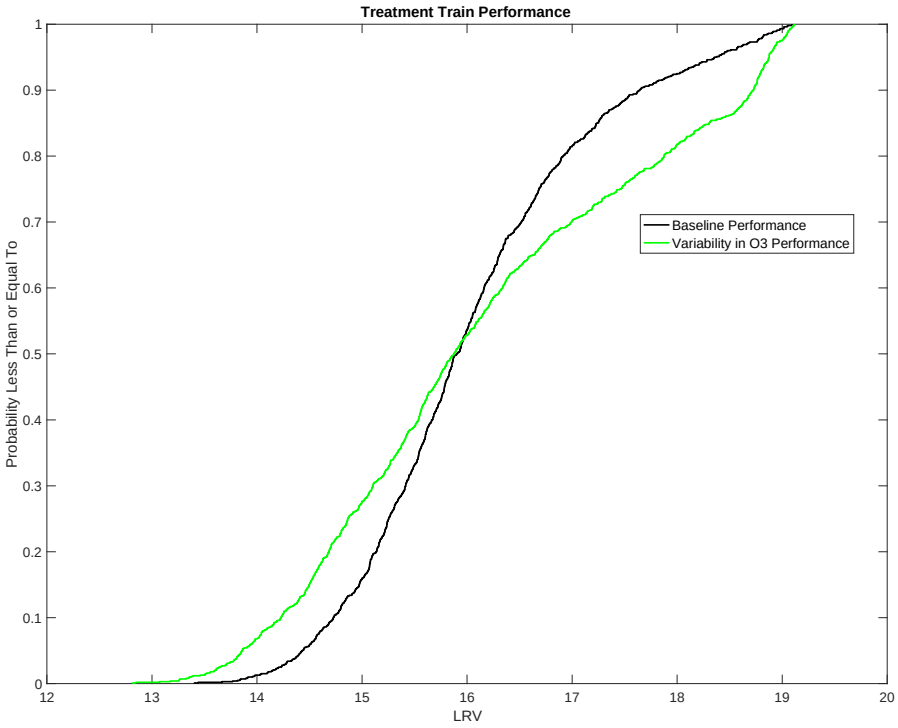
Ozone Unit Process Performance

PERFORMANCE VARIABILITY IMPACTS RISK CURVES

- If ozone performs less consistently…



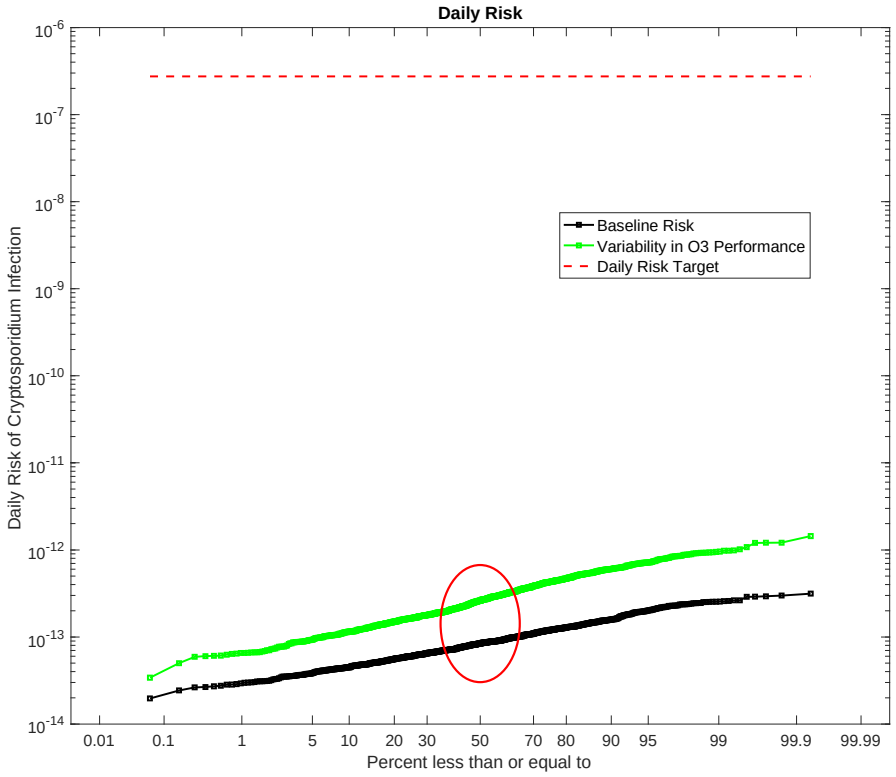
Ozone Unit Process Performance



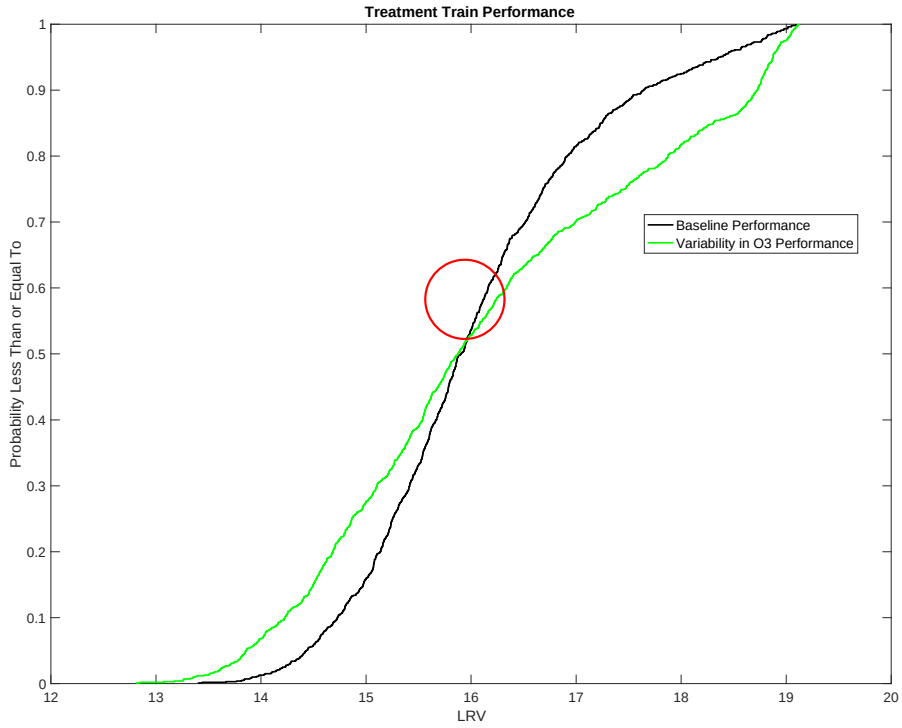
Treatment Train Performance

- …the overall treatment train shows greater variability…

PERFORMANCE VARIABILITY IMPACTS RISK CURVES

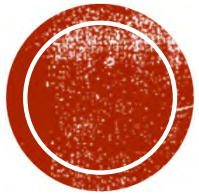


Ozone Unit Process Performance



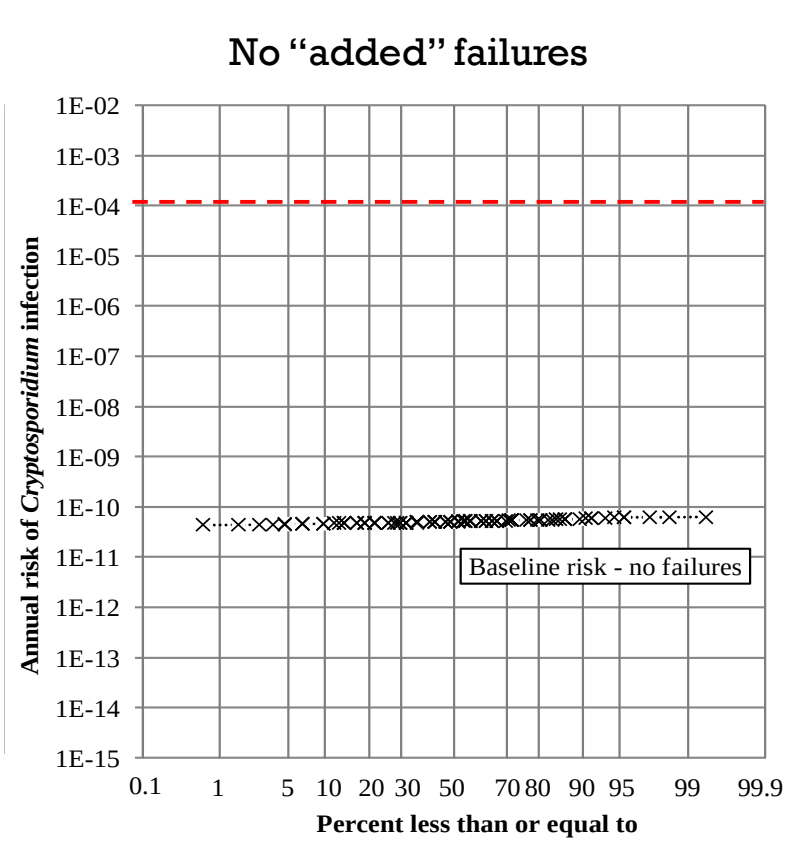
Treatment Train Performance

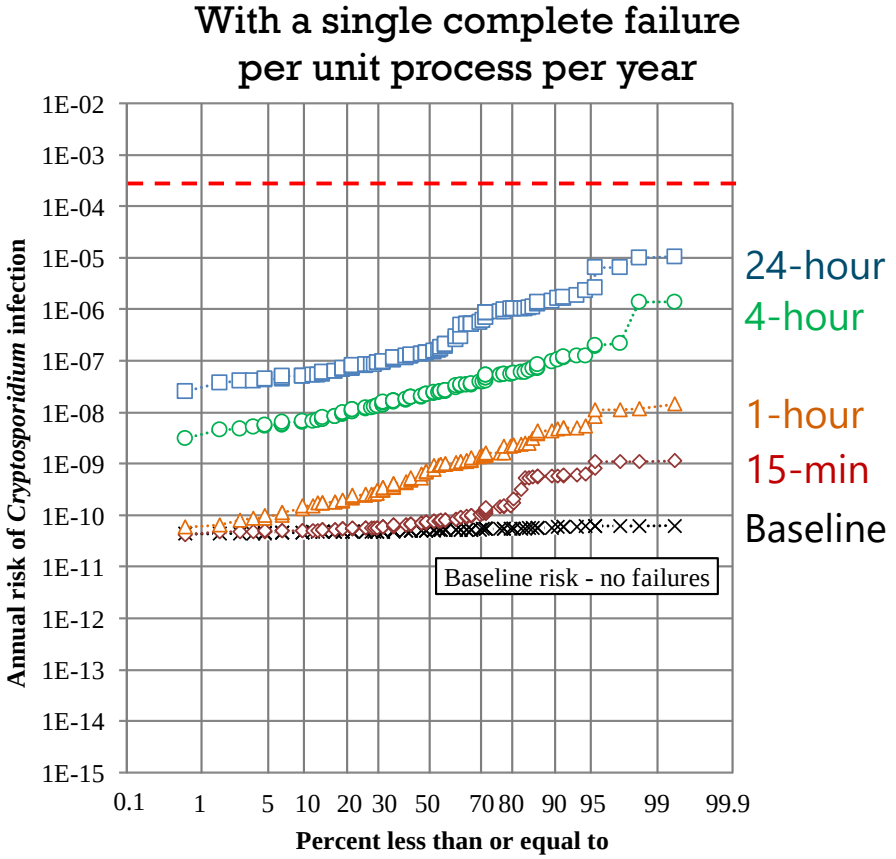
- …and greater performance variability leads to higher risk profiles



WHAT ABOUT OFF-SPEC WATER AND FAILURES?

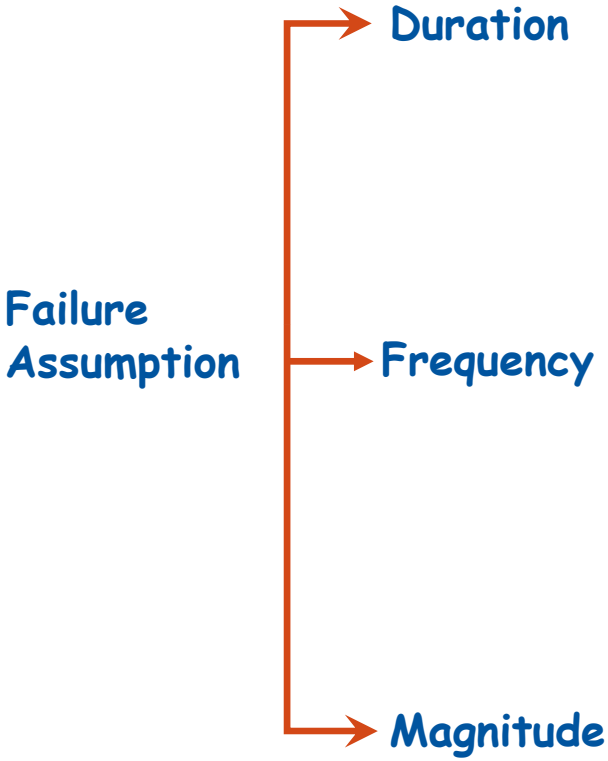
RARE FAILURES CAN DRIVE RISK



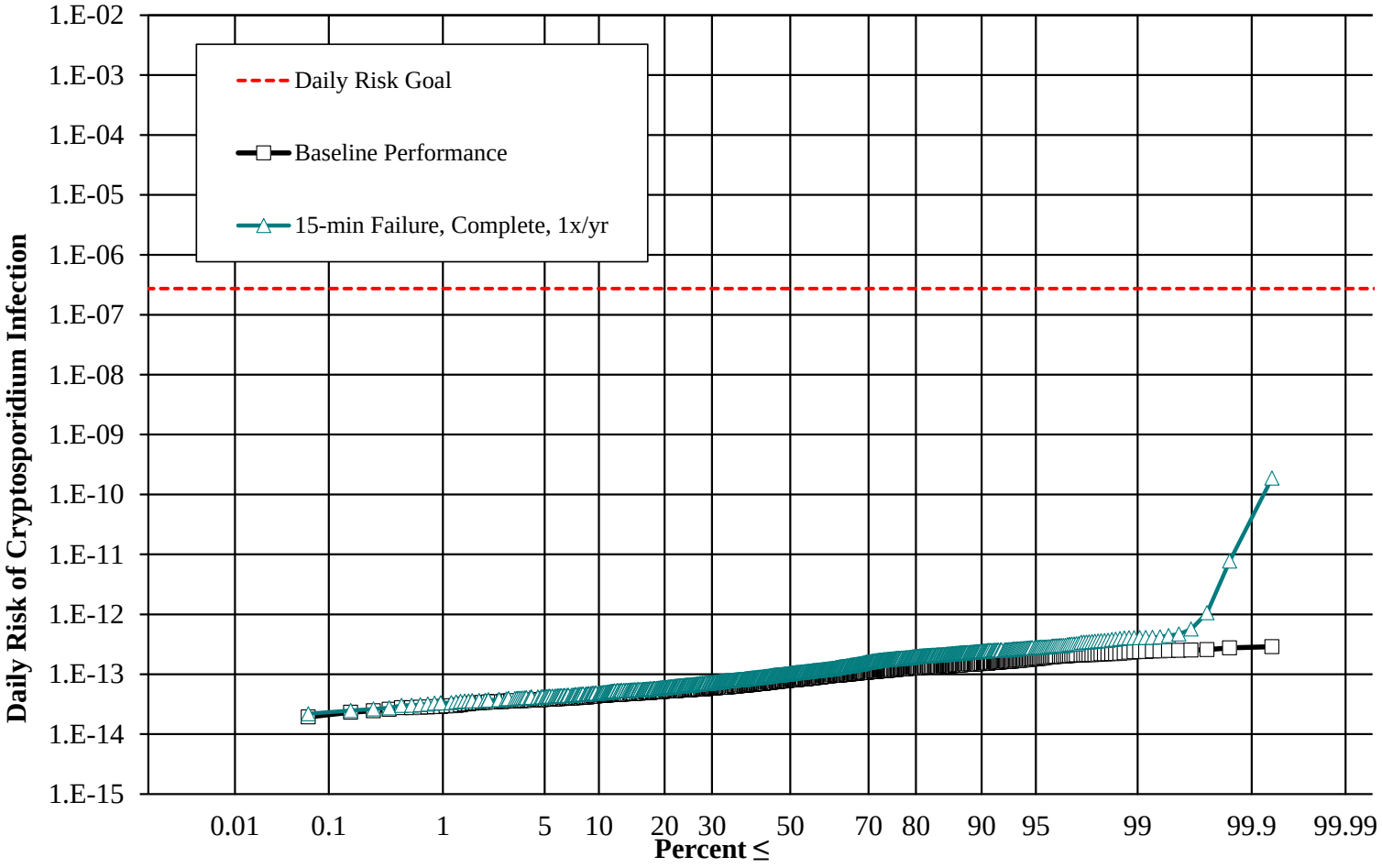


DPR QMRA from WRRF 14-12

FAILURE ASSUMPTIONS

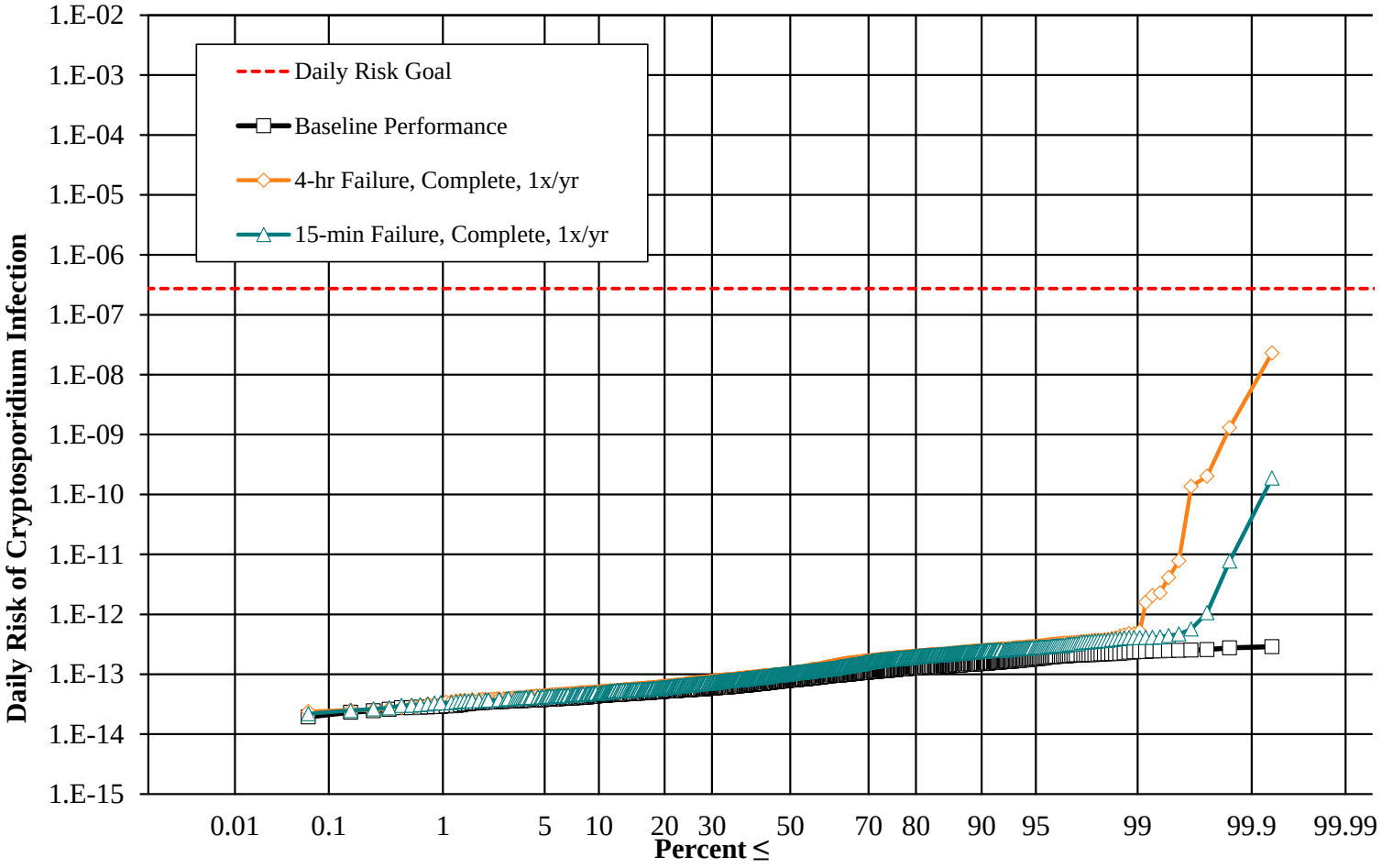


FAILURE DURATION



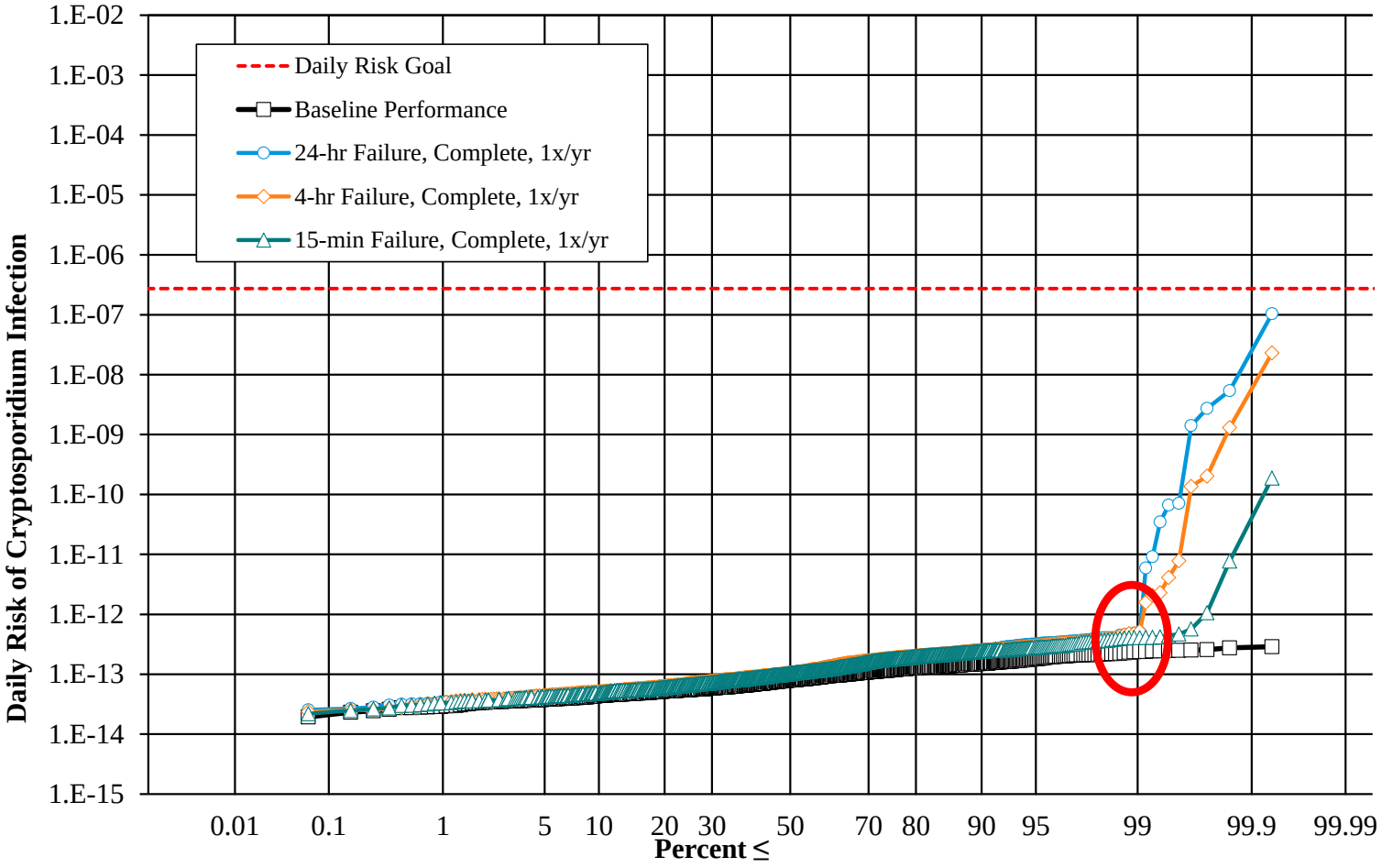
Longer failures lead to higher risk levels…

FAILURE DURATION



Longer failures lead to higher risk levels…

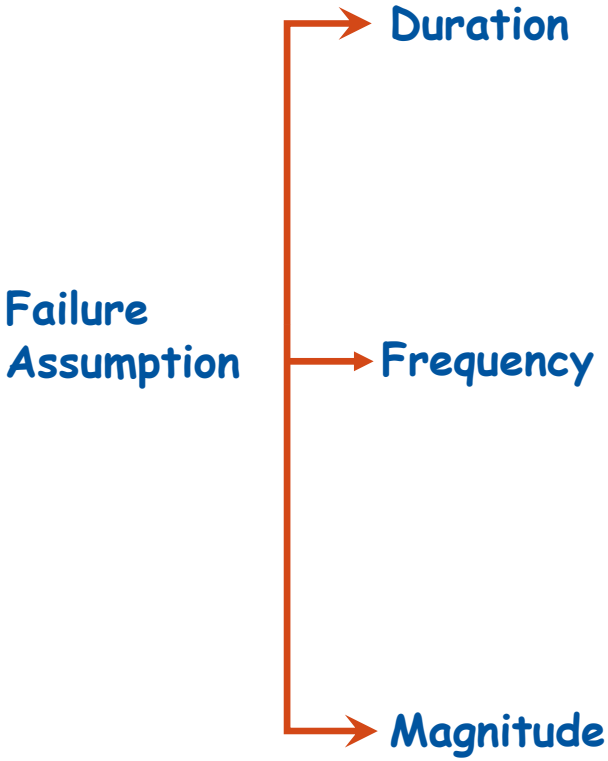
FAILURE DURATION



Longer failures lead to higher risk levels…

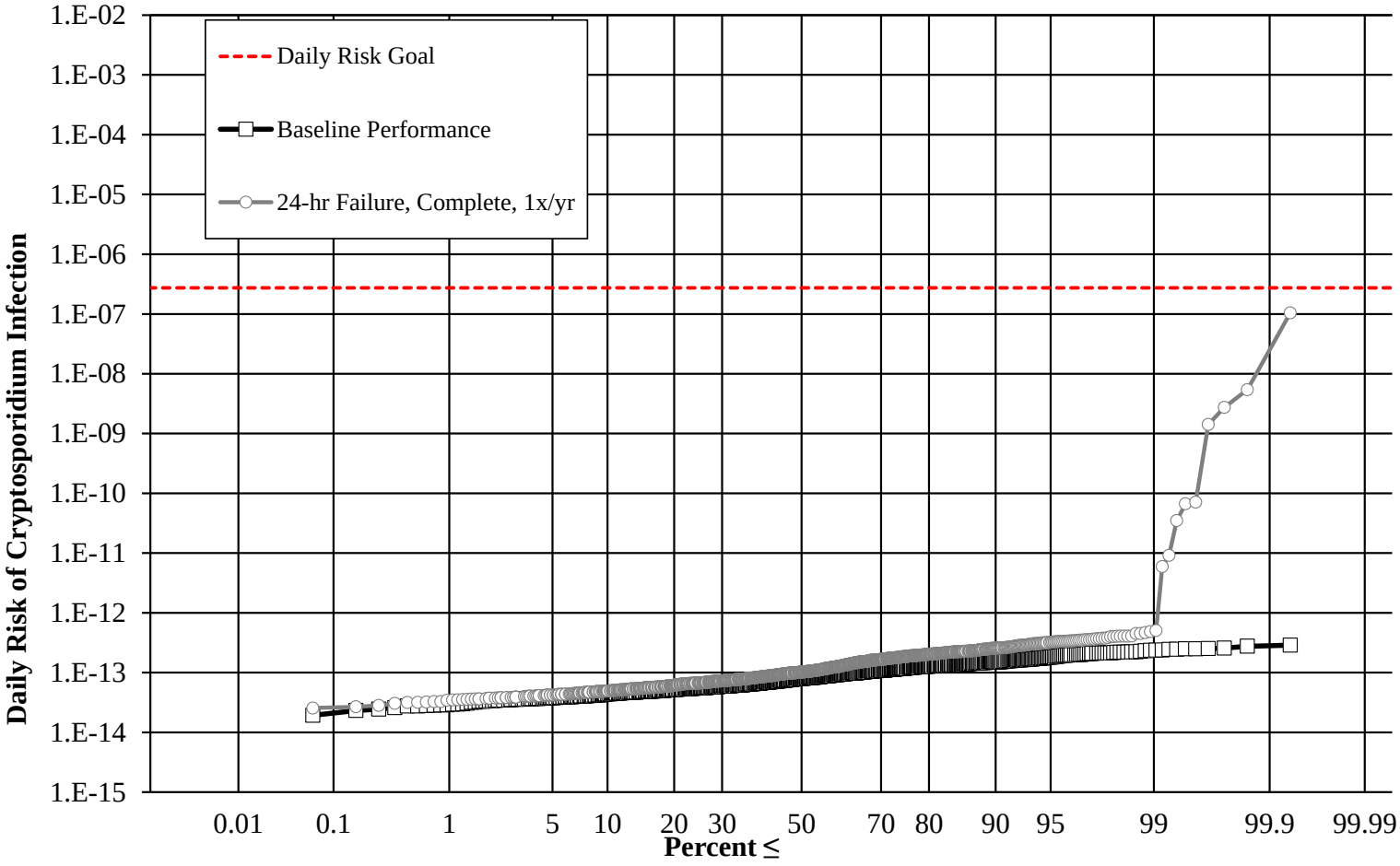
…but where the curve bends upward is the same for a given frequency of failure

FAILURE ASSUMPTIONS



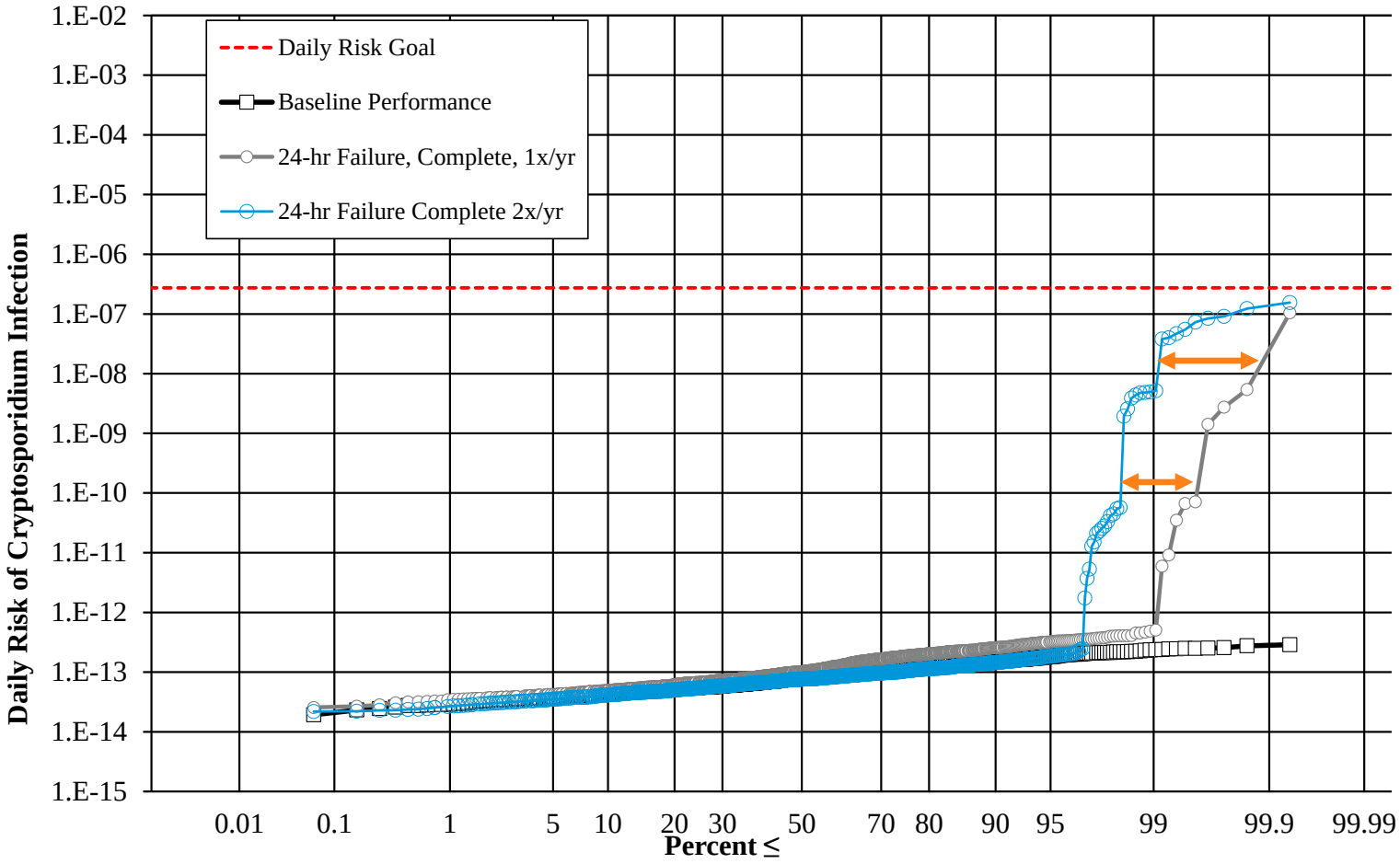
How does failure frequency impact risk?

FAILURE FREQUENCY



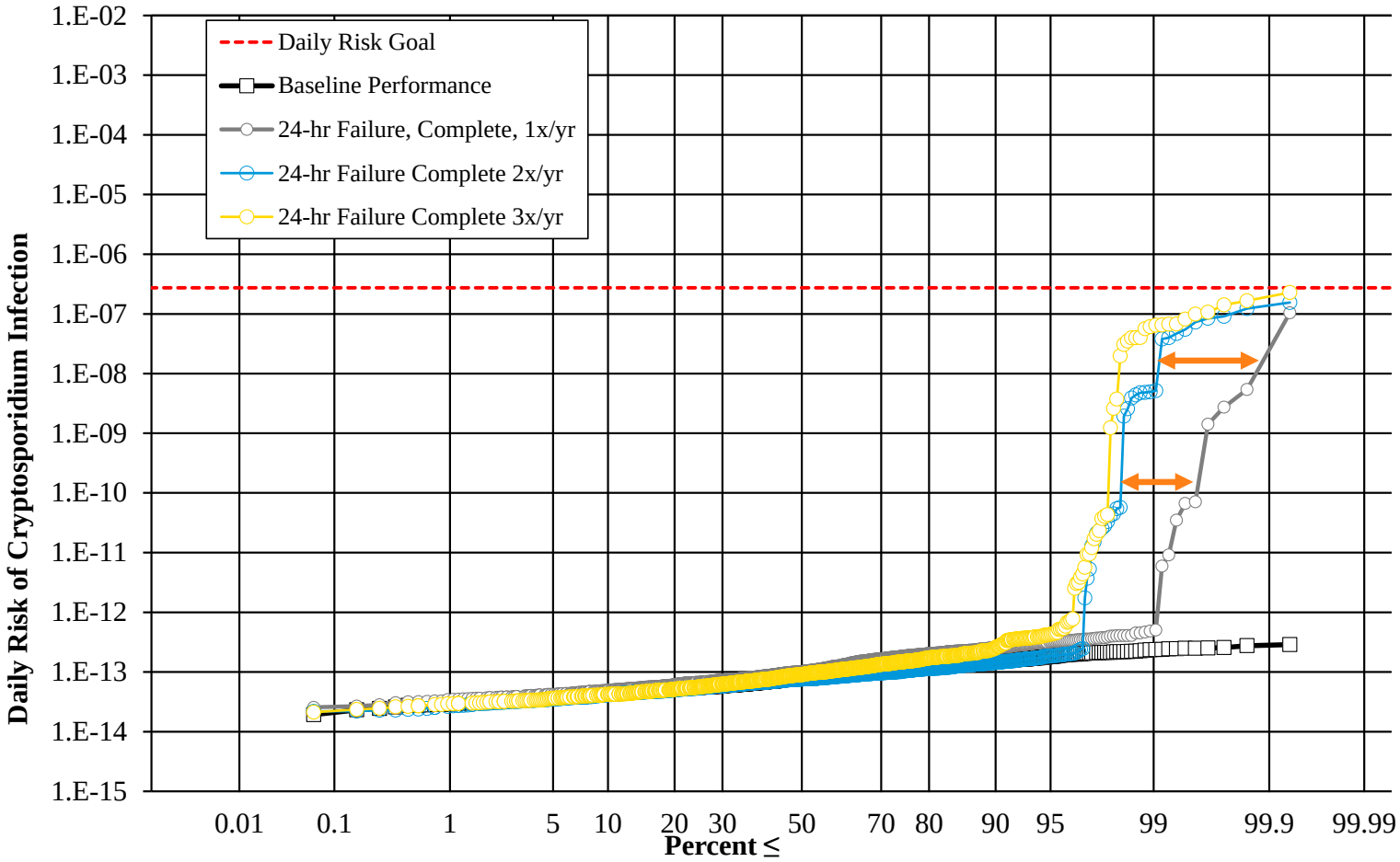
Higher <u>frequency</u> failures lead to <u>leftward</u> shifts in the risk profile

FAILURE FREQUENCY



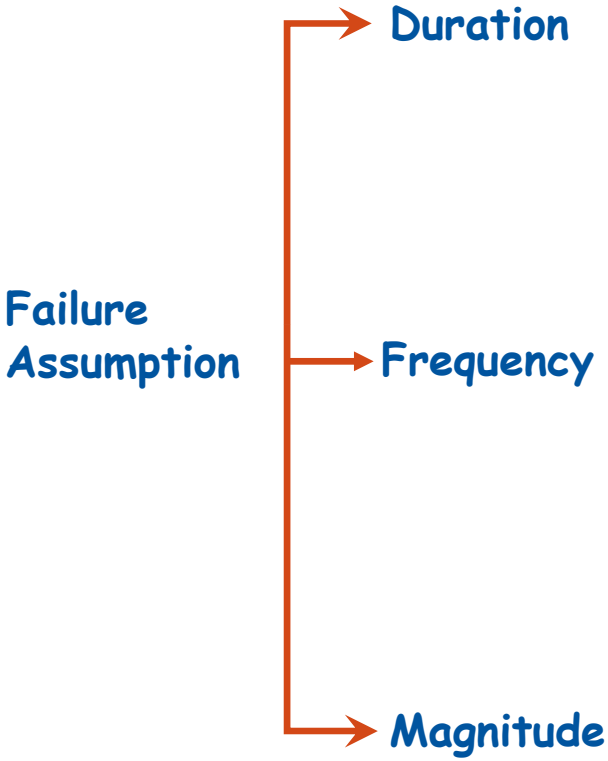
Higher frequency failures lead to leftward shifts in the risk profile

FAILURE FREQUENCY



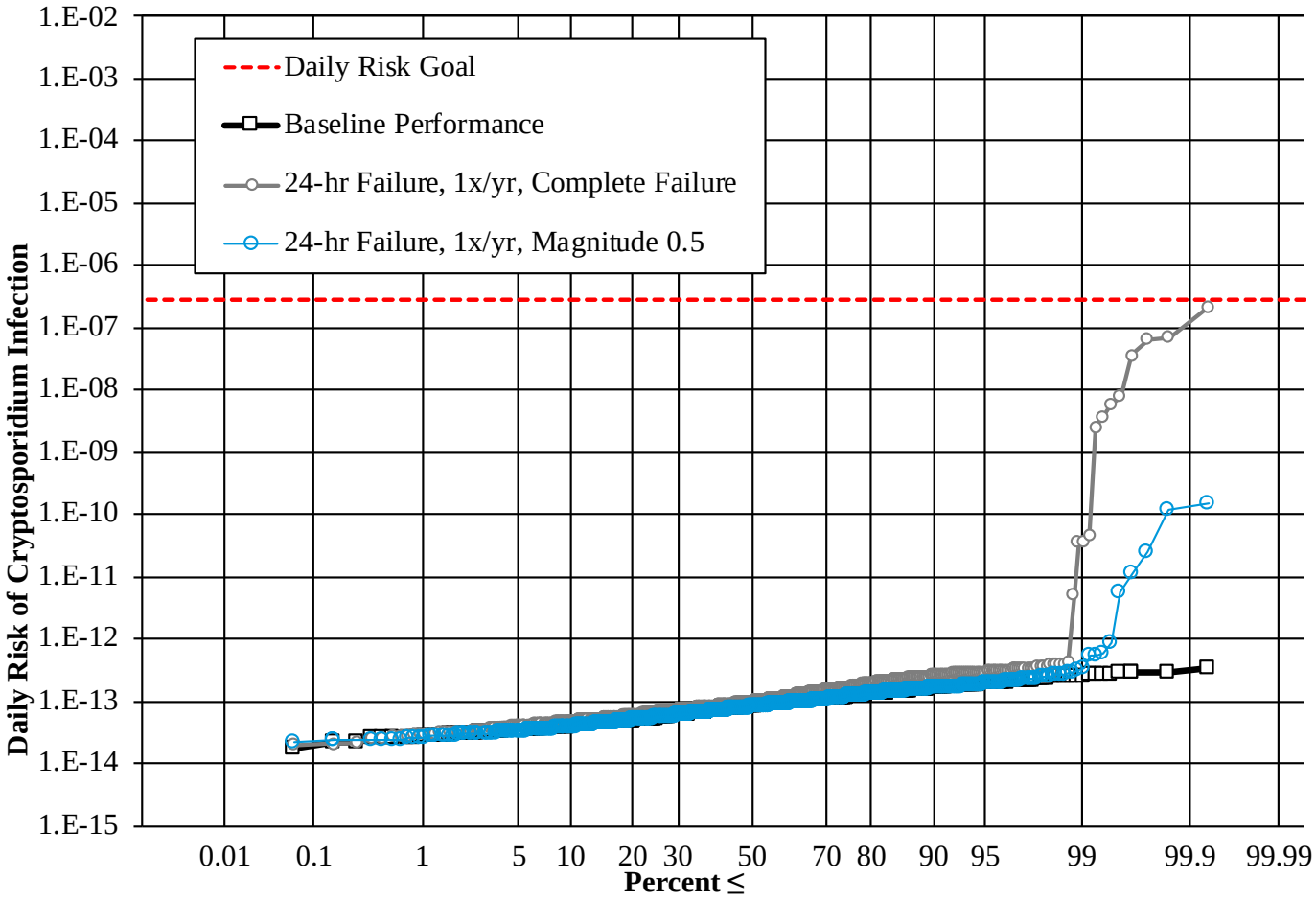
Higher frequency failures lead to leftward shifts in the risk profile

FAILURE ASSUMPTIONS



How does failure magnitude impact risk?

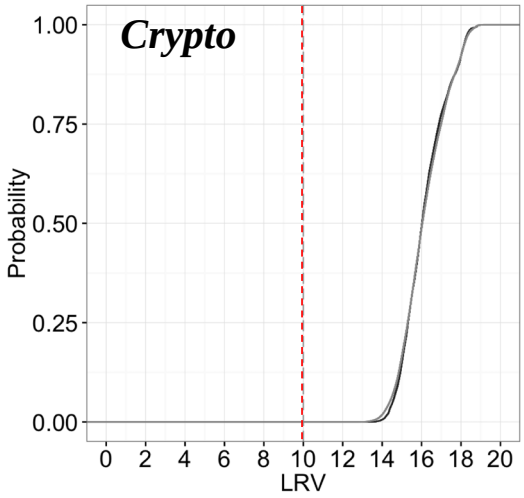
FAILURE MAGNITUDE



Higher magnitudes of failure lead to upward shifts in the risk curve

USE DPRisk TO EVALUATE DPR CRITERIA

Performance Evaluation



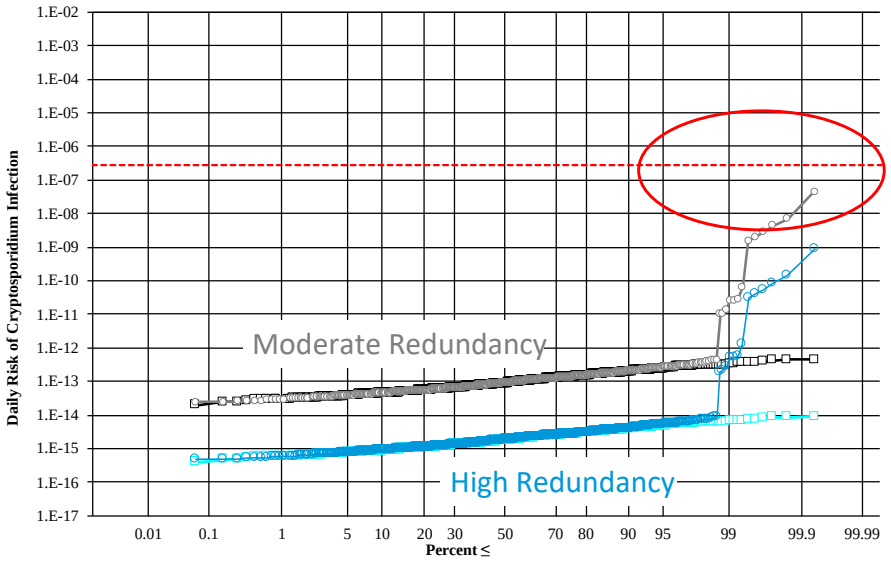
Treatment Requirements

12 / 10 / 10

13 / 11 / 11

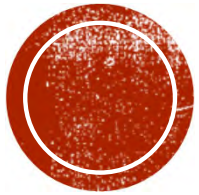
14 / 12 / 12

QMRA



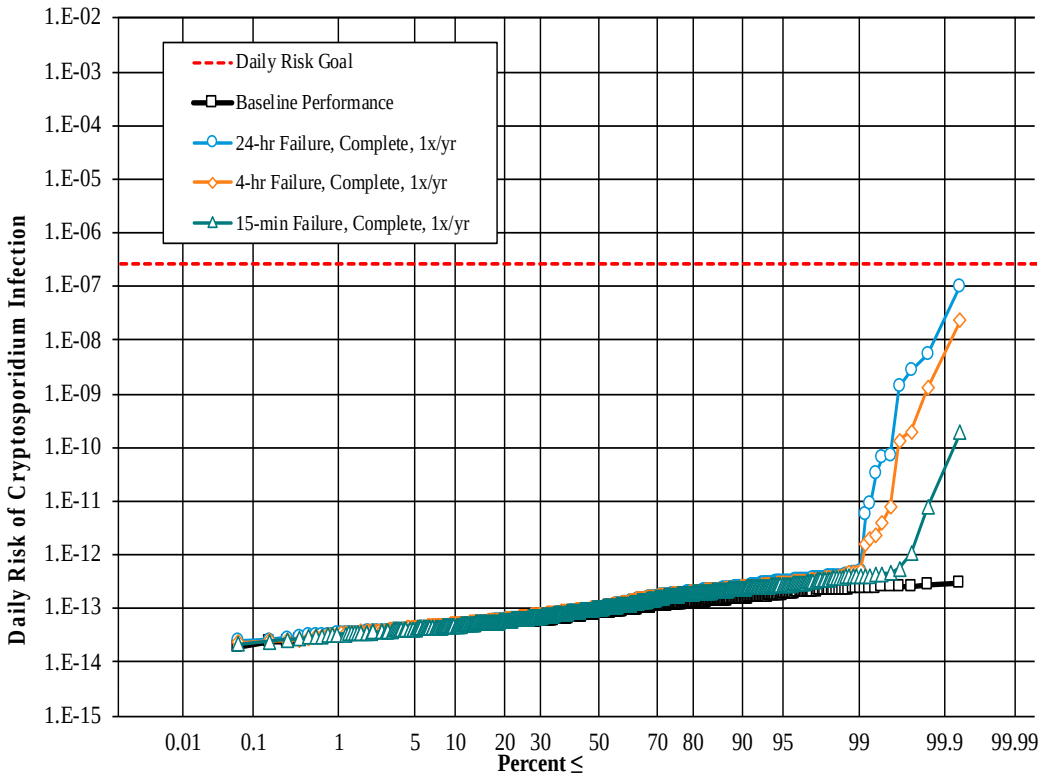
If we shift the treatment requirements….

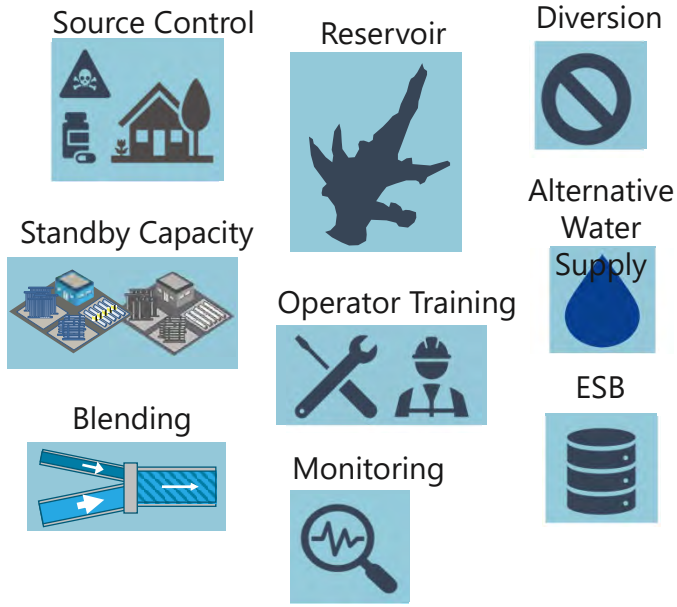
…what is the impact on public health?



MANAGEMENT BARRIERS

NON-TREATMENT BARRIERS AND RISK





These project elements may also mitigate failures and help control risk

BENEFITS OF STORAGE BUFFERS

30-day Reservoir

Improves Water Quality

Mixing of off-spec water with on-spec water dilutes contaminants

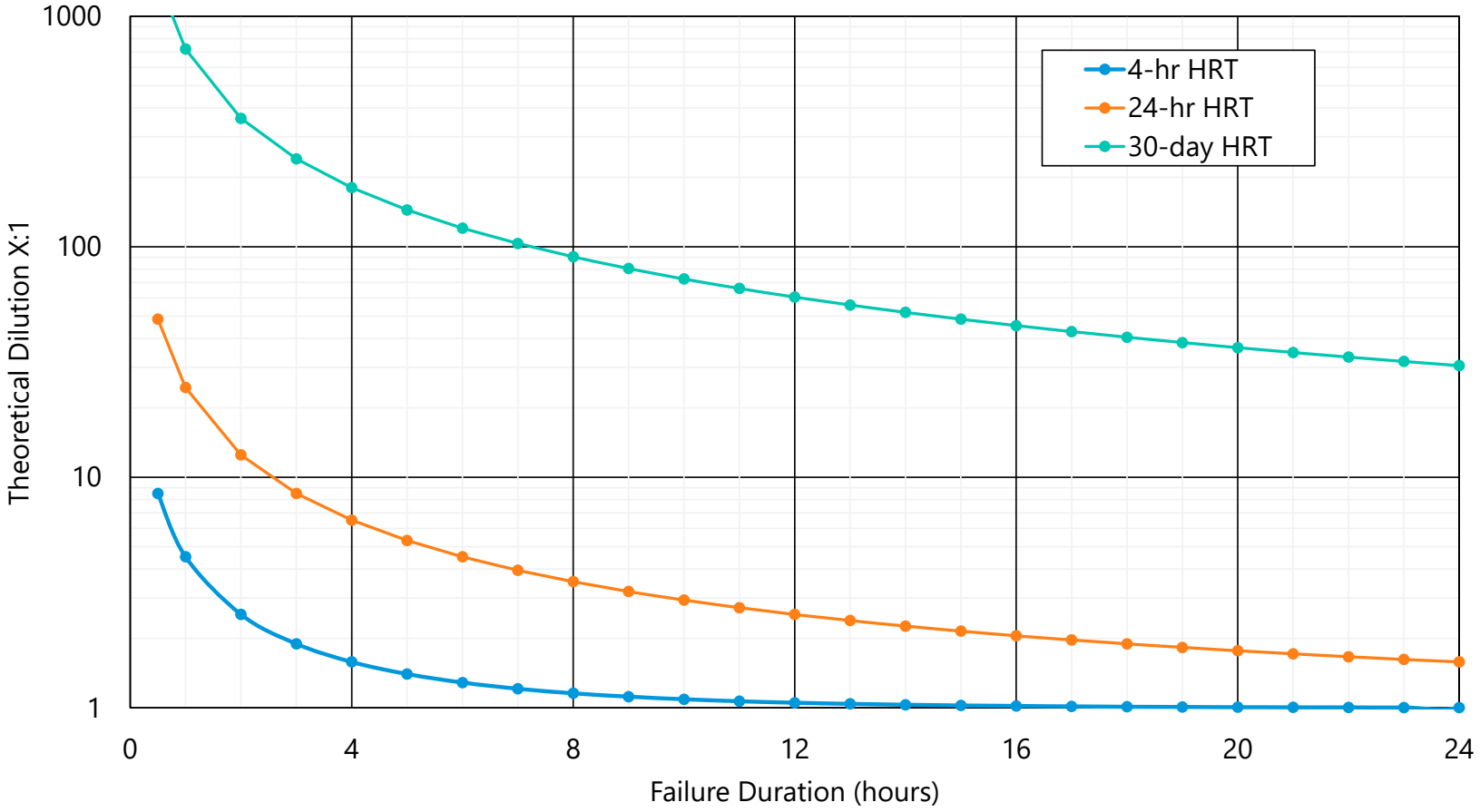
Prevents Off-Spec Water Distribution

- Provides time to respond
- Allows for decoupling

24-hr ESB

4-hr ESB

ATTENUATION OF PEAKS



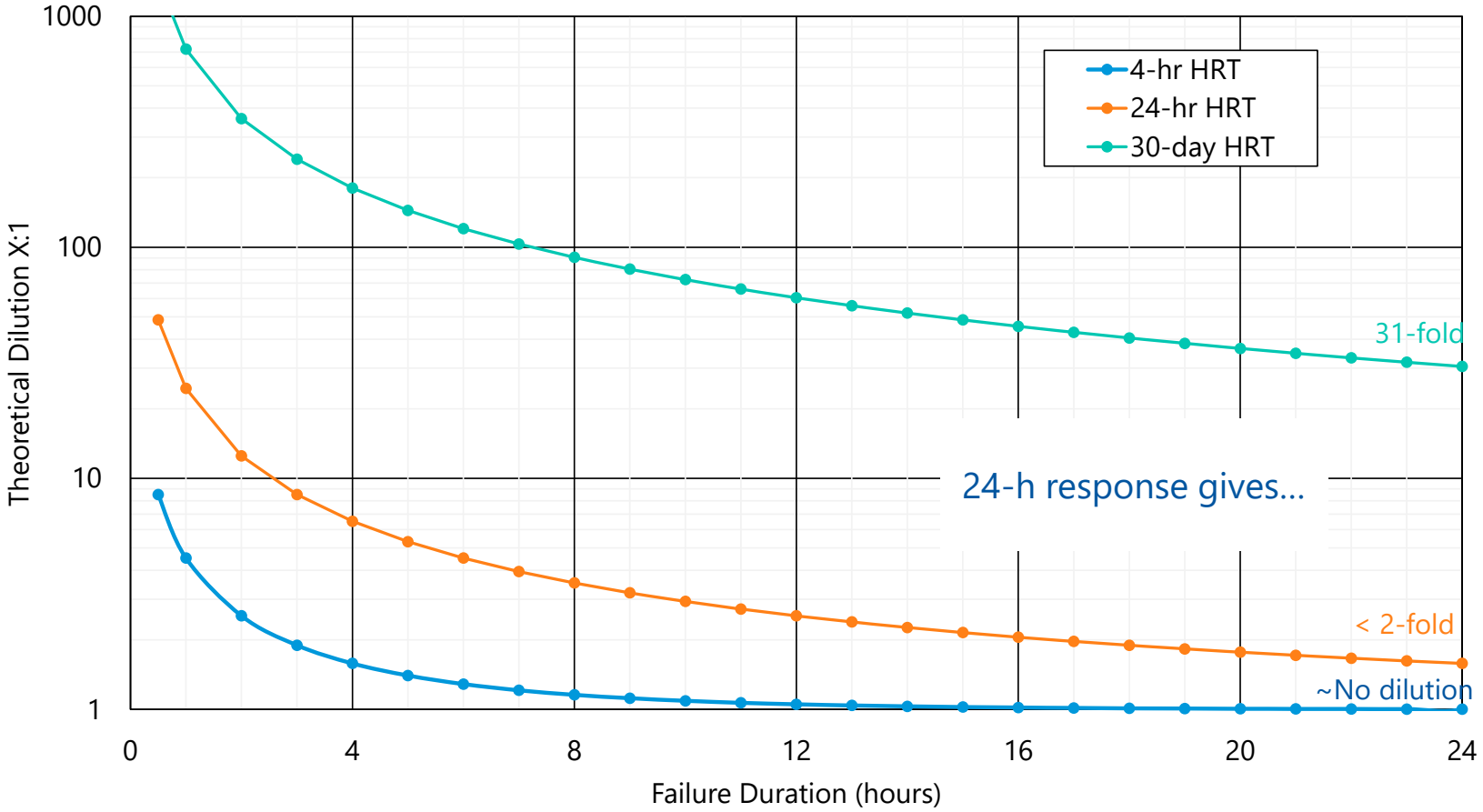
30-day Reservoir

24-hr ESB

4-hr ESB

*Assumes all storage behaves like CSTR

ATTENUATION OF PEAKS



30-day Reservoir

24-hr ESB

4-hr ESB

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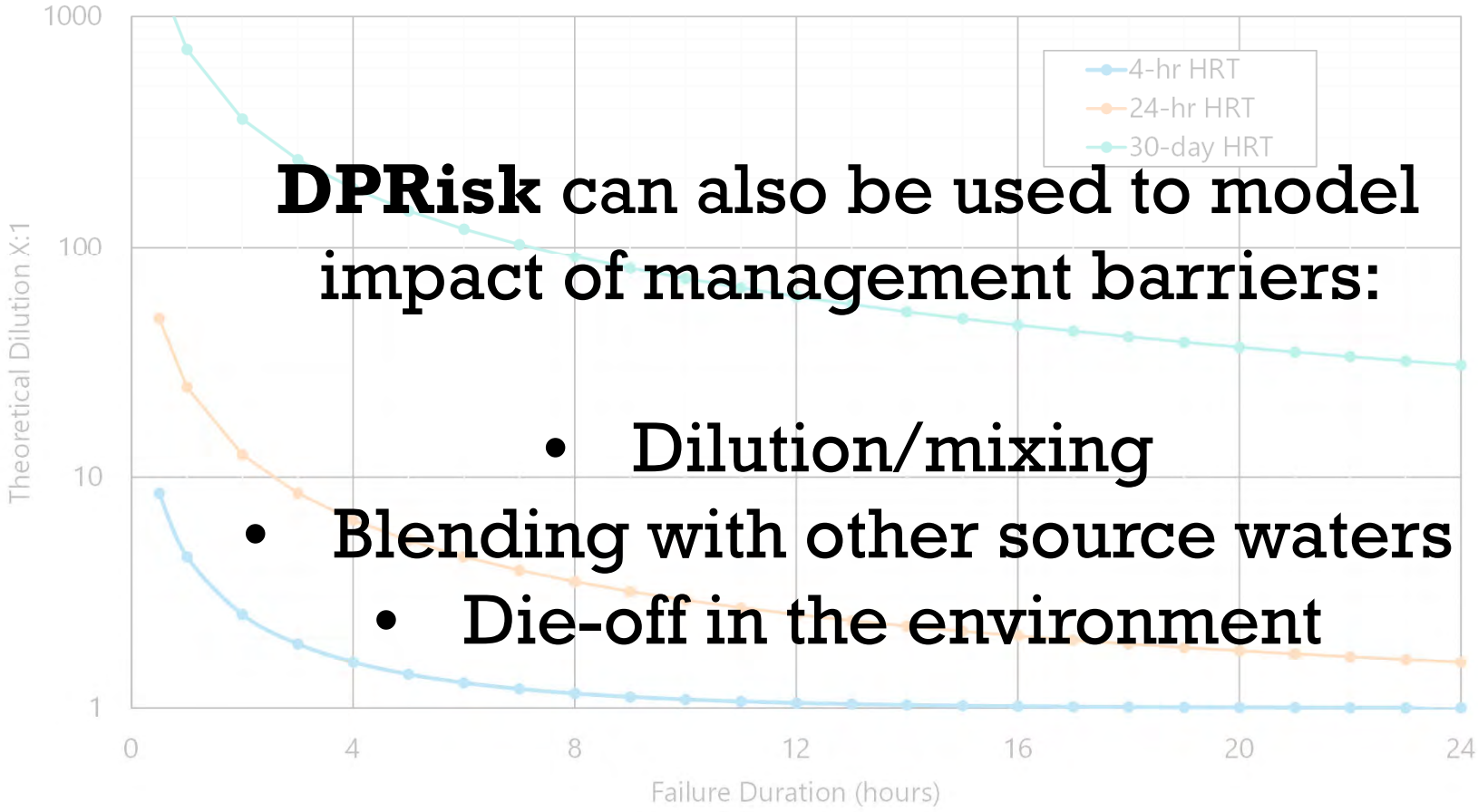
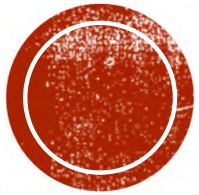
ATTENUATION OF PEAKS

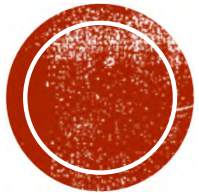


DPRisk can also be used to model impact of management barriers:

- Dilution/mixing
- Blending with other source waters
- Die-off in the environment

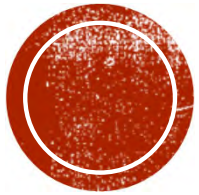


Q&A – 10 MIN



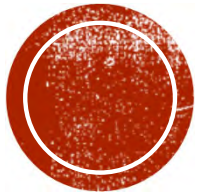
LIVE DEMO: DPRisk TOOL

Edmund Seto



CASE STUDY LIVE DEMO

Daniel Gerrity



NEXT STEPS

Brian Pecson

Adam Olivieri

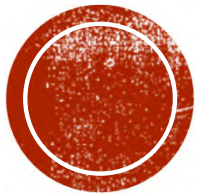
NEXT STEPS

PRESENT

- Webinar to Introduce PATTP/QMRA Tools
- Internal QA/QC of PATTP/QMRA with Research Team and Technical Working Group

FUTURE

- Distribute Guidance Manual and provide link to DPRisk Tools: **July 24, 2020**
- "Hands-on" training with PATTP/QMRA Tools: **August 4, 2020**
- Receive feedback from State Water Board on Guidance Document and tools: **August 25, 2020**
- Incorporate raw wastewater concentration data from DPR-2: **Fall/Winter, 2020**



Q&A

DPRisk Tool

Specifying Probabilistic Treatment Train Performance and Quantitative Microbial Risk Assessment Scenarios in the DPRisk Tool

Edmund Seto, PhD

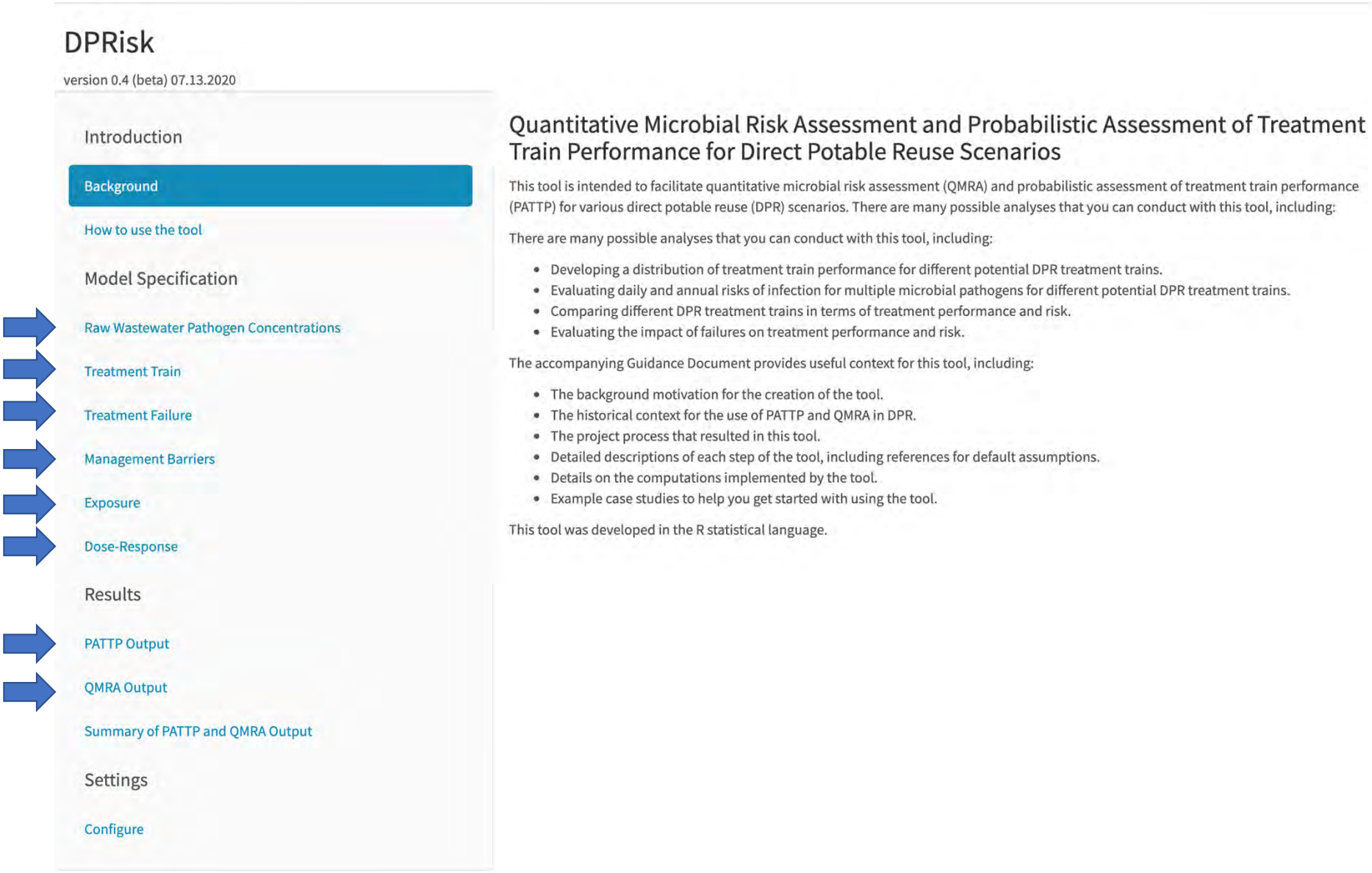
Associate Professor

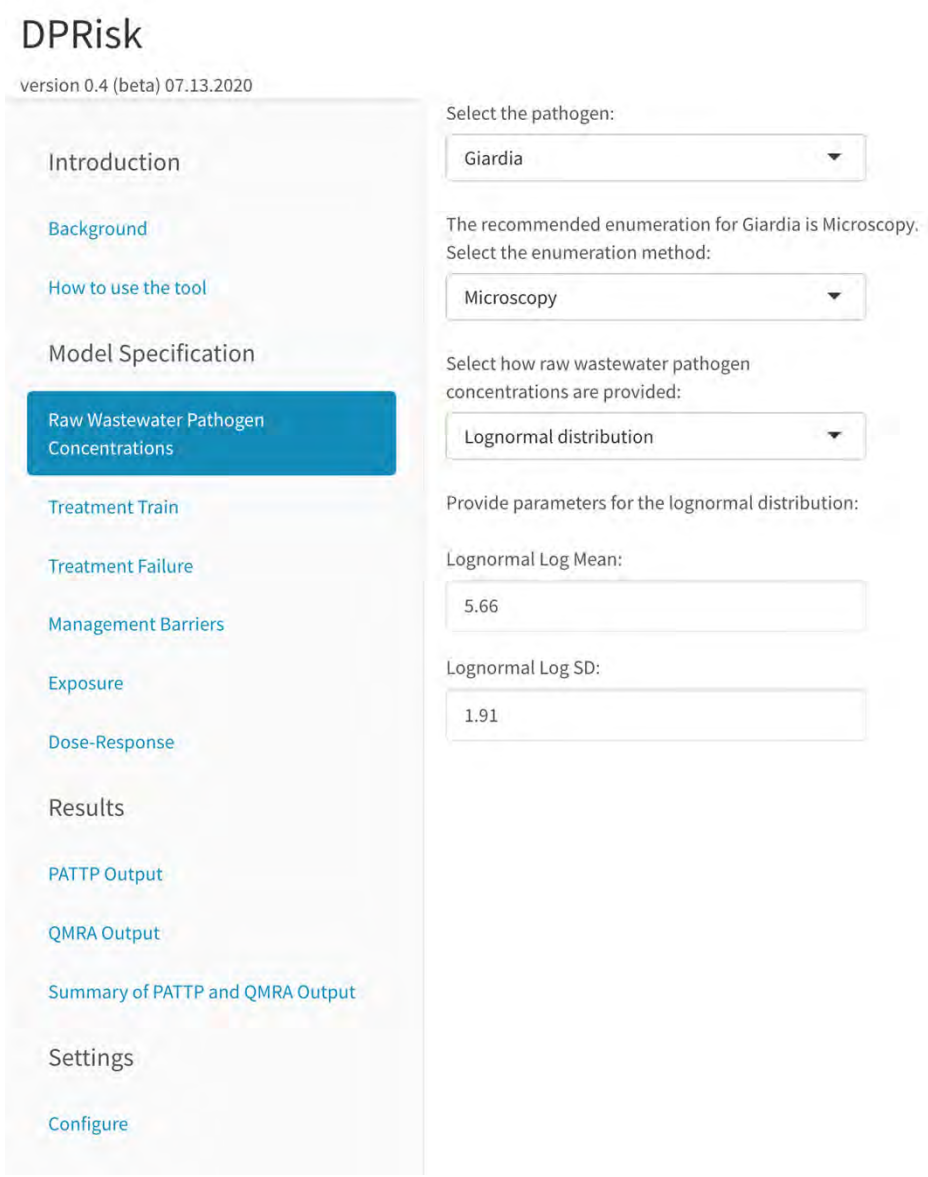
Environmental & Occupational Health Sciences

Background on Tool Development

- Goals:
  - Capable of analyses of a variety of PATTP and QMRA scenarios
  - Ease of Use, providing reasonable defaults for various parameters
  - Flexibility to incorporate a variety of user-specified inputs
  - Powerful enough to consider complex treatment failure scenarios

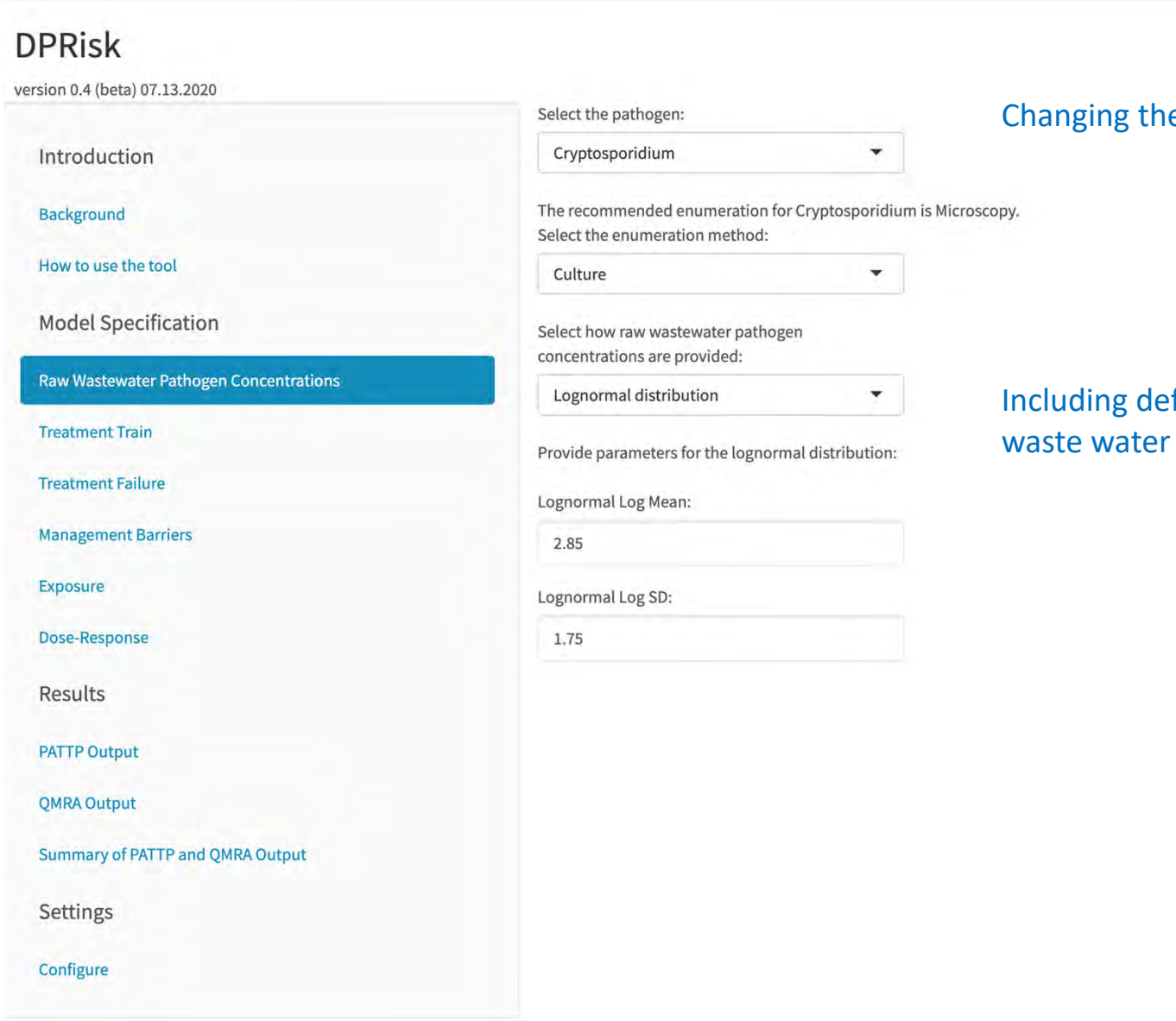
  - Based on R Shiny.
  - Can be run locally on computer, or hosted on a server and run in a web-browser.


DPRisk
version 0.4 (beta) 07.13.2020
Introduction
Background
How to use the tool
Model Specification
Raw Wastewater Pathogen Concentrations
Treatment Train
Treatment Failure
Management Barriers
Exposure
Dose-Response
Results
PATTP Output
QMRA Output
Summary of PATTP and QMRA Output
Settings
Configure
Quantitative Microbial Risk Assessment and Probabilistic Assessment of Treatment Train Performance for Direct Potable Reuse Scenarios
This tool is intended to facilitate quantitative microbial risk assessment (QMRA) and probabilistic assessment of treatment train performance (PATTP) for various direct potable reuse (DPR) scenarios. There are many possible analyses that you can conduct with this tool, including:
There are many possible analyses that you can conduct with this tool, including:
Developing a distribution of treatment train performance for different potential DPR treatment trains.
Evaluating daily and annual risks of infection for multiple microbial pathogens for different potential DPR treatment trains.
Comparing different DPR treatment trains in terms of treatment performance and risk.
Evaluating the impact of failures on treatment performance and risk.
The accompanying Guidance Document provides useful context for this tool, including:
The background motivation for the creation of the tool.
The historical context for the use of PATTP and QMRA in DPR.
The project process that resulted in this tool.
Detailed descriptions of each step of the tool, including references for default assumptions.
Details on the computations implemented by the tool.
Example case studies to help you get started with using the tool.
This tool was developed in the R statistical language.



The tool provides this recommendation based on the pathogen selected.

Including default distribution for raw waste water concentrations.



Changing the pathogen changes the defaults.

Including default distribution for raw waste water concentrations.

DPRisk

version 0.4 (beta) 07.13.2020

Introduction

Background

How to use the tool

Model Specification

Raw Wastewater Pathogen Concentrations

Treatment Train

Treatment Failure

Management Barriers

Exposure

Dose-Response

Results

PATTP Output

QMRA Output

Summary of PATTP and QMRA Output

Settings

Configure

Specify the log removal for the entire treatment train or for each process in the train.

A log removal with a point estimate of 0 indicates that the process is not used.

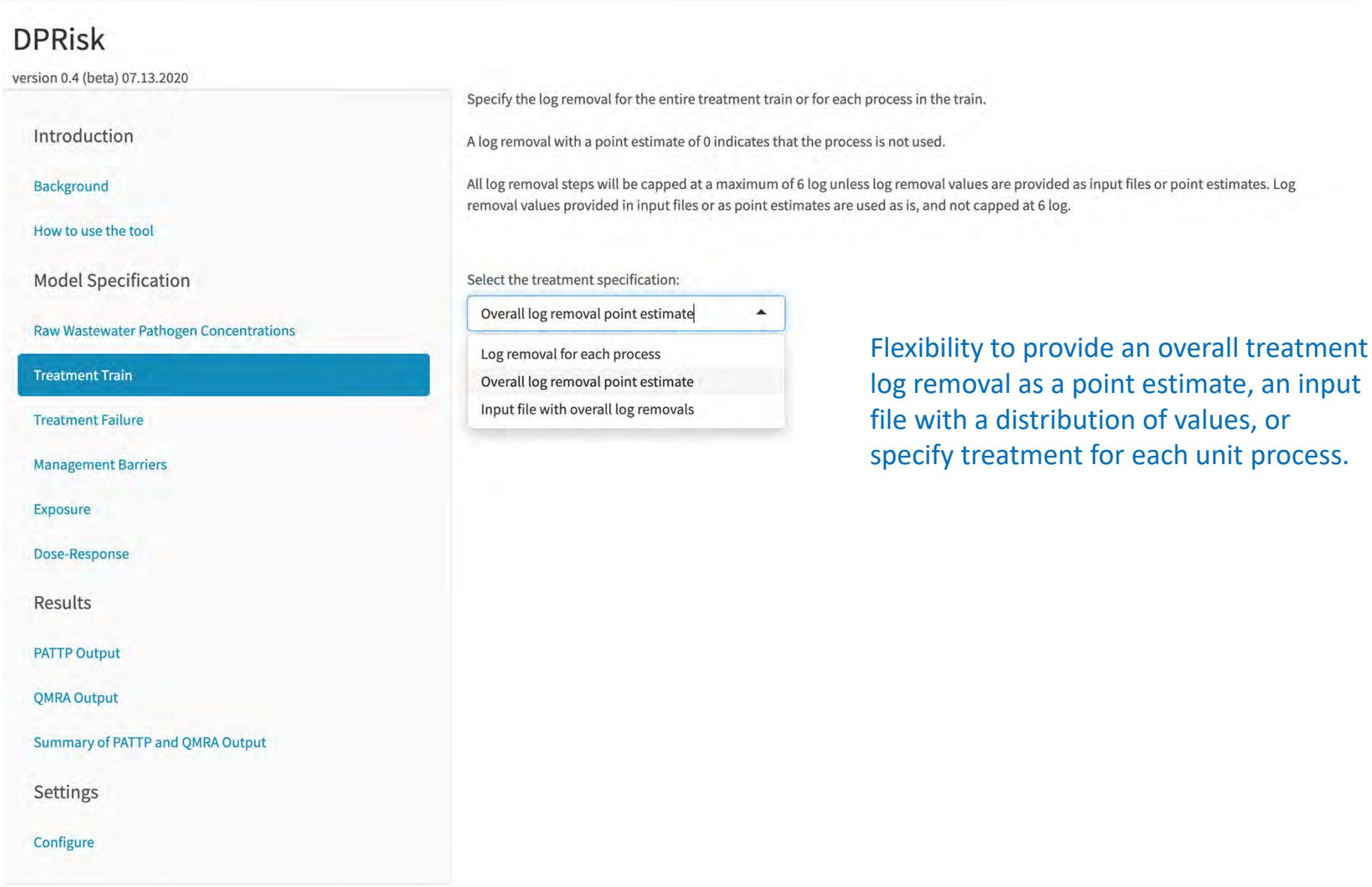
All log removal steps will be capped at a maximum of 6 log unless log removal values are provided as input files or point estimates. Log removal values provided in input files or as point estimates are used as is, and not capped at 6 log.

Select the treatment specification:

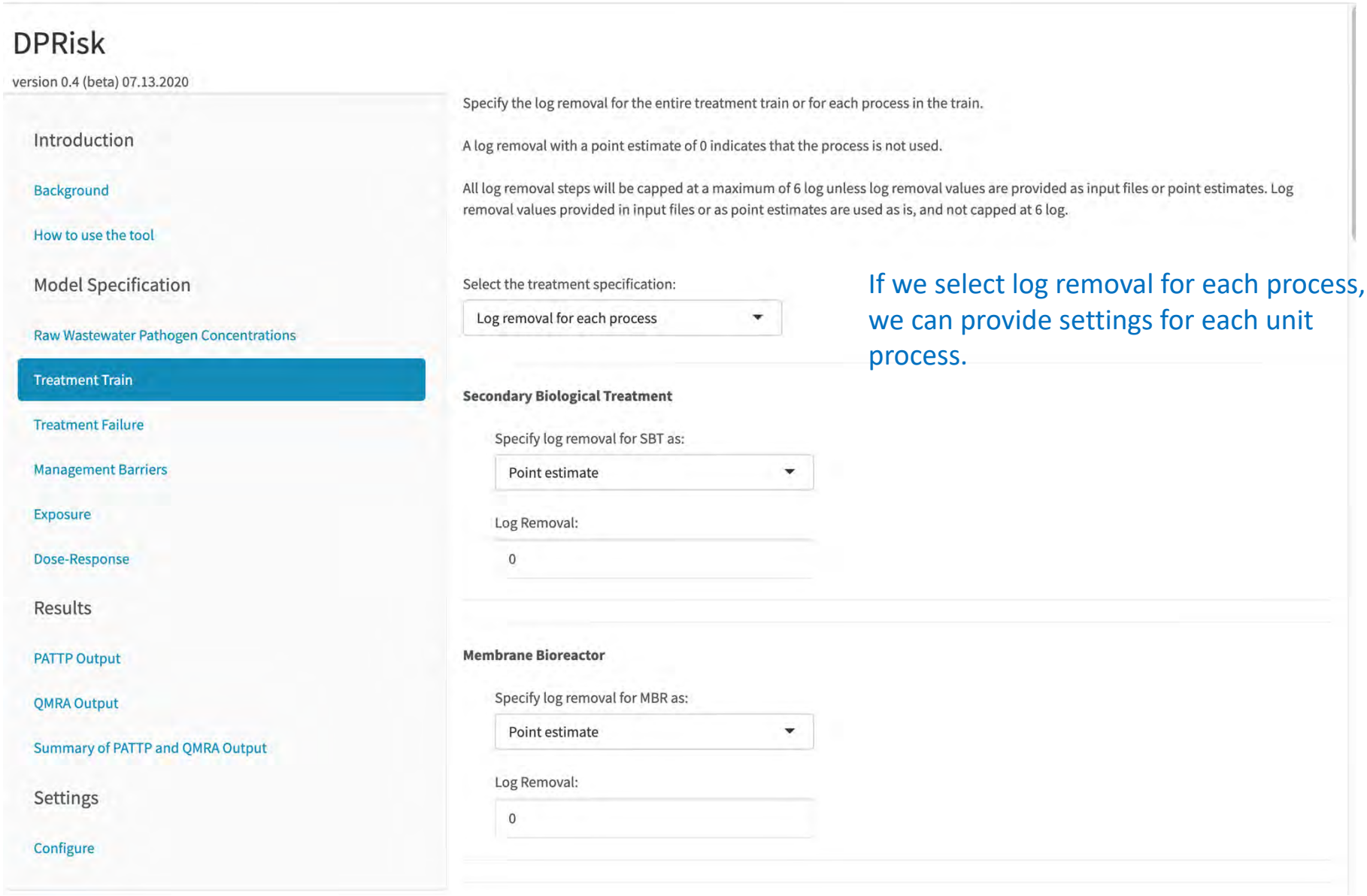
Overall log removal point estimate

Log Removal:

10



Flexibility to provide an overall treatment log removal as a point estimate, an input file with a distribution of values, or specify treatment for each unit process.

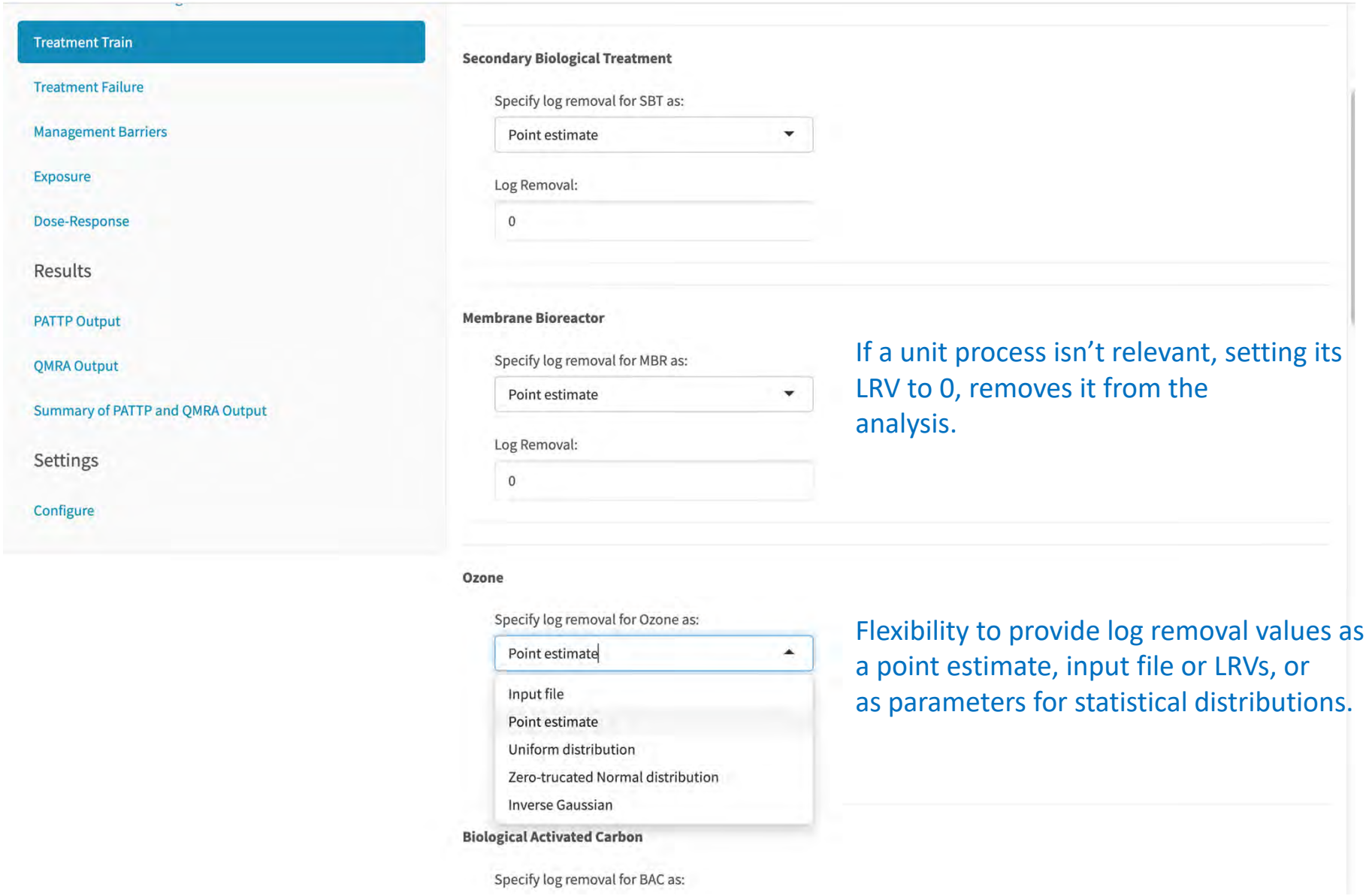


If we select log removal for each process, we can provide settings for each unit process.

Treatment Train

- Membrane bioreactor
- Ozone
- Biological activated carbon
- Membrane filtration
- Reverse Osmosis
- UV/Advanced Oxidation Process
- Pipeline Chlorine
- Flocculation/sedimentation & filtration
- Ozone 2
- Chlorine
- Custom Process #1
- Custom Process #2

There are two “custom” processes, where users can specify LRVs that are also included in the analysis, including in failure analyses.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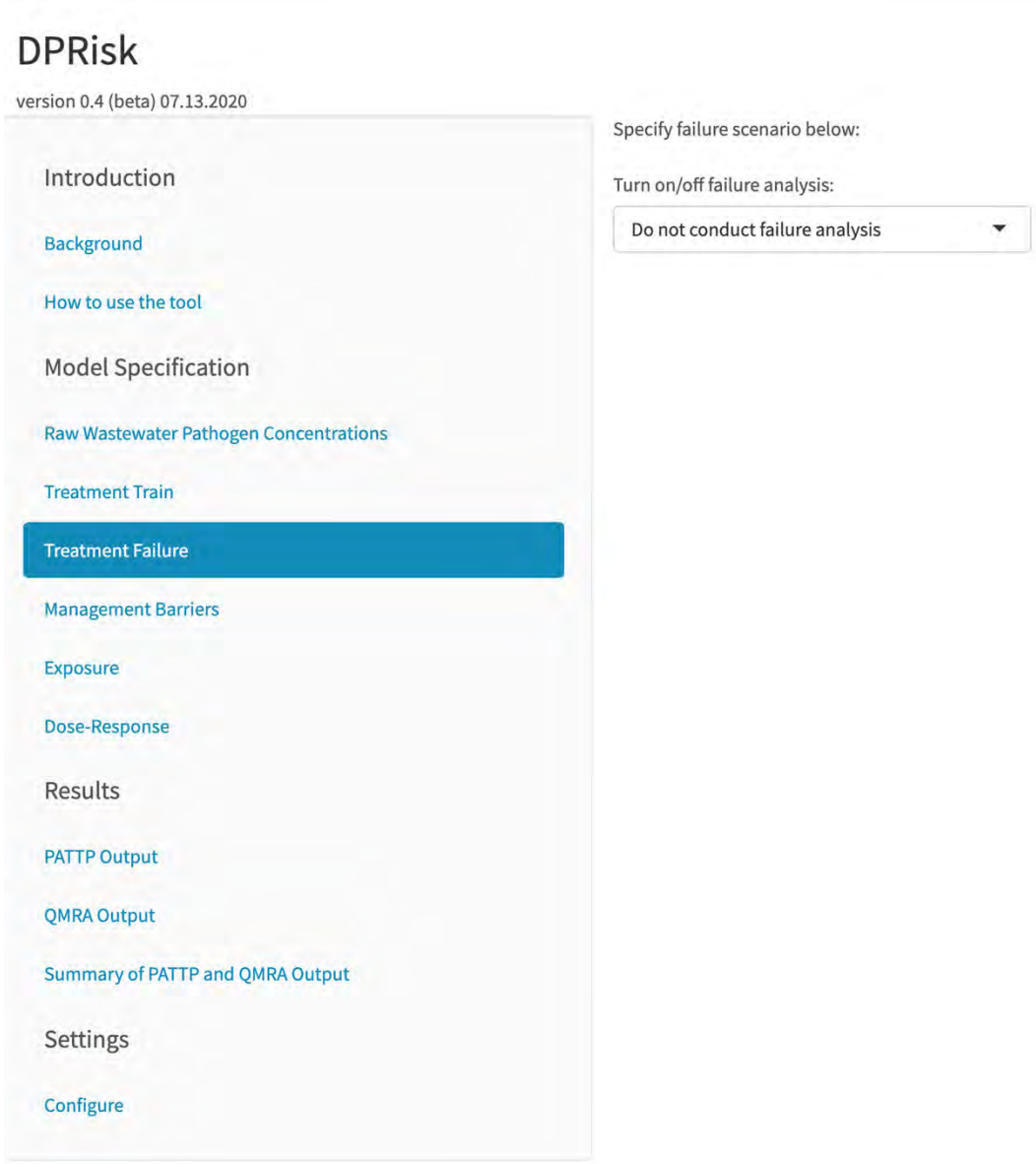
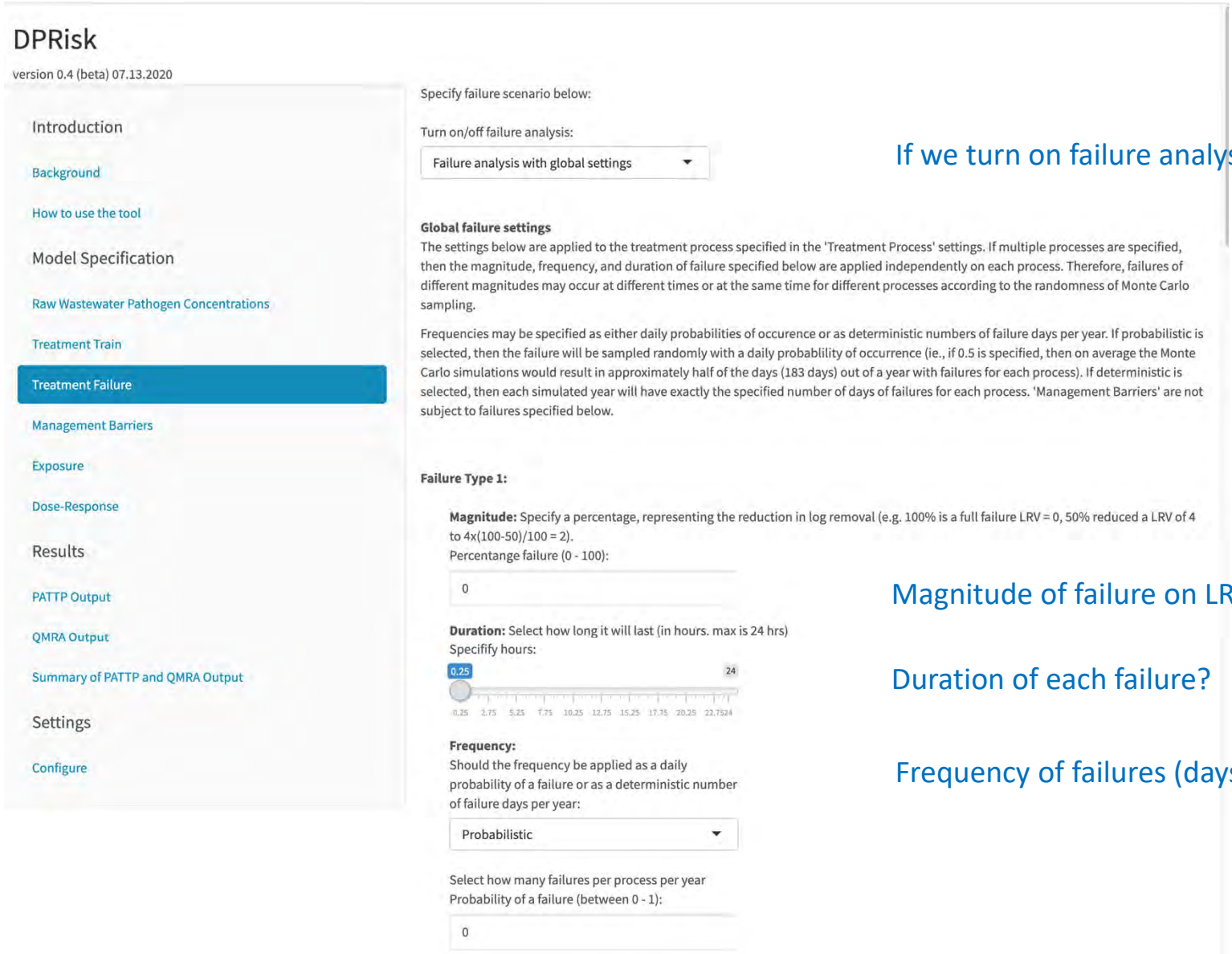
Secondary Biological Treatment
Specify log removal for SBT as:
Point estimate
Log Removal:
0
Membrane Bioreactor
Specify log removal for MBR as:
Point estimate
Log Removal:
0
Ozone
Specify log removal for Ozone as:
Point estimate
Input file
Point estimate
Uniform distribution
Zero-trucated Normal distribution
Inverse Gaussian
Biological Activated Carbon
Specify log removal for BAC as:
If a unit process isn't relevant, setting its LRV to 0, removes it from the analysis.
Flexibility to provide log removal values as a point estimate, input file or LRVs, or as parameters for statistical distributions.



Optionally, failure analyses can be performed.

We can leave this as is if we just want the tool to compute a **benchmark treatment performance** (i.e., what LRV is required for the specified raw wastewater pathogen concentrations and exposure to achieve an acceptable annualized risk, like 10^{-4} risk of infection).

We can leave as is if we just want the tool to compute **daily and annualized risk results** for the specified treatment train.



If we turn on failure analysis…

Magnitude of failure on LRV?

Duration of each failure?

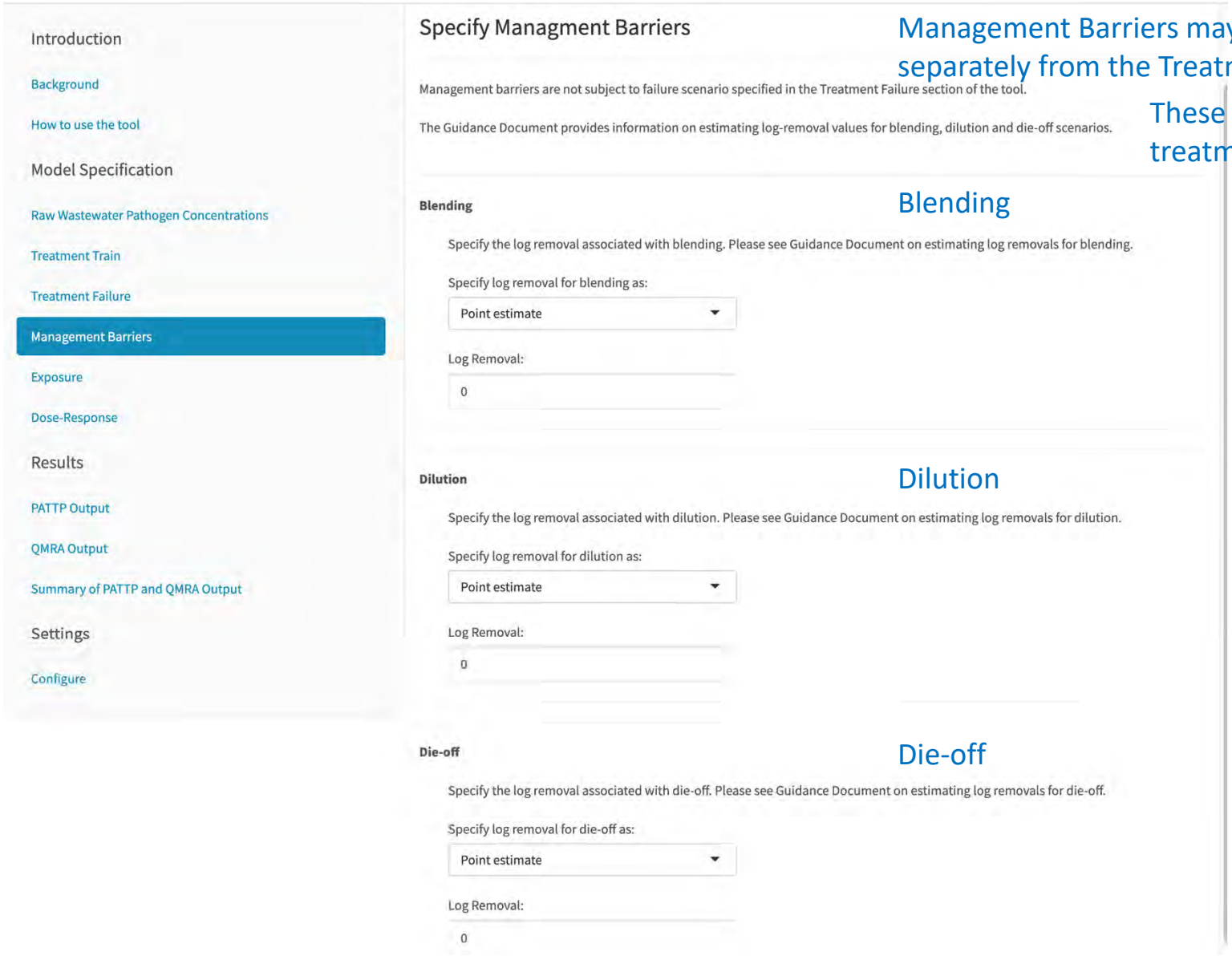
Frequency of failures (days out of the year)?

Combining “Failure Types”

- The tool allows for up to 6 Failure Types, which can be combined within a single failure analysis.

For example:

- Type 1: Magnitude: 25%, Duration: 1-hour, Frequency: 10 days/yr
- Type 2: Magnitude: 50%, Duration: 30-min, Frequency: 3 days/yr
- Type 3: Magnitude: 100%, Duration: 15-min, Frequency: 1 day/2 yrs



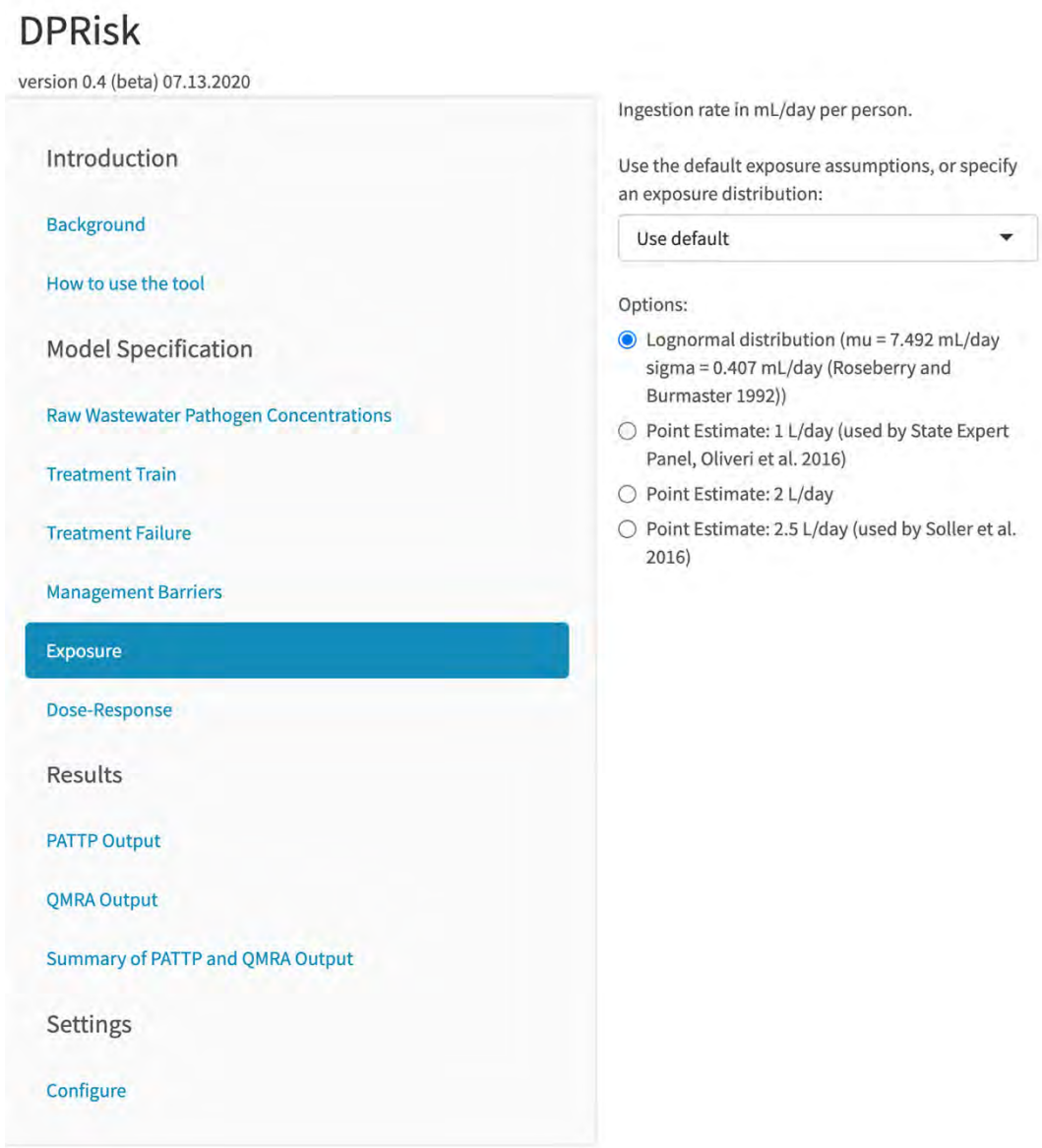
Management Barriers may be specified separately from the Treatment Train

These are not subject to treatment failures.

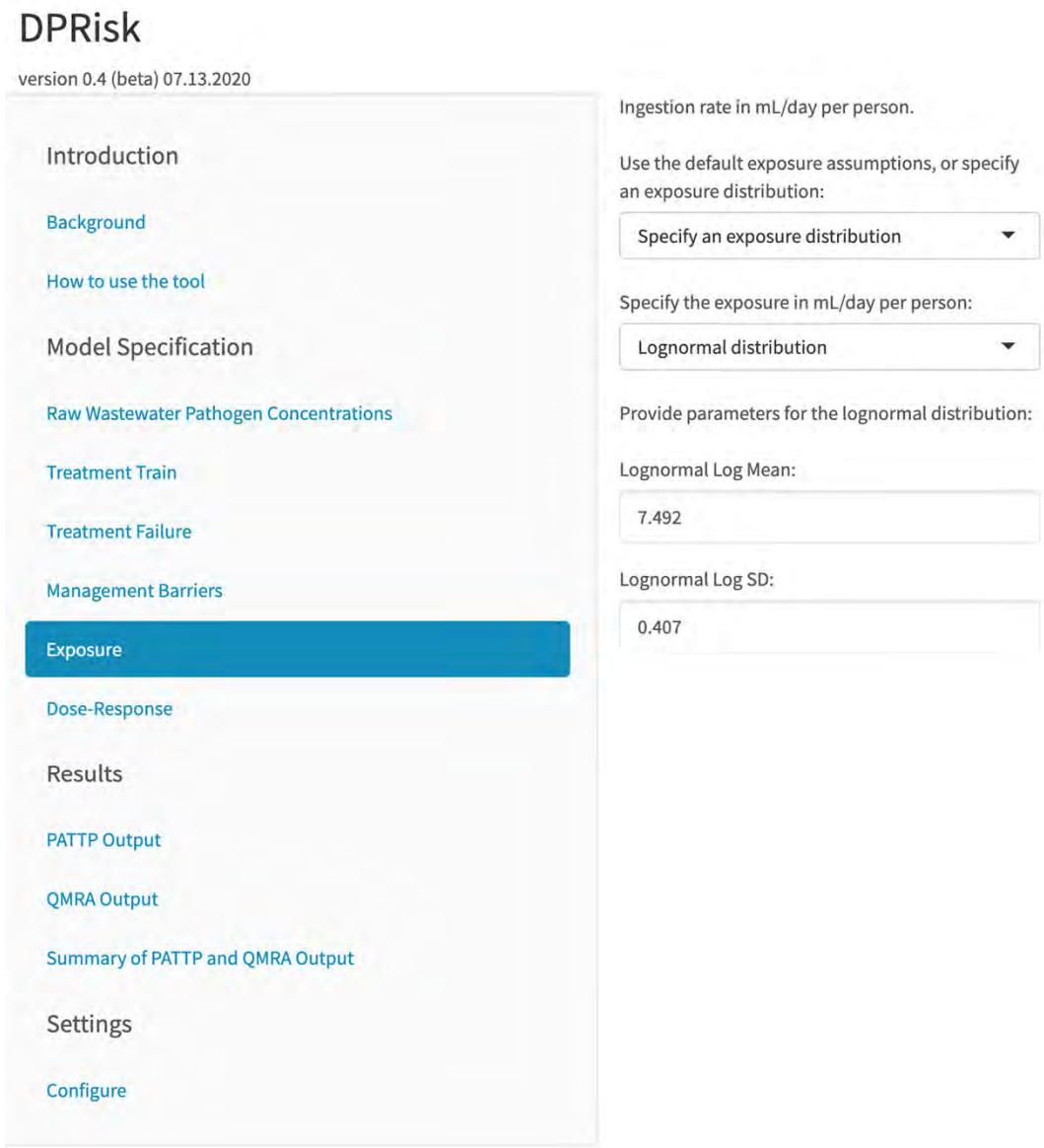
Blending

Dilution

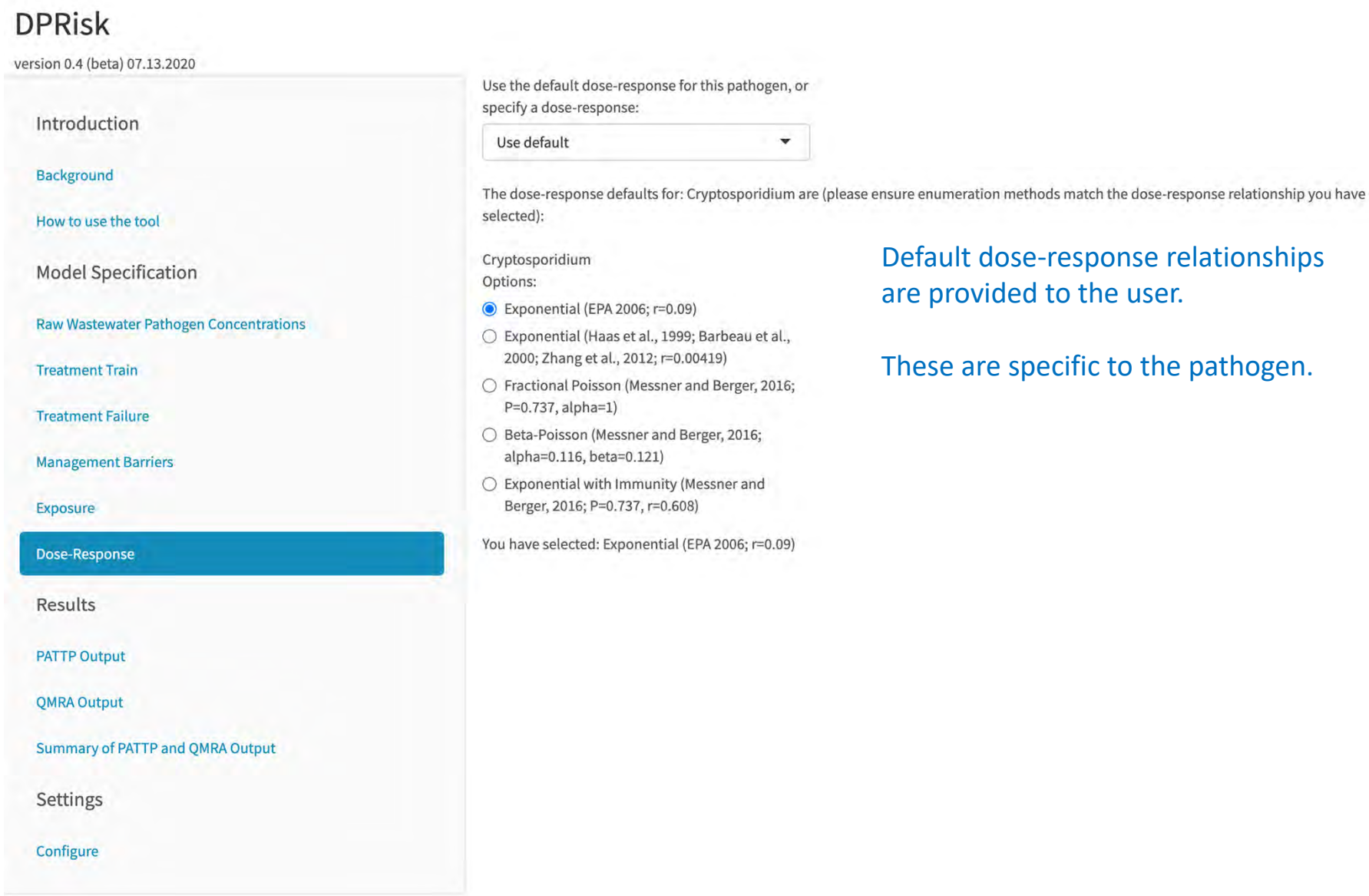
Die-off



Various defaults provided for exposure

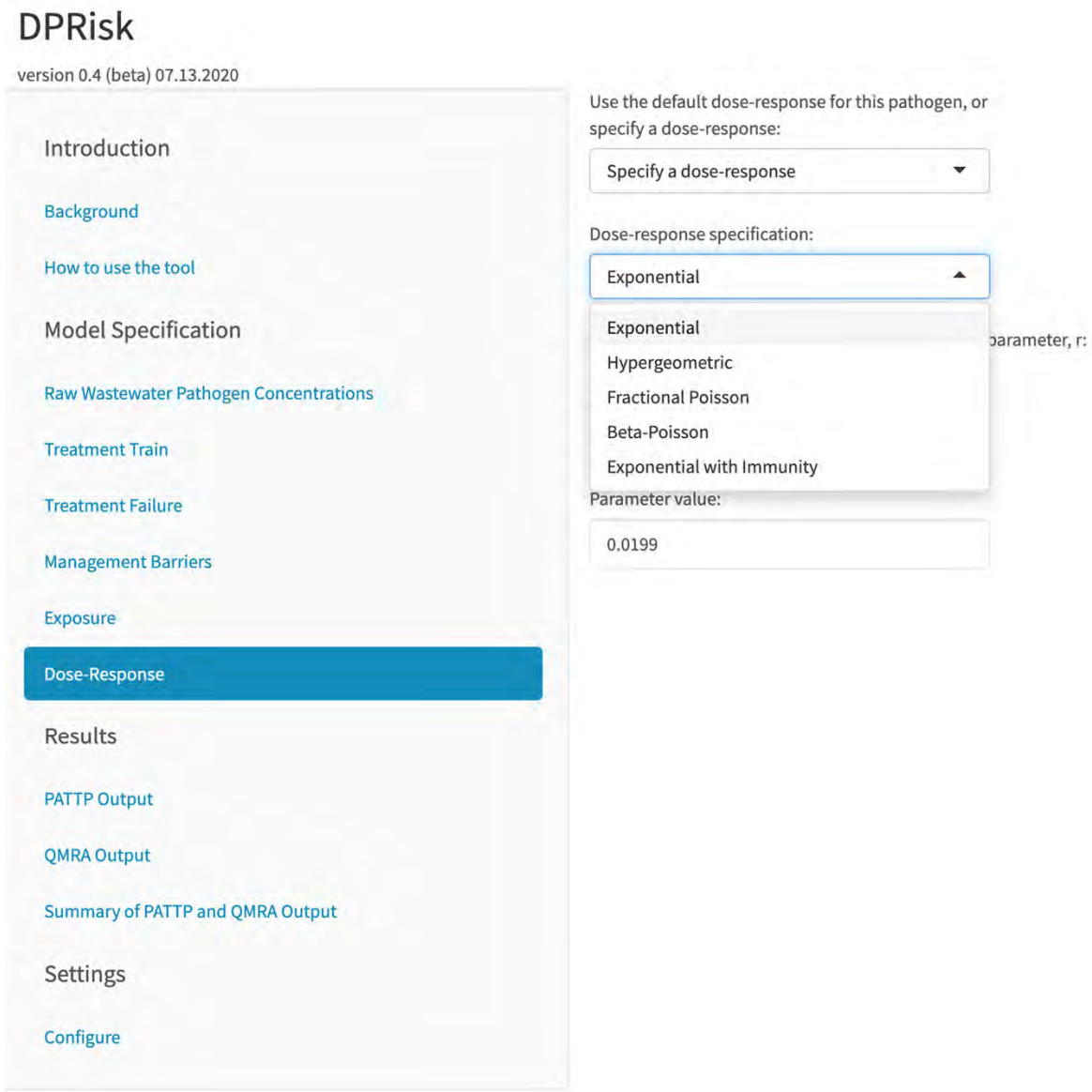


Or, the user can specify their own exposure distribution as parameters for a statistical distribution, or as an input file.



Default dose-response relationships are provided to the user.

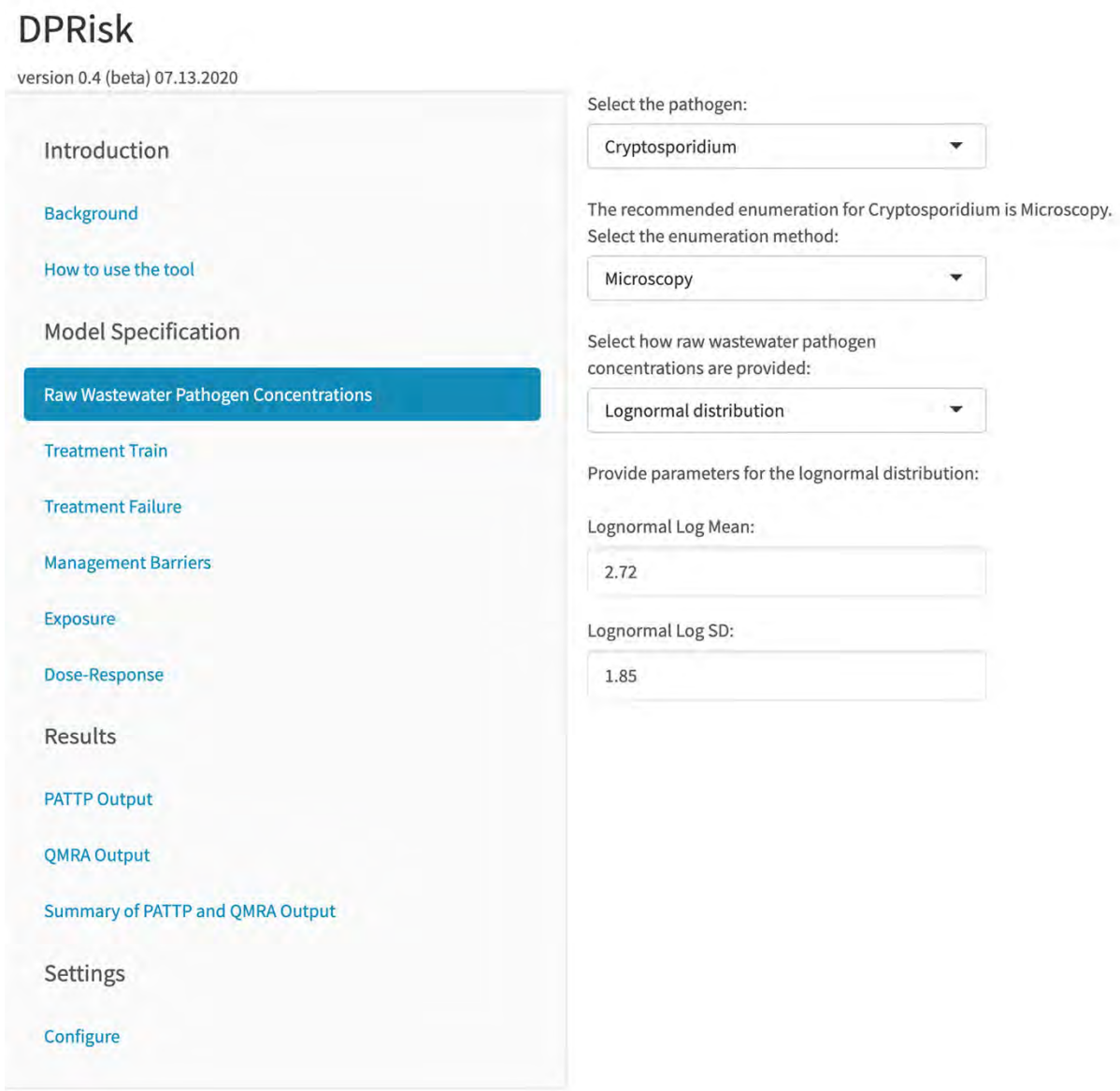
These are specific to the pathogen.



The user can provide their own dose-response relationship and parameter values.

For example, various common dose-response forms are provided by the tool.

An Example: Case Study 2 from the Guidance Document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Configure
Select the pathogen:
Cryptosporidium
The recommended enumeration for Cryptosporidium is Microscopy.
Select the enumeration method:
Microscopy
Select how raw wastewater pathogen concentrations are provided:
Lognormal distribution
Provide parameters for the lognormal distribution:
Lognormal Log Mean:
2.72
Lognormal Log SD:
1.85

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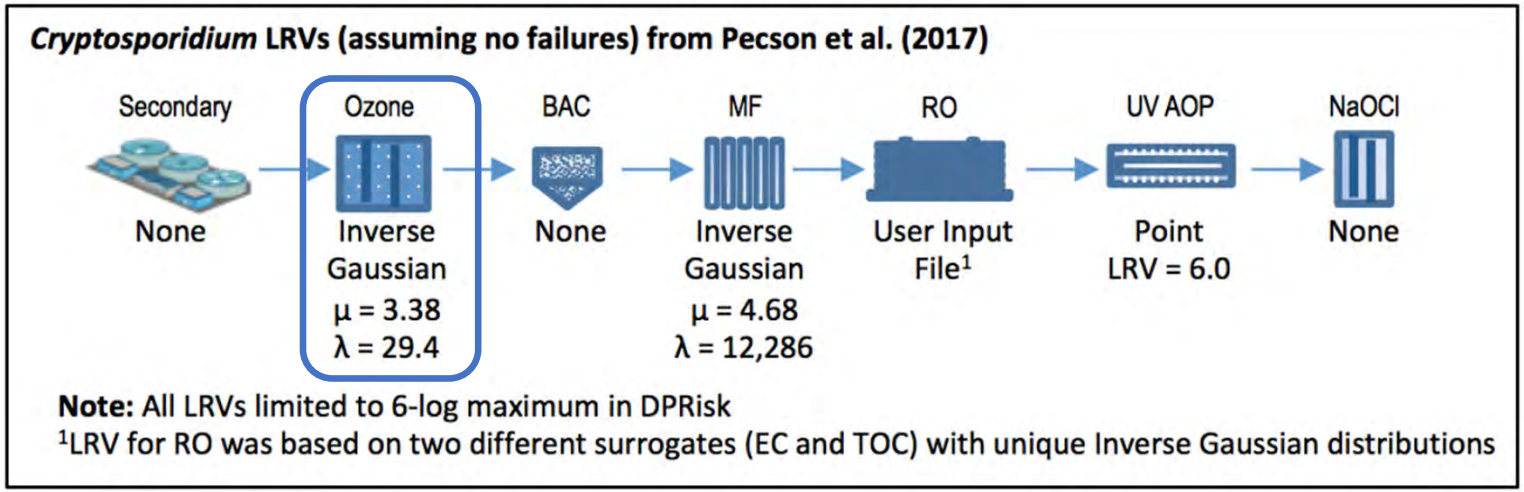


Specify log removal for MBR as:

Point estimate

Log Removal:

0

Ozone

Specify log removal for Ozone as:

Inverse Gaussian

Provide parameters for the Inverse Gaussian distribution:

mu:

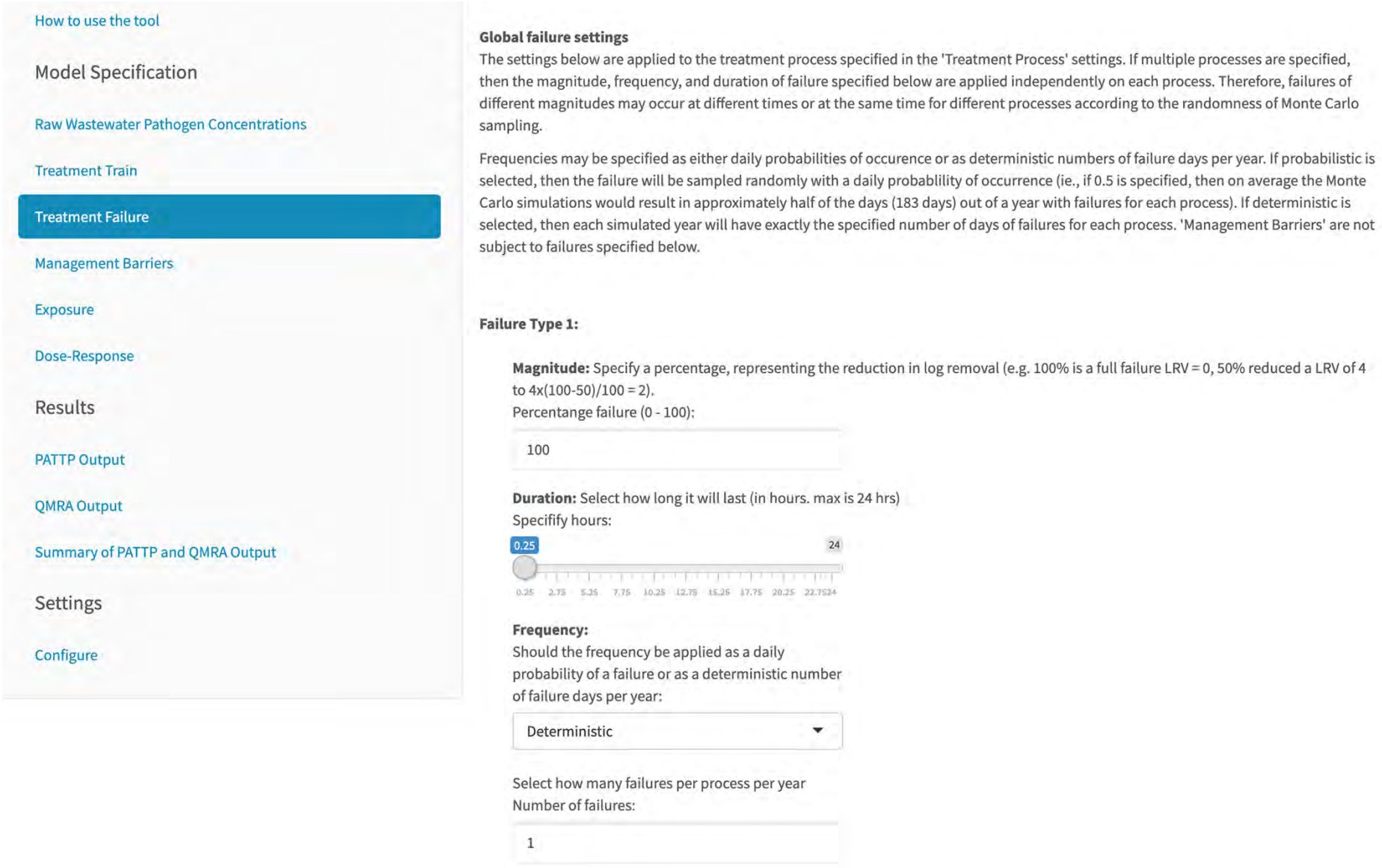
3.38

lambda:

29.4

Specification for Ozone in the treatment train

… and similarly for other unit processes.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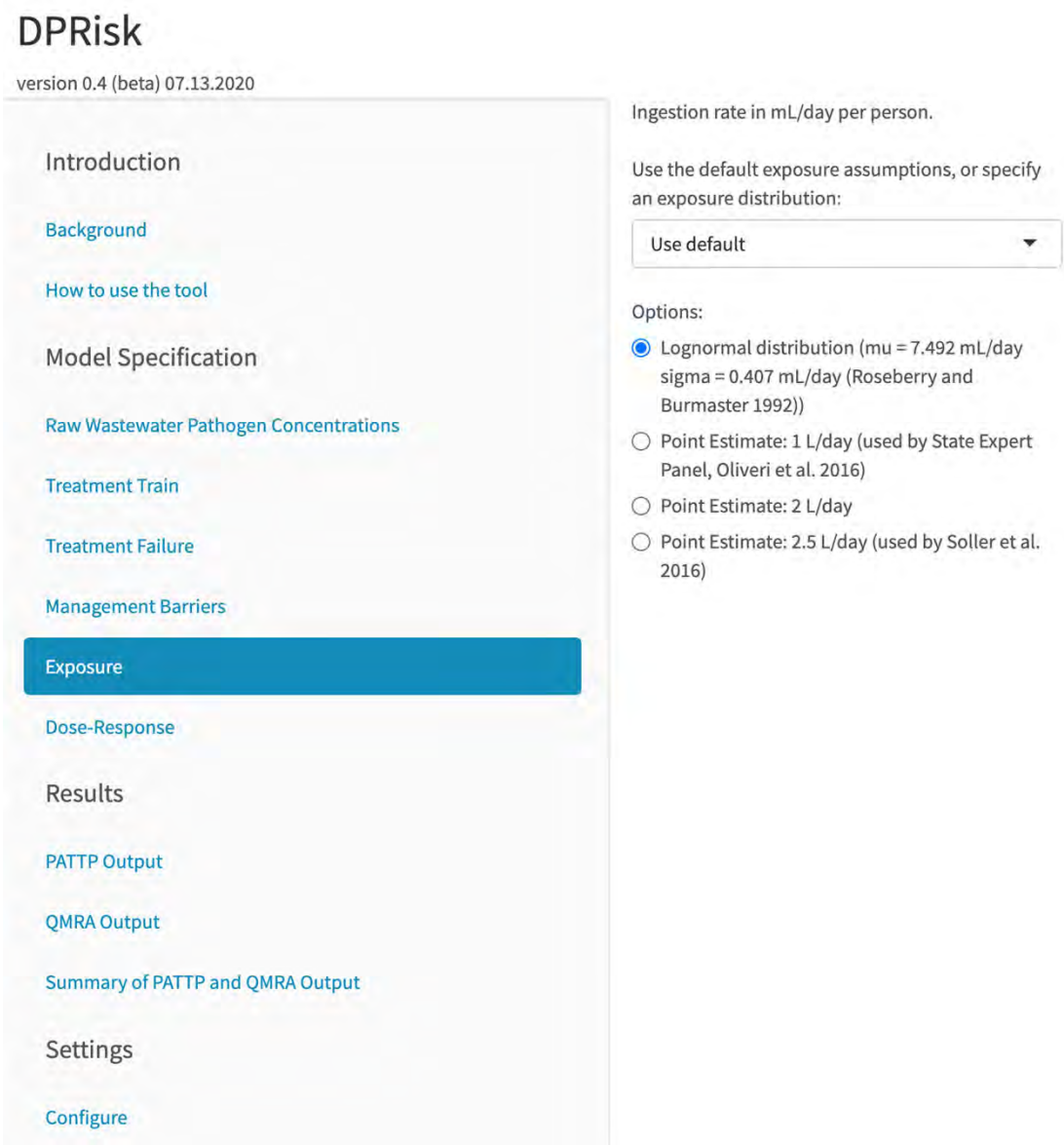
Global failure settings
The settings below are applied to the treatment process specified in the 'Treatment Process' settings. If multiple processes are specified, then the magnitude, frequency, and duration of failure specified below are applied independently on each process. Therefore, failures of different magnitudes may occur at different times or at the same time for different processes according to the randomness of Monte Carlo sampling.
Frequencies may be specified as either daily probabilities of occurence or as deterministic numbers of failure days per year. If probabilistic is selected, then the failure will be sampled randomly with a daily probablility of occurrence (ie., if 0.5 is specified, then on average the Monte Carlo simulations would result in approximately half of the days (183 days) out of a year with failures for each process). If deterministic is selected, then each simulated year will have exactly the specified number of days of failures for each process. 'Management Barriers' are not subject to failures specified below.
Failure Type 1:
Magnitude: Specify a percentage, representing the reduction in log removal (e.g. 100% is a full failure LRV = 0, 50% reduced a LRV of 4 to 4x(100-50)/100 = 2).
Percentange failure (0 - 100):
100
Duration: Select how long it will last (in hours. max is 24 hrs)
Specifify hours:
0.25
24
0.25 2.75 5.25 7.75 10.25 12.75 15.25 17.75 20.25 22.75 24
Frequency:
Should the frequency be applied as a daily probability of a failure or as a deterministic number of failure days per year:
Deterministic
Select how many failures per process per year
Number of failures:
1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Ingestion rate in mL/day per person.
Use the default exposure assumptions, or specify an exposure distribution:
Use default
Options:
Lognormal distribution (mu = 7.492 mL/day sigma = 0.407 mL/day (Roseberry and Burmaster 1992))
Point Estimate: 1 L/day (used by State Expert Panel, Oliveri et al. 2016)
Point Estimate: 2 L/day
Point Estimate: 2.5 L/day (used by Soller et al. 2016)

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Use the default dose-response for this pathogen, or specify a dose-response:

Use default

The dose-response defaults for: Cryptosporidium are (please ensure enumeration methods match the dose-response relationship you have selected):

Cryptosporidium
Options:

- ○ Exponential (EPA 2006; r=0.09)
- ○ Exponential (Haas et al., 1999; Barbeau et al., 2000; Zhang et al., 2012; r=0.00419)
- ○ Fractional Poisson (Messner and Berger, 2016; P=0.737, alpha=1)
- ◉ Beta-Poisson (Messner and Berger, 2016; alpha=0.116, beta=0.121)
- ○ Exponential with Immunity (Messner and Berger, 2016; P=0.737, r=0.608)

You have selected: Beta-Poisson (Messner and Berger, 2016; alpha=0.116, beta=0.121)

Outputs from the Analysis

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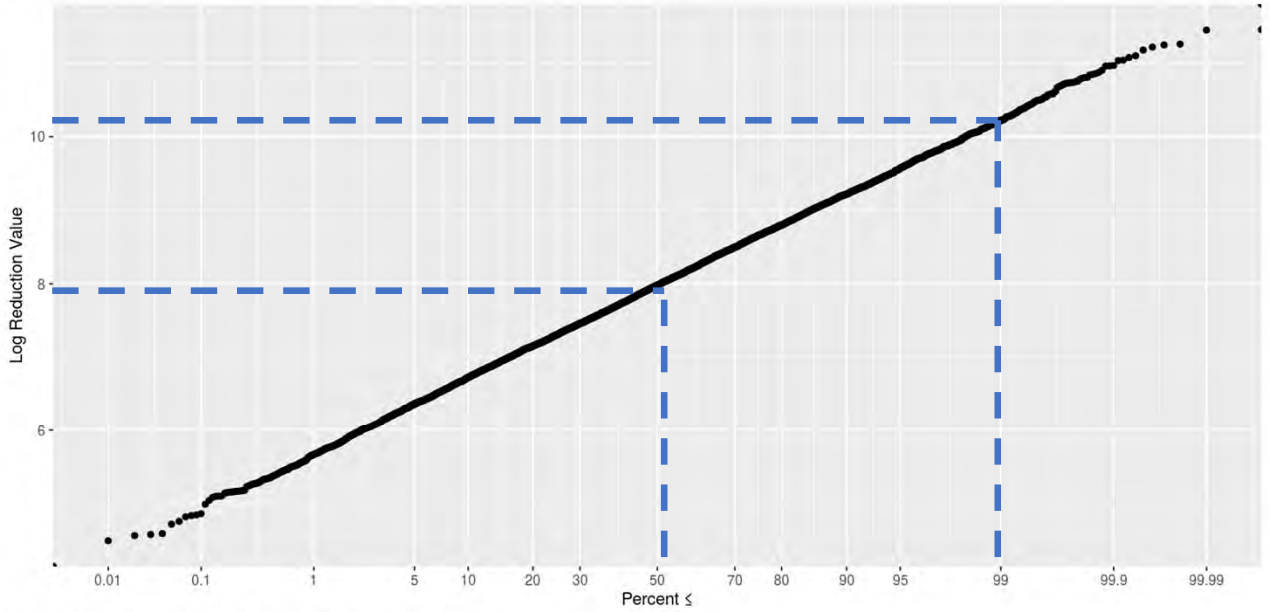
Note: You must click on, and double-check the model specifications before PATTP output will be computed.

Benchmark Treatment Train Performance

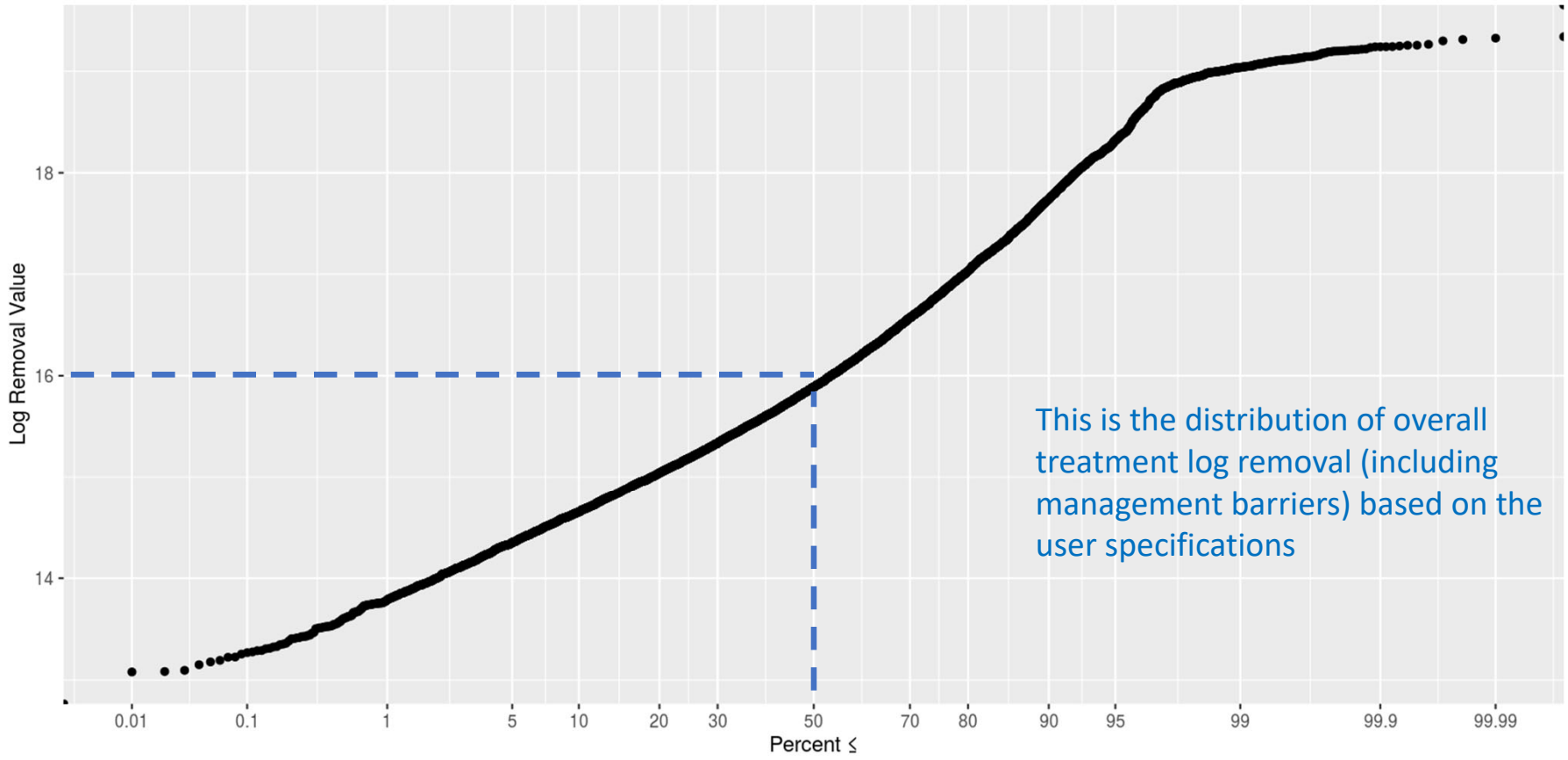
Distribution of Log Removal Values to achieve 10^{-4} annual risk:



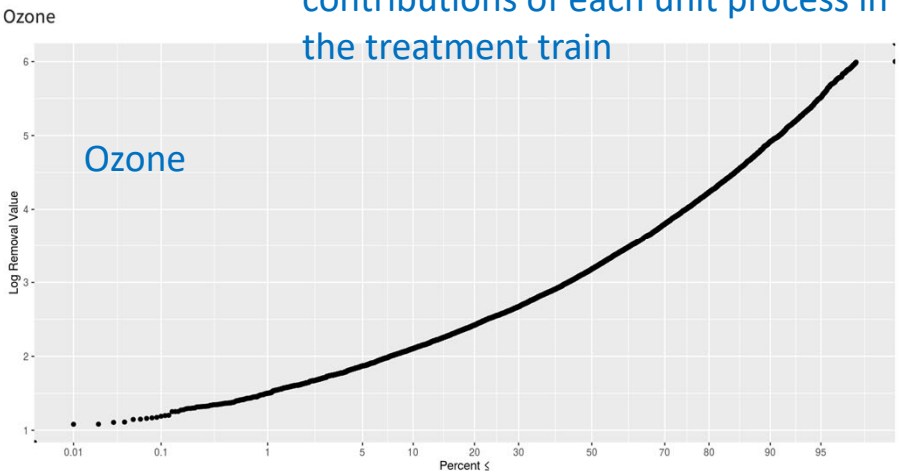
Summary statistics for Log Removal Values to achieve 10^{-4} annual risk:

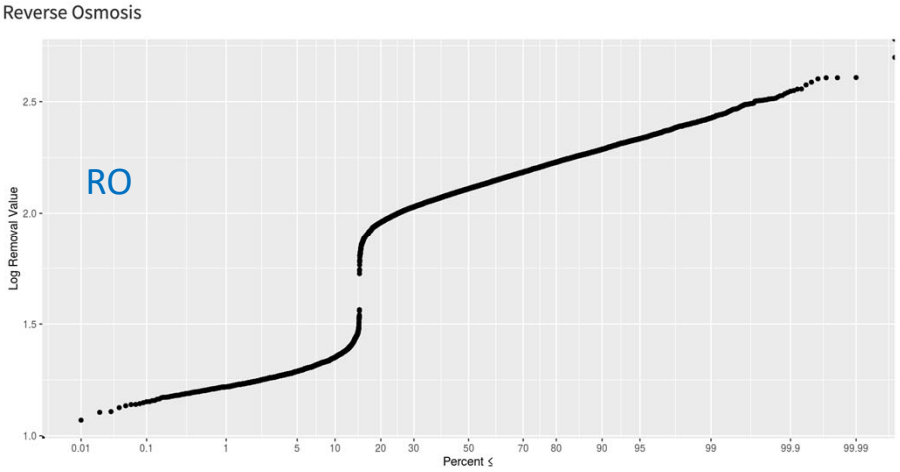
```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  4.496   7.313   7.980   7.976   8.647  11.455
```

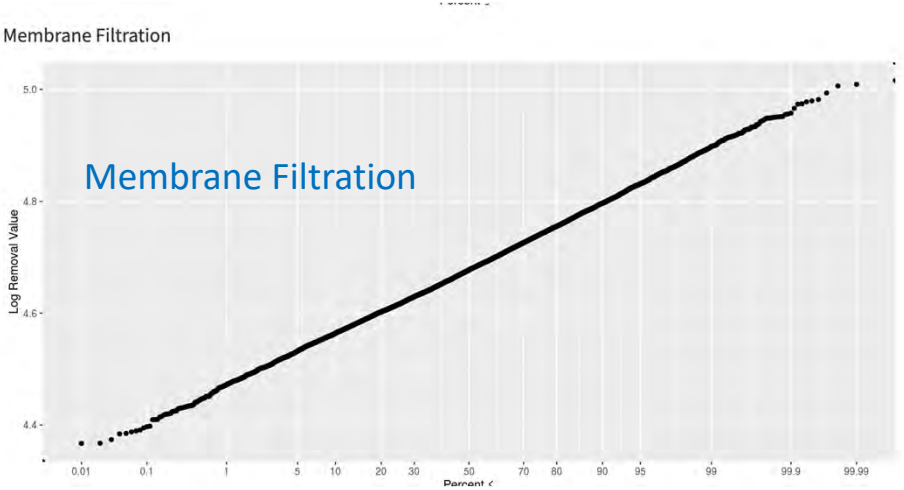
Below is the performance of the overall treatment train (including Management Barriers):

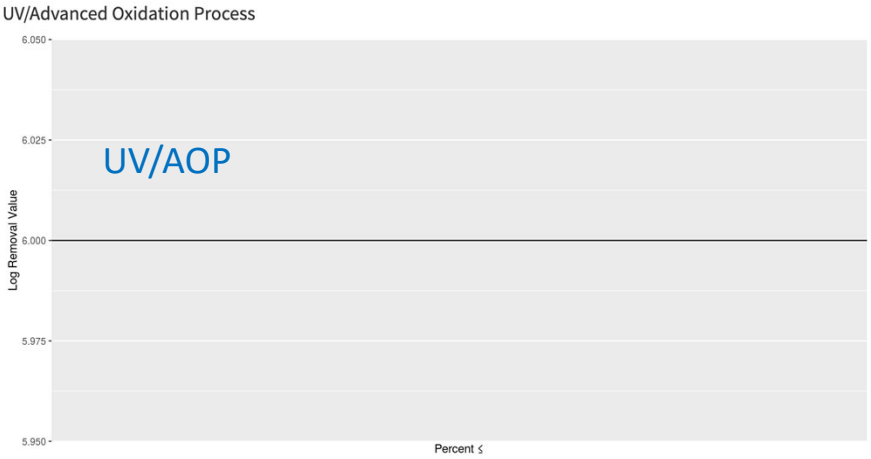


Figures show the individual LRV contributions of each unit process in the treatment train









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Note: You must click on, and double-check the model specifications before QMRA output will be computed.

Risk (With/Without Treatment Failure)

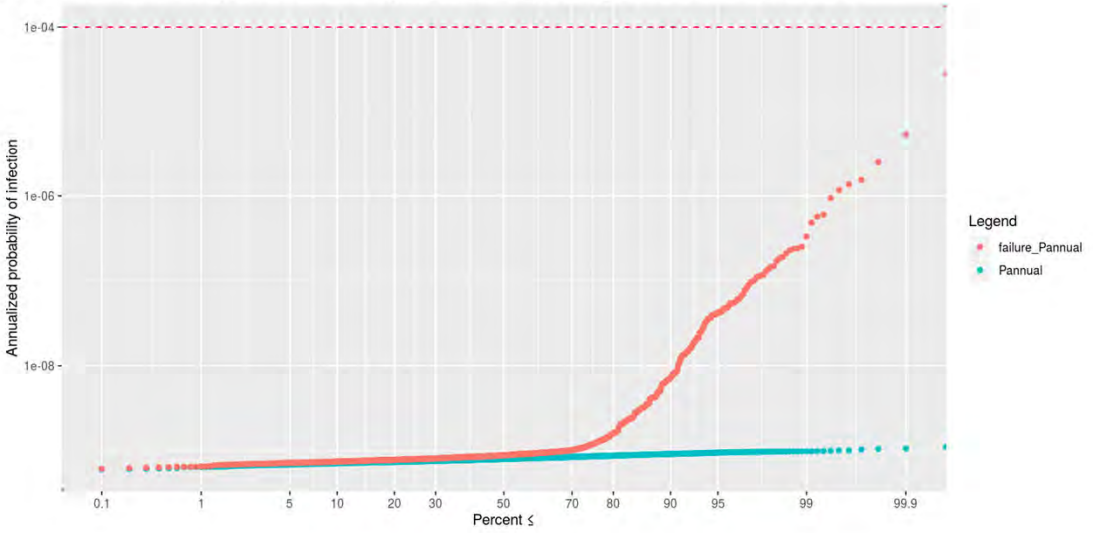
Below are annualized risks based on 1000 Monte Carlo samples of the 10,000 15-min exposure events (with and without failure).

Annual Risk:

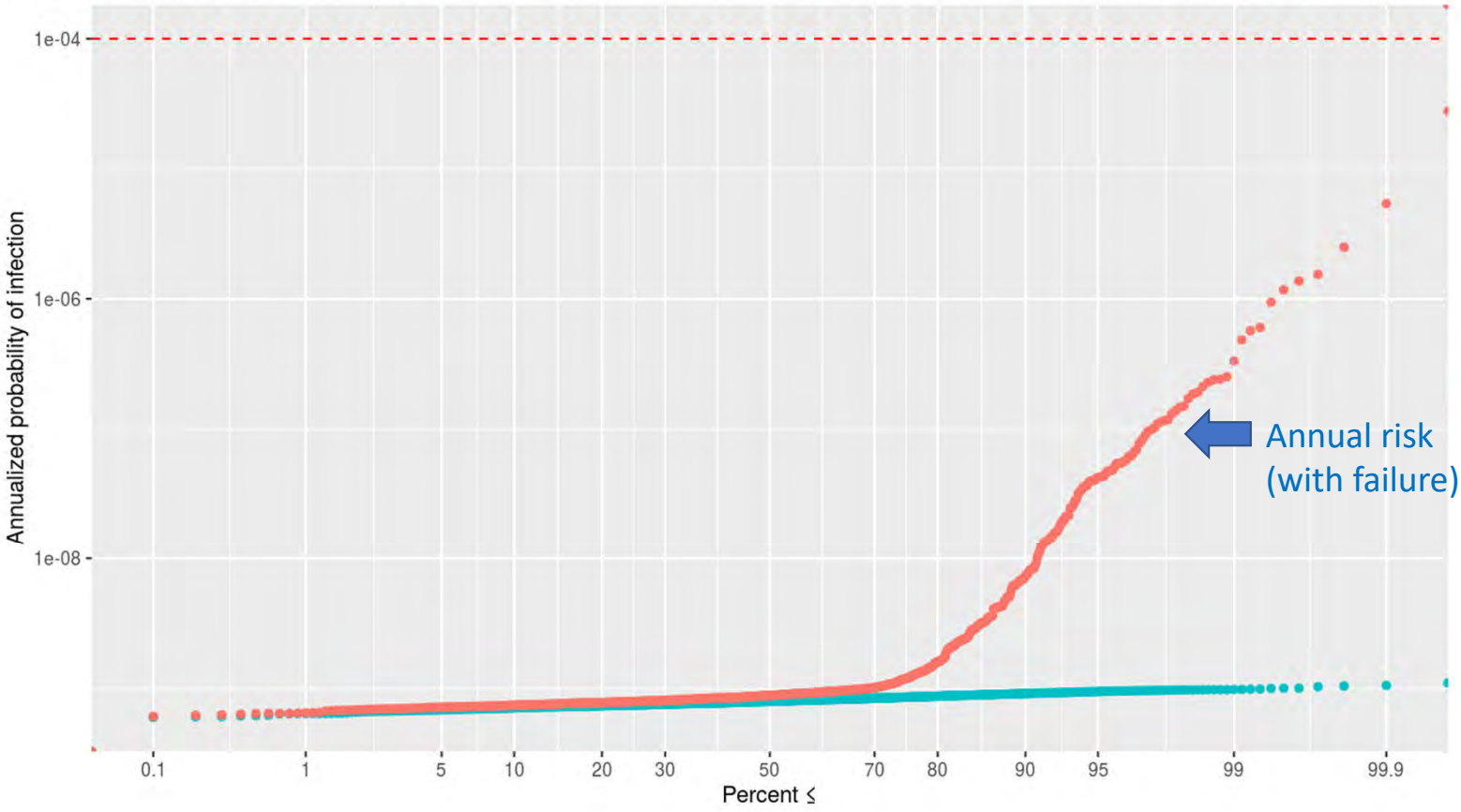
Summary statistics for annual risk, Pannual (with/without failure):

```
    Pannual          failure_Pannual
Min.   :6.057e-10   Min.   :6.160e-10
1st Qu.:7.523e-10   1st Qu.:8.010e-10
Median :8.029e-10   Median :8.900e-10
Mean   :8.100e-10   Mean   :4.901e-08
3rd Qu.:8.621e-10   3rd Qu.:1.188e-09
Max.   :1.109e-09   Max.   :2.782e-05
```

Plot of annual risk, Pannual (with/without failure) (dashed red line depicts target annual risk threshold at 10^{-4}):



Plot of annual risk, Pannual (with/without failure) (dashed red line depicts target annual risk threshold at 10^{-4}):



Target risk of 10^{-4}

Annual risk (with failure)

Annual risk (without failure)

Pannual Table for Failure Simulations

Show 5 entries

Search:

	failure_Pannual	Pannual
1	1.16827458818136e-9	7.94848187268826e-10
2	1.26478660877893e-9	7.01320557183749e-10
3	8.52424575370492e-10	8.36166469397881e-10
4	8.03628608103679e-10	7.64679652931477e-10
5	7.42635286599125e-10	7.4180639408894e-10

Showing 1 to 5 of 1,000 entries

Previous 1 2 3 4 5 … 200 Next

Download Failure Data

The tool allows you to download the data for further analyses, visualization, etc.

The tool allows you visualize the factors that contribute to risk…

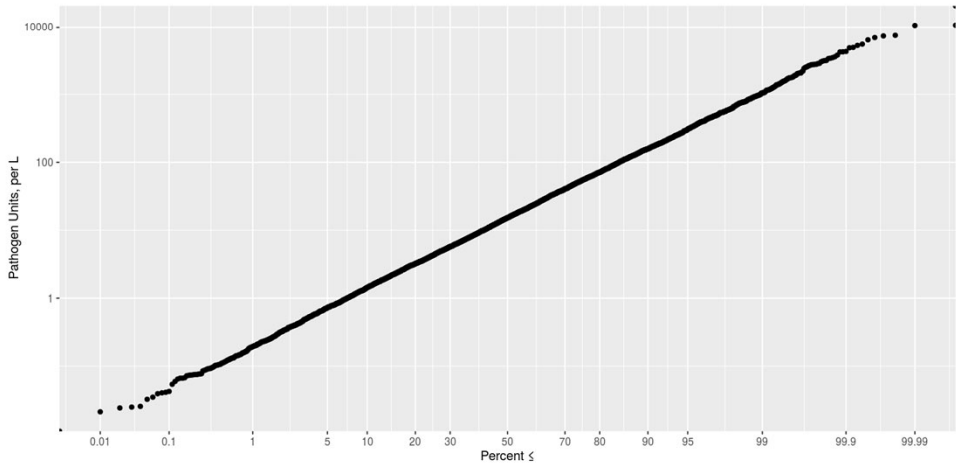
Raw Wastewater Pathogen Concentration

Pathogen: Cryptosporidium
Enumeration method: Microscopy
Input specification: Lognormal distribution
The user-provided log mean value: 2.72
The user-provided log SD value: 1.85

Summary statistics:

```
     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
    0.021     4.325    15.233    80.266    53.612 10742.003
```

Plot of concentration data used:



Exposure

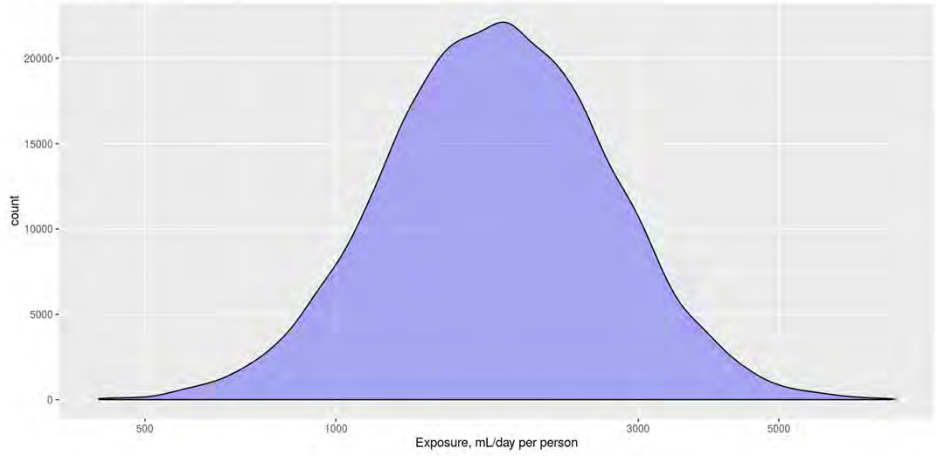
Exposure specification: Lognormal distribution

The default used: Lognormal distribution (mu = 7.492 mL/day sigma = 0.407 mL/day (Roseberry and Burmaster 1992))

Summary statistics:

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
  422.4  1360.7  1795.0  1945.2  2367.5  7597.9
```

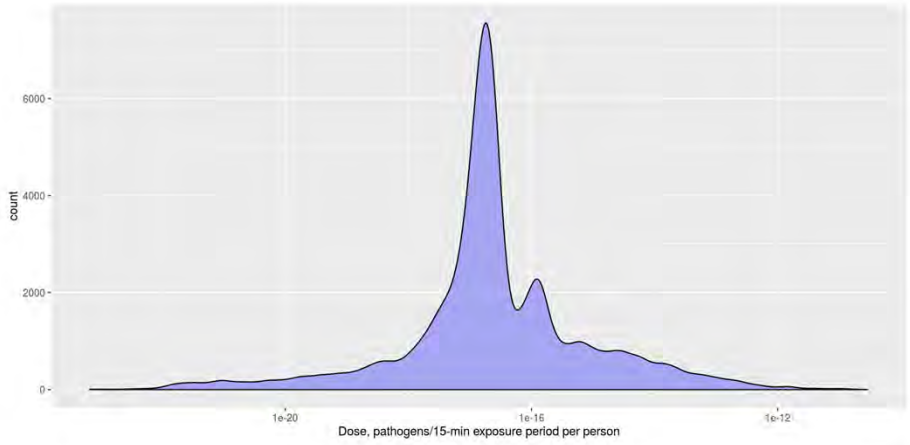
Plot of exposure data used:

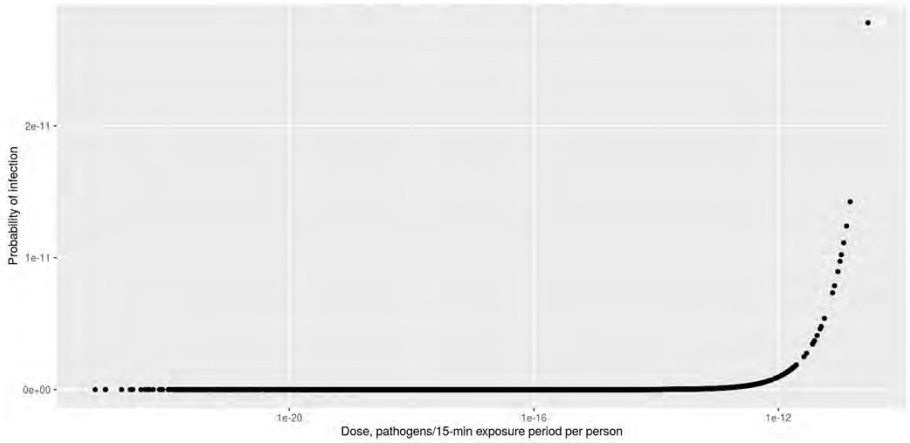


Dose-Response

Dose-Response specification: Exponential
Dose data used (per 15-min exposure period) (Without Treatment Failure), and calculated Response:
Summary statistics:

```
     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.000e+00 8.000e-18 2.000e-17 2.416e-14 1.200e-16 2.902e-11
```





SOUTHERN NEVADA WATER AUTHORITY

DPRisk Tool: Guidance Document and Case Studies

Daniel Gerrity, Ph.D.
Principal Research Scientist, Water Quality R&D
Southern Nevada Water Authority

Guidance Document Components

Guidance Document for DPRisk

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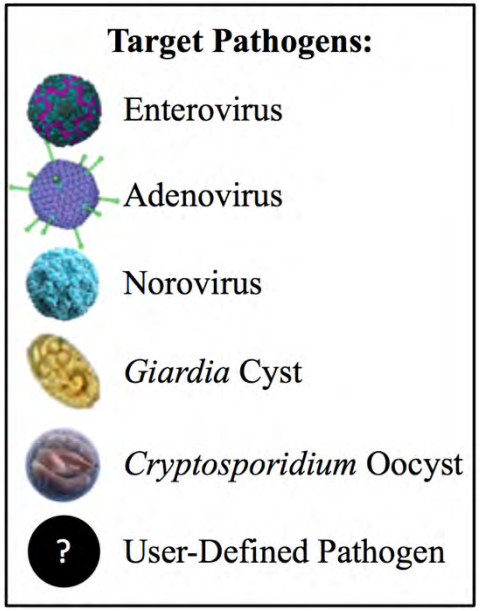
10 Key Components of a QMRA/PATTP

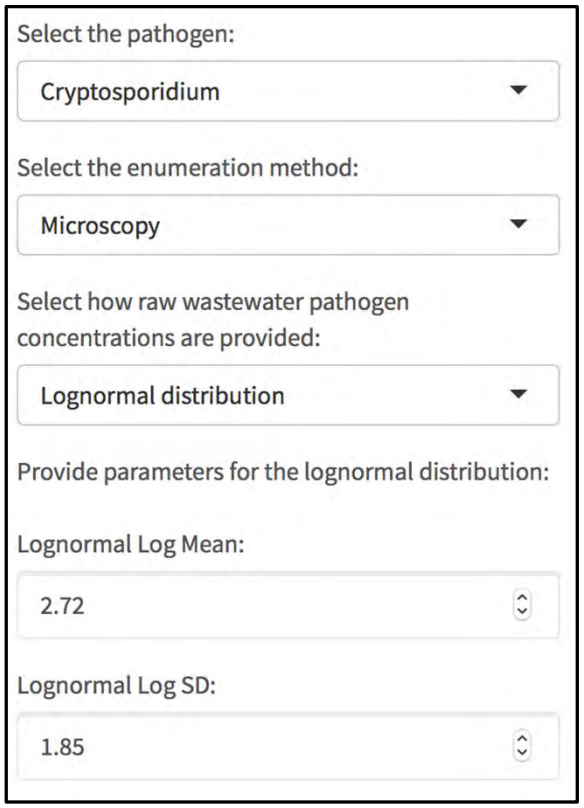
1. Target pathogens
2. Raw wastewater pathogen datasets
3. Raw wastewater pathogen distributions
4. Identifying unit processes for the treatment train
5. Assigning treatment process LRVs
6. Treatment process failure framework
7. Management barriers (blending, dilution, die-off)
8. Drinking water ingestion rate and frequency
9. Pathogen-specific dose response models
10. Risk characterization

Section Breakdowns

- **Background**
  - Literature review (e.g., target pathogens in recently published QMRAs)
  - Important concepts (e.g., uncertainty vs. variability)
- **Integration into DPRisk Tool**
  - Implementation (e.g., target pathogens actually included in DPRisk)
  - Flexibility to expand beyond defaults

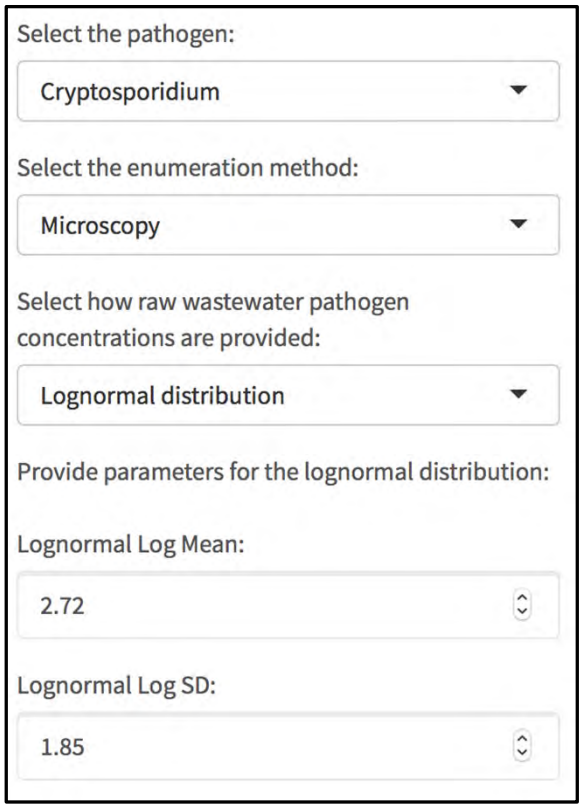


Default User Inputs vs. Flexibility



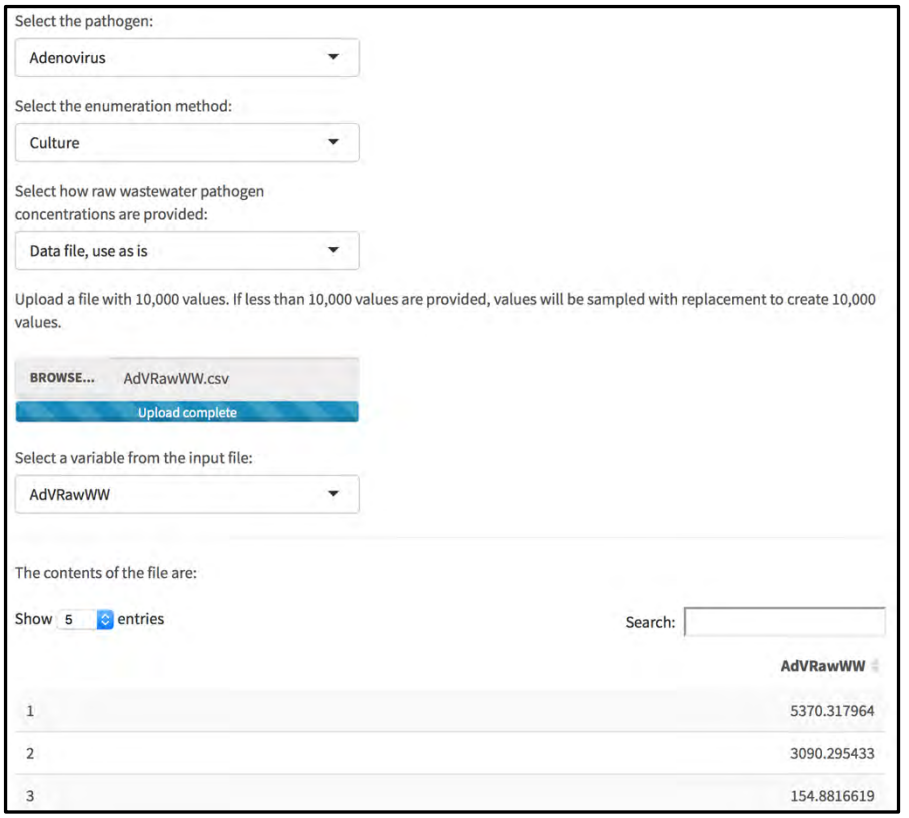
Default User Inputs:
To be updated and autopopulated with data from DPR-2
(shown: *Cryptosporidium* in Case Study 2)

Default User Inputs vs. Flexibility



Default User Inputs:
To be updated and autopopulated with data from DPR-2
(shown: *Cryptosporidium* in Case Study 2)

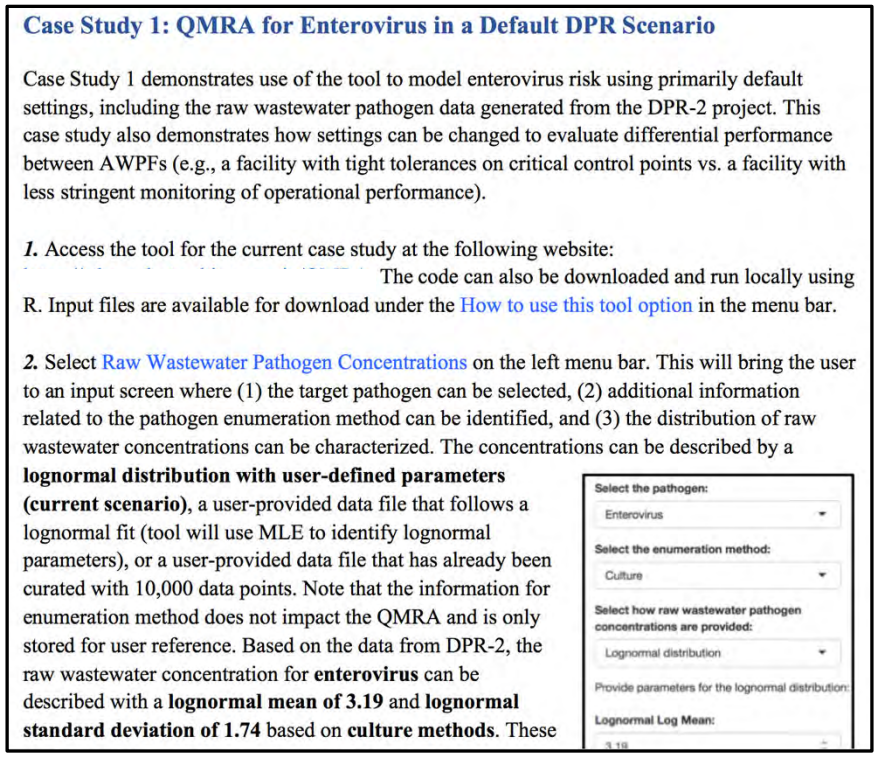
Flexibility:
Input files to allow for alternative distributions
(shown: log_{10}uniform distribution for adenovirus in Case Study 3)



Case Study Goals

- 3 case studies included in Guidance Document
- Demonstrate overall functionality of DPRisk tool (walk user through inputs)
- Show example inputs from regulatory frameworks/published literature
- Show example outputs from tool (screenshots in Guidance Document)
- Allow for direct comparison of tool output with published data
- Explain alternative modeling options and potential for sensitivity analyses

Case Study 1: Enterovirus in a Default DPR Scenario



Case Study 1: QMRA for Enterovirus in a Default DPR Scenario

Case Study 1 demonstrates use of the tool to model enterovirus risk using primarily default settings, including the raw wastewater pathogen data generated from the DPR-2 project. This case study also demonstrates how settings can be changed to evaluate differential performance between AWPFs (e.g., a facility with tight tolerances on critical control points vs. a facility with less stringent monitoring of operational performance).

1. Access the tool for the current case study at the following website: The code can also be downloaded and run locally using R. Input files are available for download under the How to use this tool option in the menu bar.

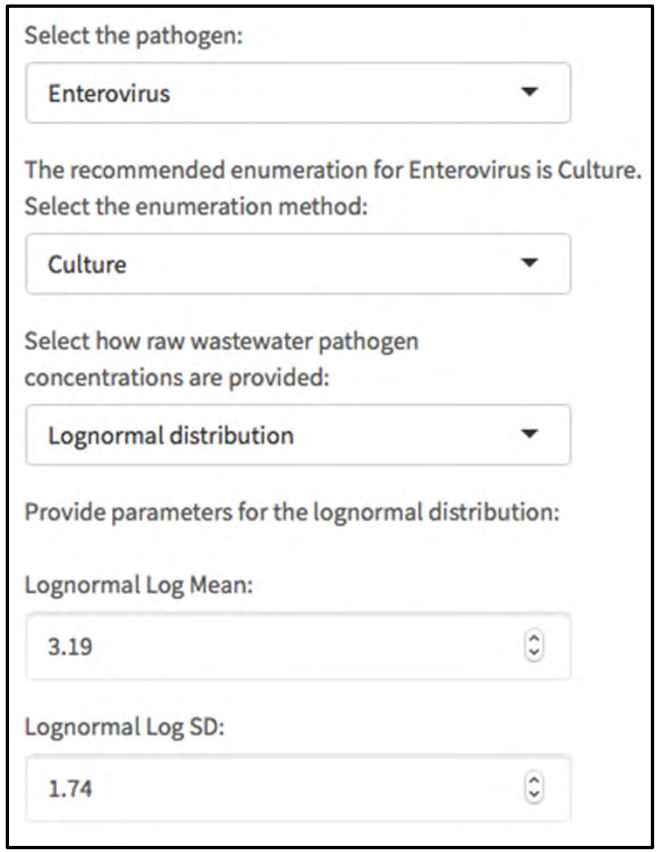
2. Select Raw Wastewater Pathogen Concentrations on the left menu bar. This will bring the user to an input screen where (1) the target pathogen can be selected, (2) additional information related to the pathogen enumeration method can be identified, and (3) the distribution of raw wastewater concentrations can be characterized. The concentrations can be described by a **lognormal distribution with user-defined parameters (current scenario)**, a user-provided data file that follows a lognormal fit (tool will use MLE to identify lognormal parameters), or a user-provided data file that has already been curated with 10,000 data points. Note that the information for enumeration method does not impact the QMRA and is only stored for user reference. Based on the data from DPR-2, the raw wastewater concentration for **enterovirus** can be described with a **lognormal mean of 3.19** and **lognormal standard deviation of 1.74** based on **culture methods**. These

Select the pathogen:
Enterovirus
Select the enumeration method:
Culture
Select how raw wastewater pathogen concentrations are provided:
Lognormal distribution
Provide parameters for the lognormal distribution:
Lognormal Log Mean:

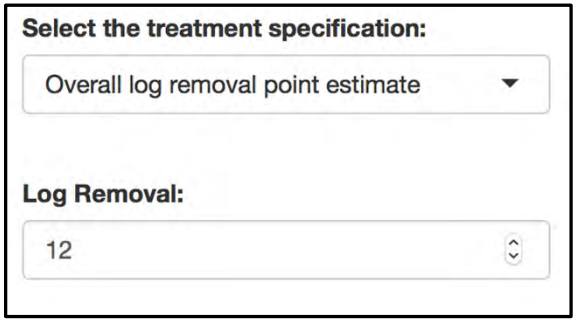
- Use default enterovirus data from DPR-2
- Focus on a common LRV benchmark
  - Example: Point estimate → LRV = 12
- Sensitivity analysis to evaluate tolerances on LRV target
  - Demonstrates input file upload for treatment train LRV
  - Example: 12±0.0, 12±0.5, 12±1.0, 12±1.5
  - Simultaneous comparison of risk curves

Case Study 1: Inputs

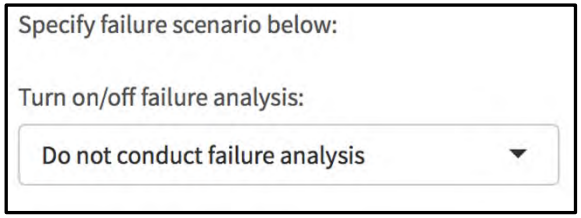
1. Raw WW Pathogen Concentration



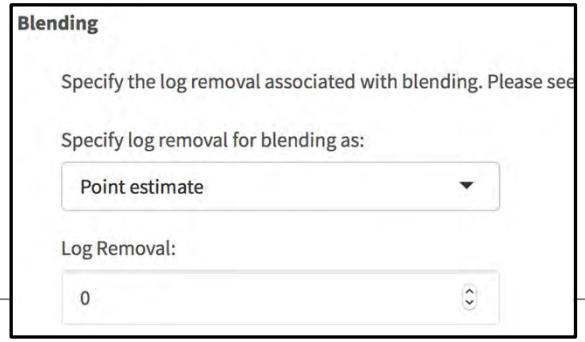
2. Treatment Train (Point Estimate)



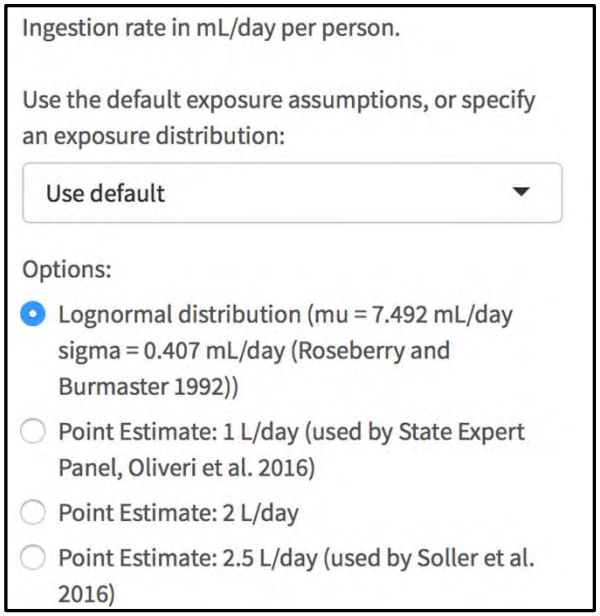
3. Treatment Failure (None)



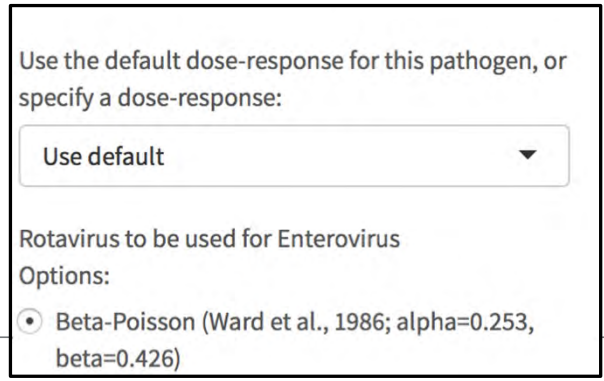
4. Management Barriers (None)



5. Exposure (Default)



6. Dose Response (Default)



Case Study 1: Example Output

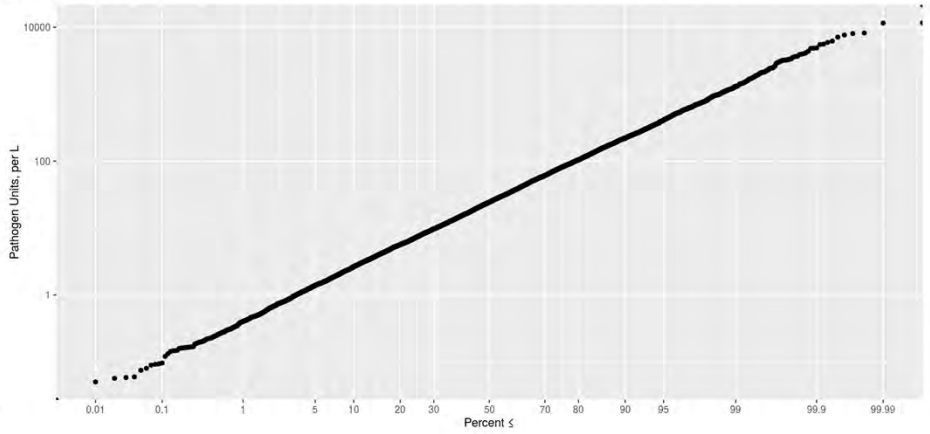
Raw Wastewater Pathogen Concentration

Pathogen: Enterovirus
Enumeration method: Culture
Input specification: Lognormal distribution
The user-provided log mean value: 3.19
The user-provided log SD value: 1.74

Summary statistics:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.050	7.457	24.368	106.247	79.578	11634.718

Plot of concentration data used:



Dose-Response

Dose-Response specification: Beta-Poisson
Dose data used (per 15-min exposure period) (Without Treatment Failure), and calculated
Summary statistics:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
2.000e-16	1.057e-13	4.556e-13	4.218e-12	1.963e-12	9.208e-10

(Distribution of enterovirus doses)

Processing Table (Without Treatment Failure) (Raw data available for download)

Each row represents a 15-min risk calculation.
Show 5 entries Search:

	input	lr	blending_lr	dilution_lr	dieoff_lr	lr_with_mb	Ceff	exposur
1	2.18142236193674	12	0	0	0	12	2.18142236193674e-12	1020.732982230
2	25.9632567082336	12	0	0	0	12	2.59632567082336e-11	1821.831394193
3	6.43870554439972	12	0	0	0	12	6.43870554439972e-12	1314.809048653
4	35.1425510125799	12	0	0	0	12	3.51425510125799e-11	1955.514476548
5	290.161035111467	12	0	0	0	12	2.90161035111467e-10	3204.123818815

Showing 1 to 5 of 10,000 entries Previous 1 2 3 4 5 … 2000 Next
Download Data (Without Treatment Failure)

Case Study 1: Sensitivity Analysis

- **User Input Files**
  - A series of user input files will be provided on the tool website for users to reproduce the case studies
  - Case Study 1: implications of a normally distributed treatment train LRV of 12 with different standard deviations

2. Treatment Train (Alternative)

Select the treatment specification:

Input file with overall log removals

BROWSE... LRVMean12StDev05.csv

Upload complete

Normal Distribution:
68% of LRVs fall within
+/- 1 standard deviation of mean

95% of LRVs fall within
+/- 2 standard deviations of mean

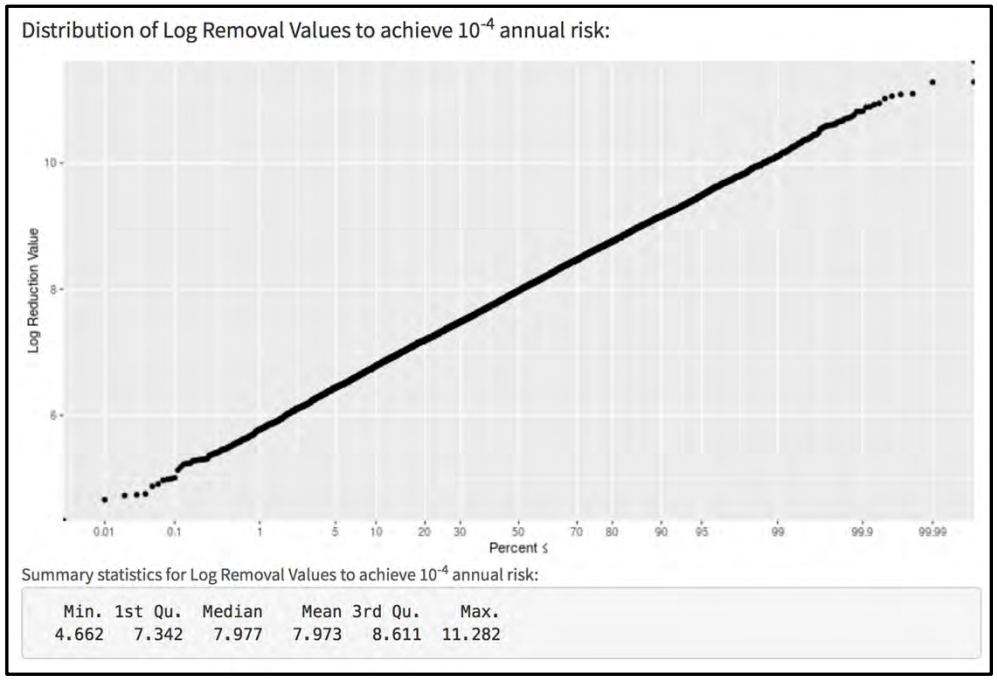
Treatment specification: Overall log removal point estimate

Treatment Process Summary of overall log removal:

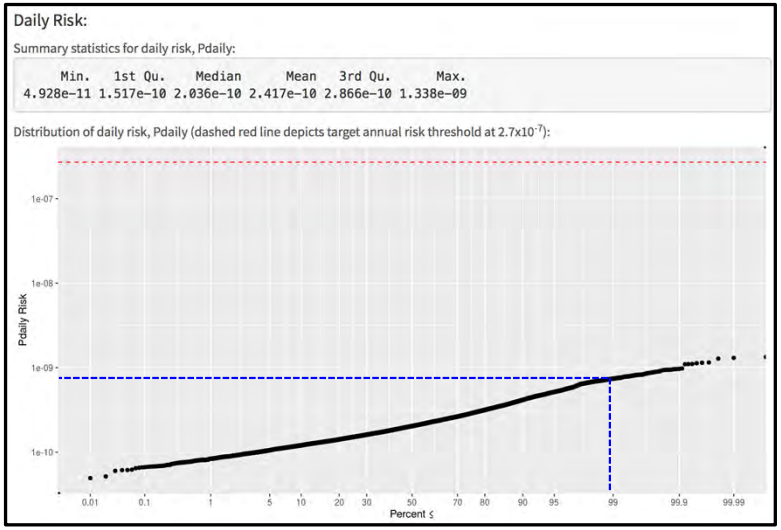
Min.	1st Qu.	Median	Mean	3rd Qu.	Max.		
12	12	12	12	12	12	$\mu = 12.0$	$\sigma = 0.0$
10.19	11.65	11.99	11.99	12.33	13.80	$\mu = 12.0$	$\sigma = 0.5$
8.379	11.308	11.979	11.981	12.650	15.590	$\mu = 12.0$	$\sigma = 1.0$
6.719	11.026	12.000	12.015	13.018	17.530	$\mu = 12.0$	$\sigma = 1.5$

Case Study 1: QMRA

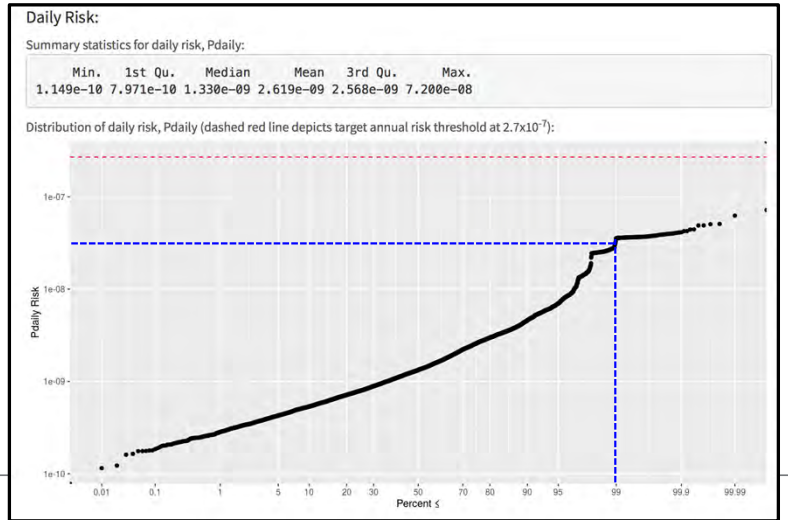
Benchmark LRVs to Achieve 10^{-4} Annual Risk of Infection



LRV = 12±0.0
LRV_{min} = 12.0
$P_{daily,99}$ = 9×10^{-10}



LRV = 12±1.0
LRV_{min} = 8.4
$P_{daily,99}$ = 5×10^{-8}

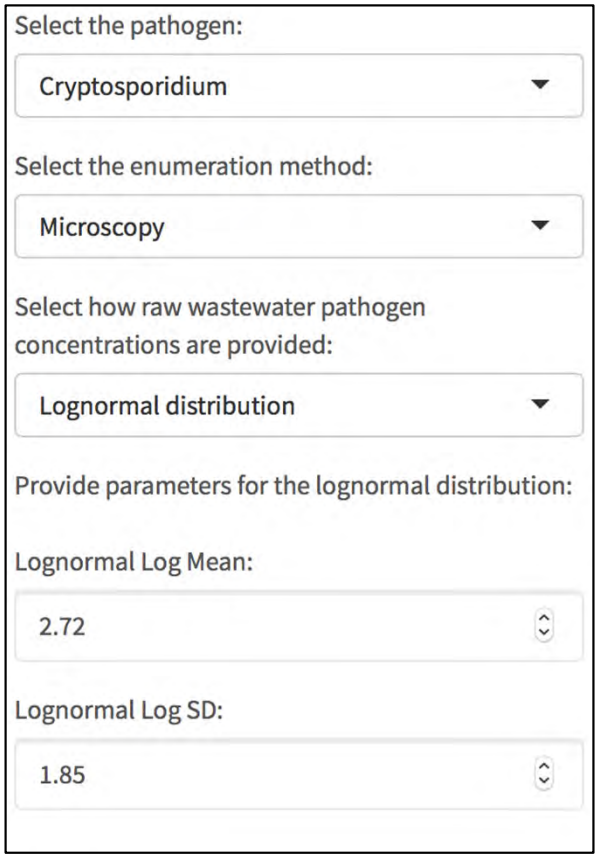


Case Study 2: Crypto in a FAT-Based DPR Scenario

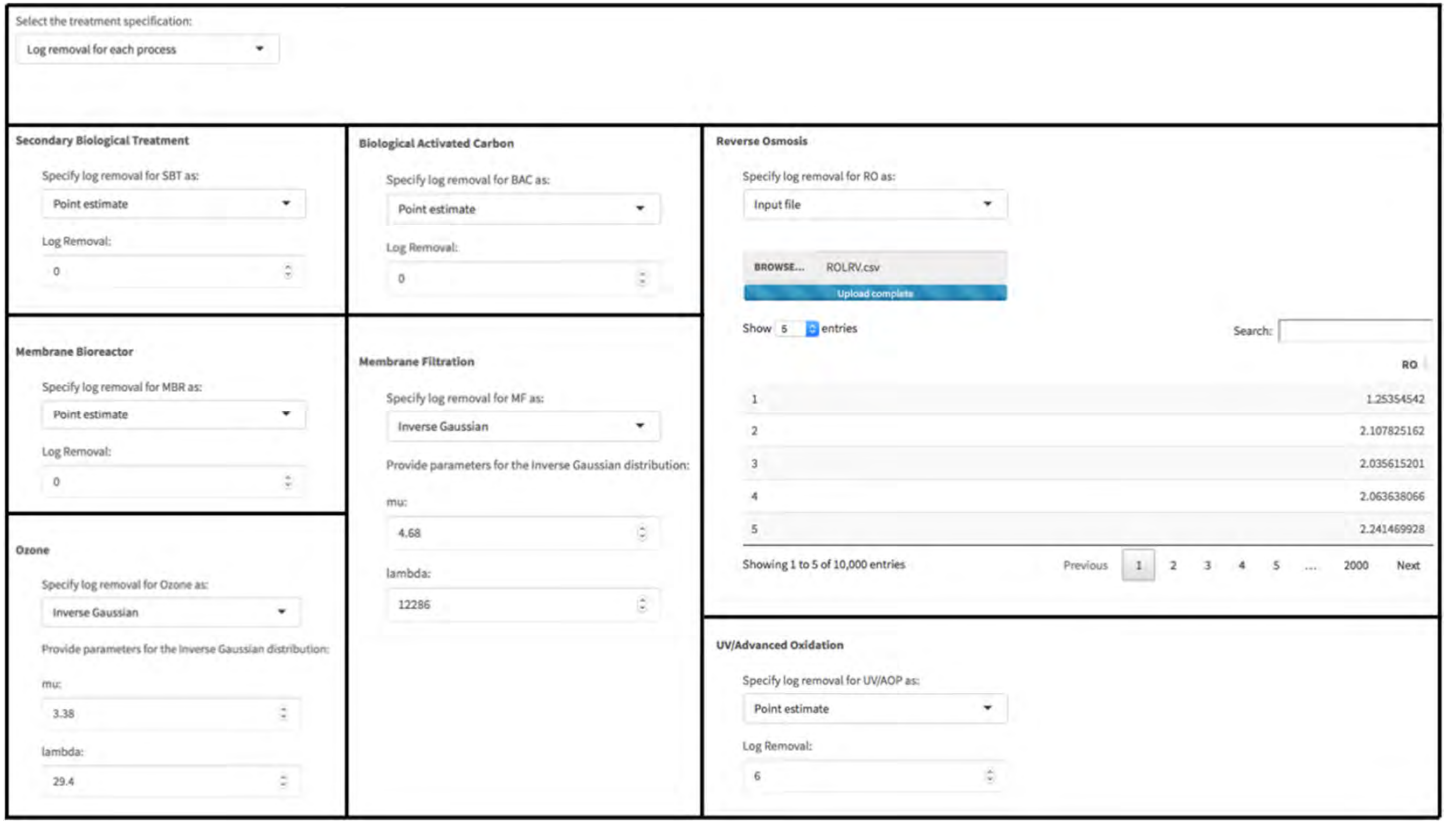
- Direct comparison with published data from City of San Diego demo facility (Pecson et al., 2017)
- LRVs for each unit treatment process
  - Inverse Gaussian distributions/point estimates from publication
  - Input file upload for RO treatment (bimodal: TOC surrogate used 85% of the time and EC surrogate used 15% of the time)
- Failure framework
  - Global failures of specified magnitude, frequency, and duration

Case Study 2: Inputs

1. Raw WW Pathogen Conc.



2. Treatment Train (Point Estimate)



Case Study 2: Inputs

3. Treatment Failure

Magnitude: Specify a percentage, representing the reduction LRV = 0, 50% reduced a LRV of 4 to 4x(100-50)/100 = 2).
Percentange failure (0 - 100):

100

Duration: Select how long it will last (in hours. max is 24 hrs)
Specifify hours:

0.25 — 24

0.25 2.75 5.25 7.75 10.25 12.75 15.25 17.75 20.25 22.7524

Frequency:
Should the frequency be applied as a daily probability of a failure or as a deterministic number of failure days per year:

Deterministic

Select how many failures per process per year
Number of failures:

1

4. Management Barriers (None)

Blending

Specify the log removal associated with blending. Please see

Specify log removal for blending as:

Point estimate

Log Removal:

0

5. Exposure (Default)

Ingestion rate in mL/day per person.

Use the default exposure assumptions, or specify an exposure distribution:

Use default

Options:

- (•) Lognormal distribution (mu = 7.492 mL/day sigma = 0.407 mL/day (Roseberry and Burmaster 1992))
- ( ) Point Estimate: 1 L/day (used by State Expert Panel, Oliveri et al. 2016)
- ( ) Point Estimate: 2 L/day
- ( ) Point Estimate: 2.5 L/day (used by Soller et al. 2016)

6. Dose Response (Default)

Use the default dose-response for this pathogen, or specify a dose-response:

Specify a dose-response

Dose-response specification:

Beta-Poisson

The Beta-Poisson dose-response is characterized by parameter, alpha:

Parameter specification:

Point estimate

Parameter value:

0.116

The Beta-Poisson dose-response is characterized by parameter, beta:

Parameter specification:

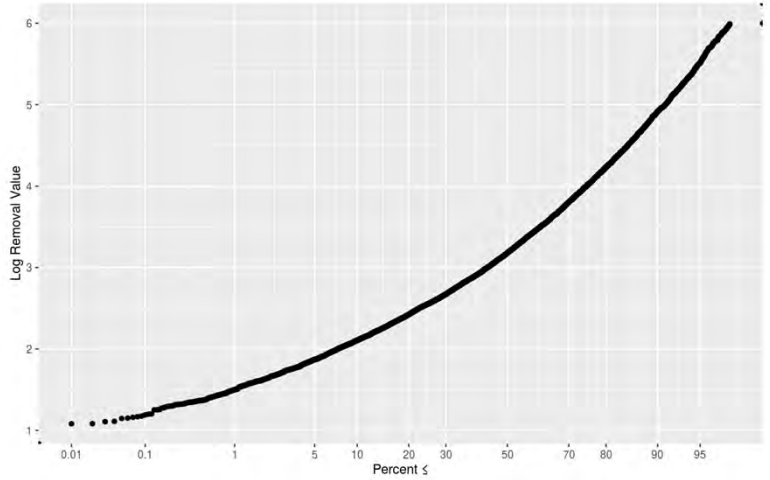
Point estimate

Parameter value:

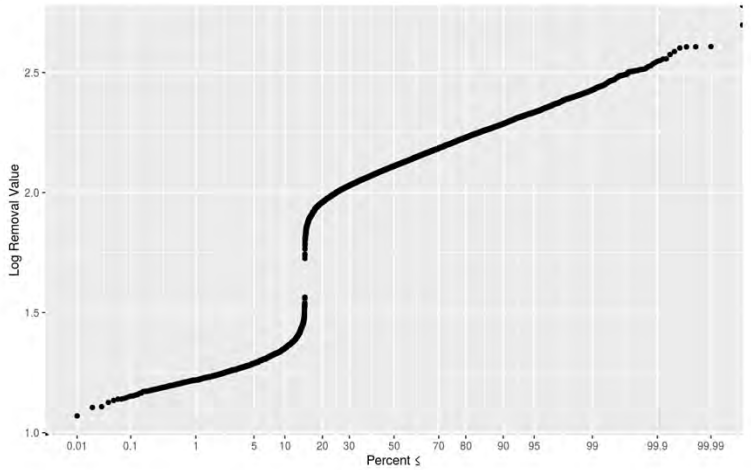
0.121

Case Study 2: PATTP Results

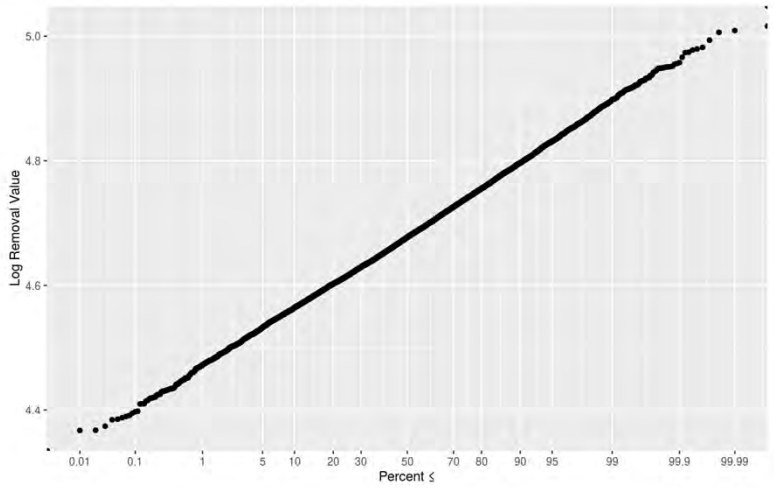
Ozone



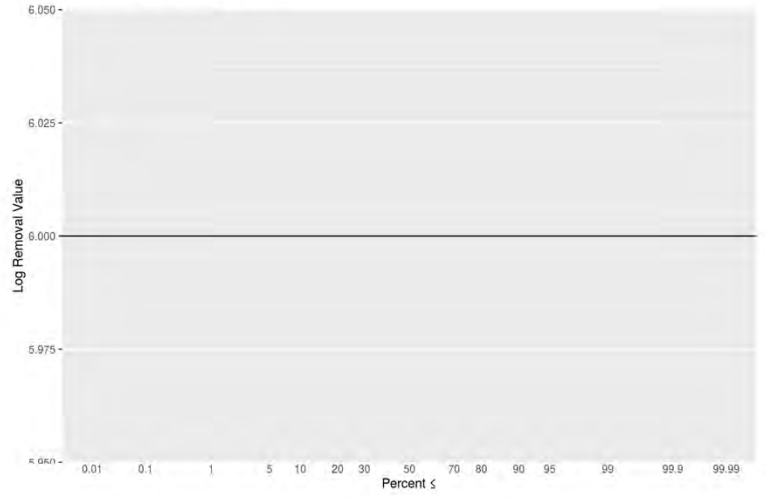
Reverse Osmosis



Membrane Filtration

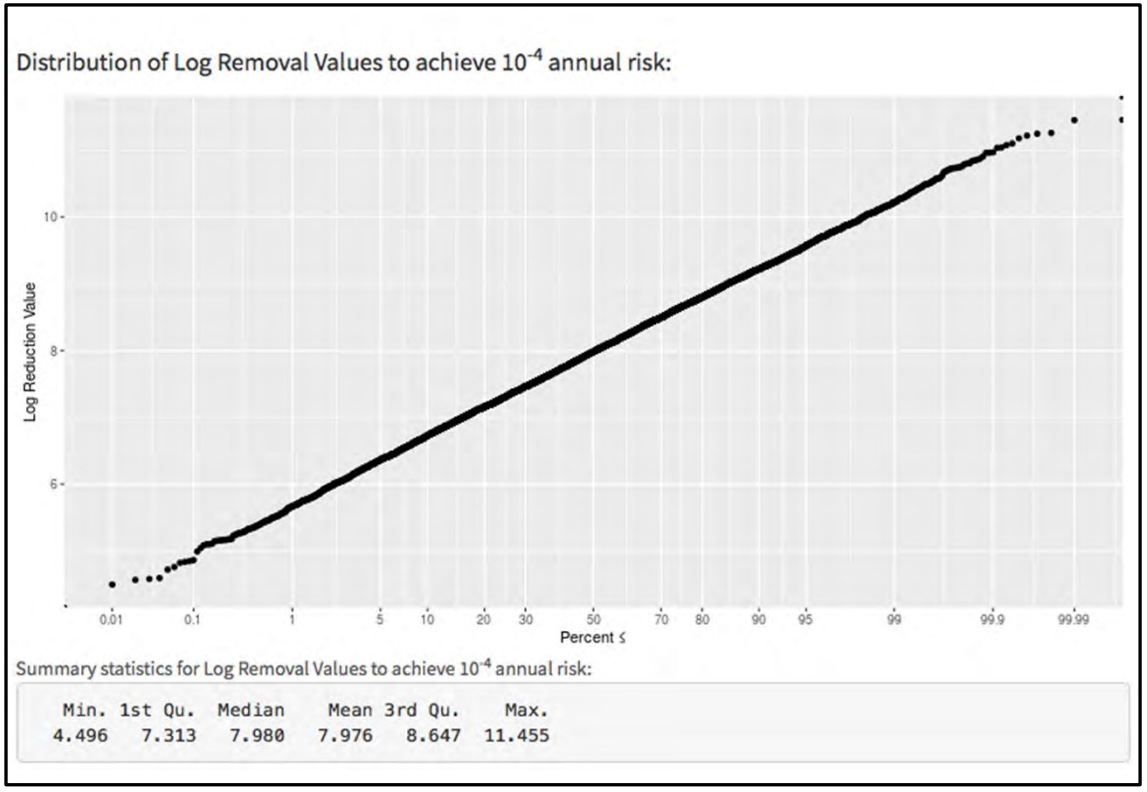


UV/Advanced Oxidation Process



Case Study 2: PATTP Results

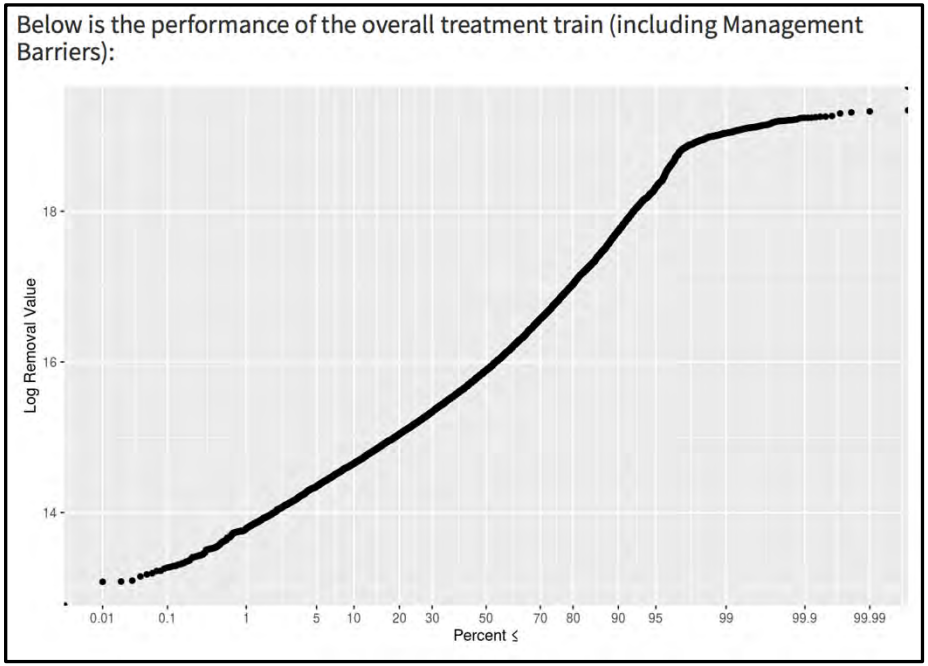
Benchmark LRVs



Summary statistics for Log Removal Values to achieve 10^{-4} annual risk:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
4.496	7.313	7.980	7.976	8.647	11.455

Simulated LRVs



What LRVs are needed to achieve 10^{-4} annual risk target?

What LRVs are actually achieved by the treatment train?

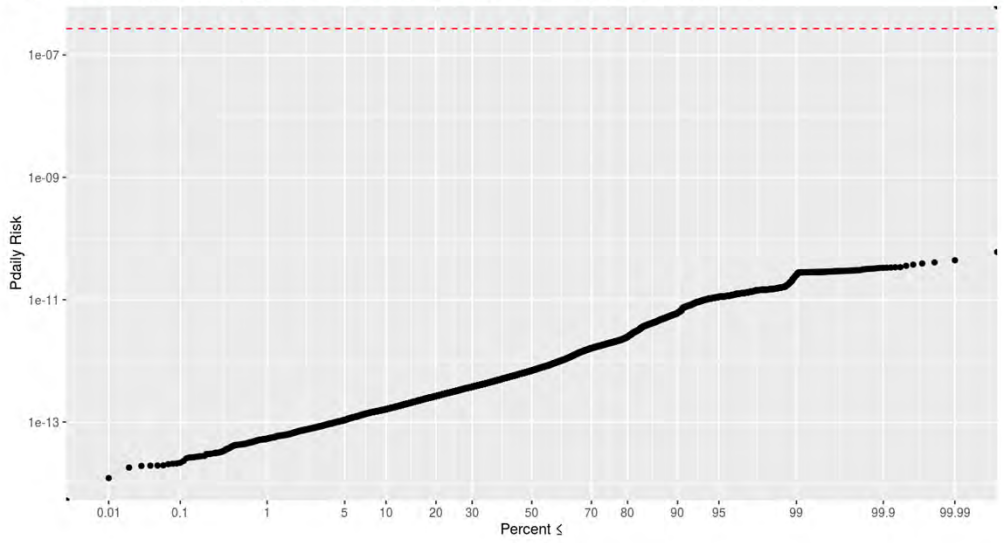
Case Study 2: QMRA (No Failures)

Daily Risk:

Summary statistics for daily risk, Pdaily:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
1.210e-14	3.185e-13	6.932e-13	2.265e-12	1.933e-12	5.993e-11

Distribution of daily risk, Pdaily (dashed red line depicts target annual risk threshold at 2.7×10^{-7}):

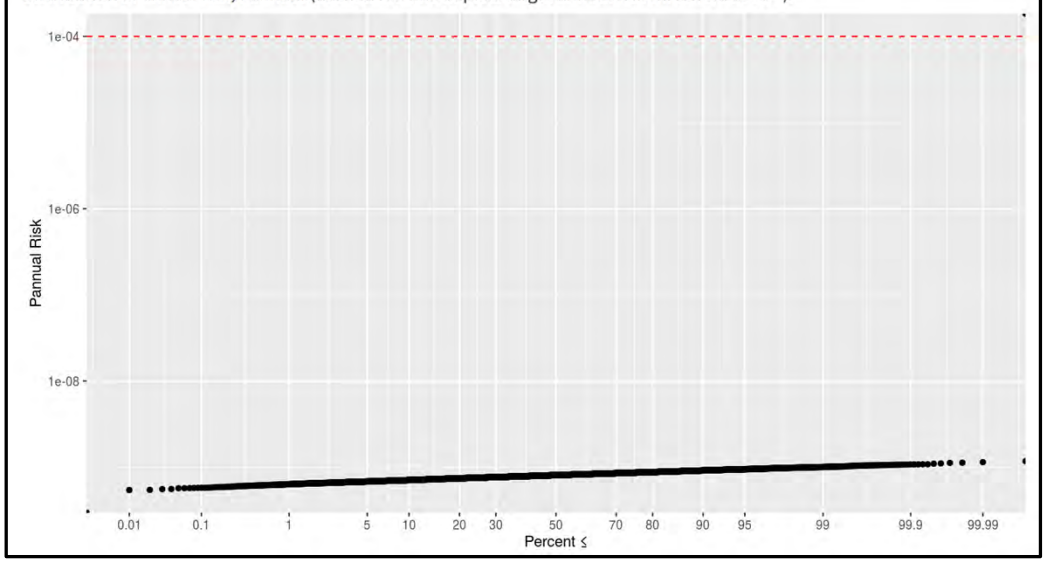


Annual Risk:

Summary statistics for annual risk, Pannual:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
5.429e-10	7.555e-10	8.076e-10	8.105e-10	8.633e-10	1.176e-09

Distribution of annual risk, Pannual (dashed red line depicts target annual risk threshold at 10^{-4}):



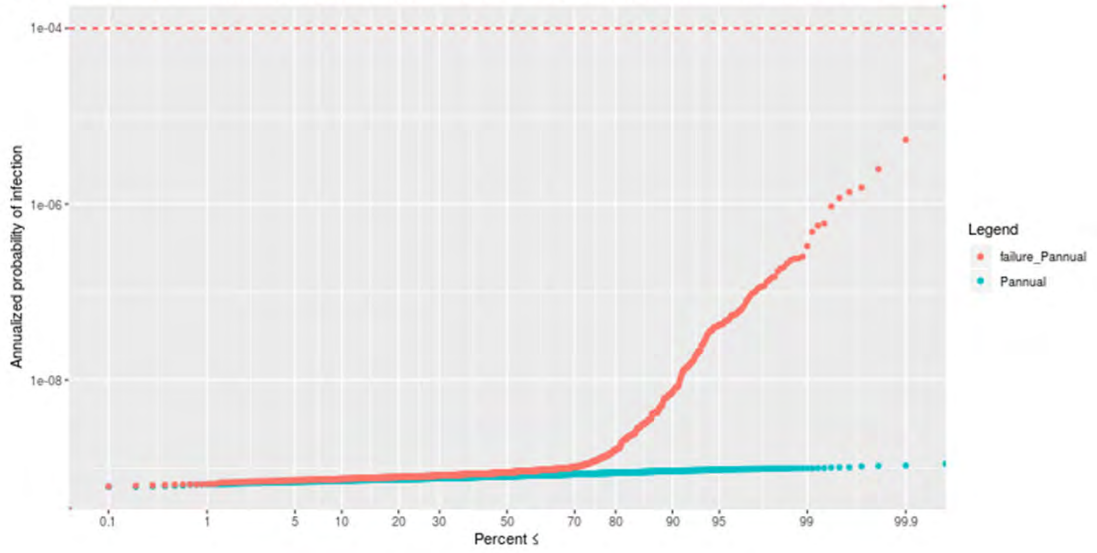
Case Study 2: Failure Results and Comparison

Annual Risk:

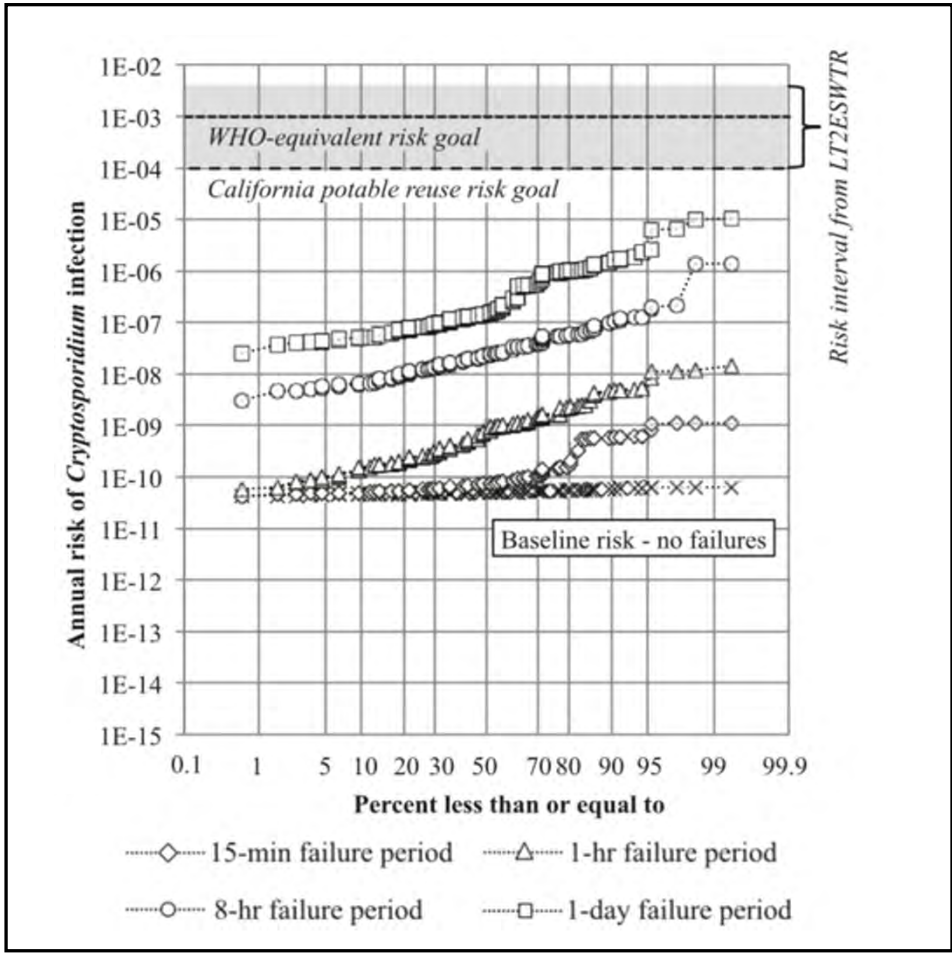
Summary statistics for annual risk, Pannual (with/without failure):

```
    Pannual          failure_Pannual
Min.   :6.057e-10   Min.   :6.160e-10
1st Qu.:7.523e-10   1st Qu.:8.010e-10
Median :8.029e-10   Median :8.900e-10
Mean   :8.100e-10   Mean   :4.901e-08
3rd Qu.:8.621e-10   3rd Qu.:1.188e-09
Max.   :1.109e-09   Max.   :2.782e-05
```

Plot of annual risk, Pannual (with/without failure) (dashed red line depicts target annual risk threshold at 10^{-4}):



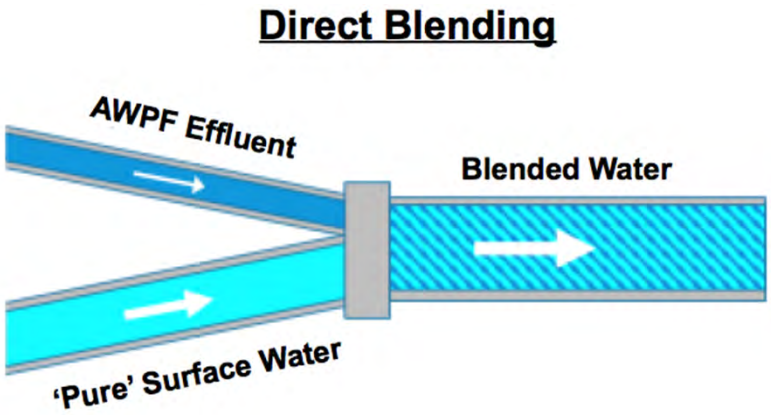
QA/QC Approach?

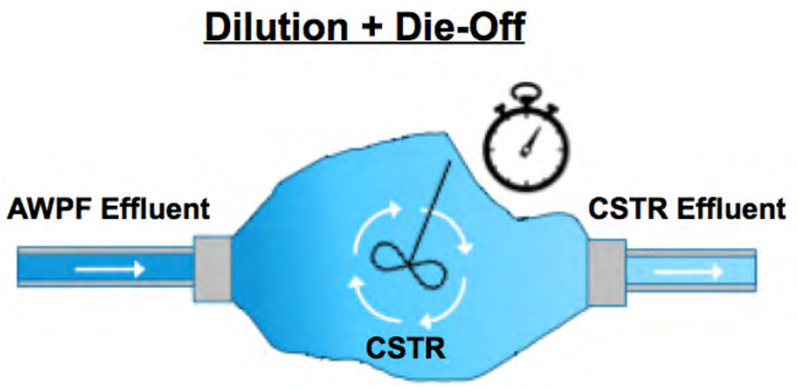


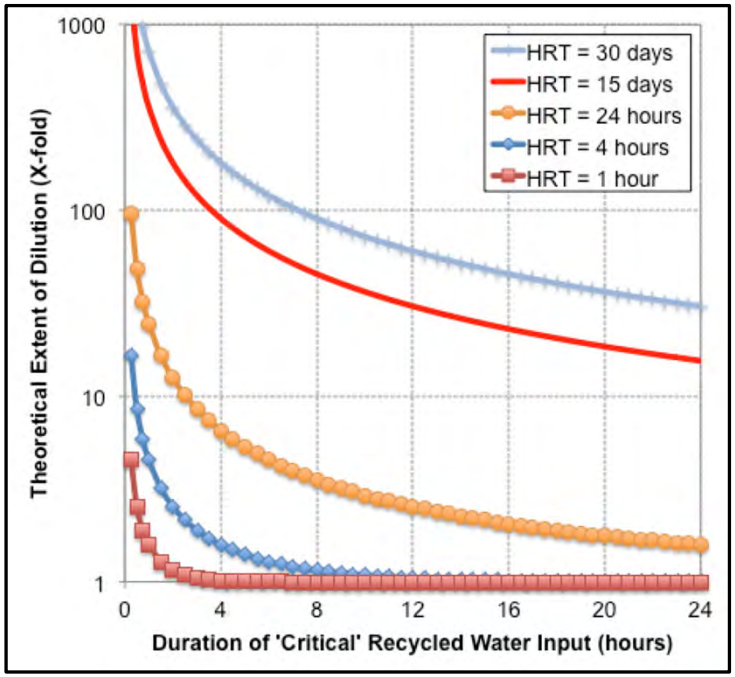
Case Study 3: Adenovirus in a FAT-Based DPR Scenario

- Direct comparison with published data from Soller et al. (2018)
- Combination of default model inputs vs. customized model inputs
  - Default inputs for treatment LRVs: uniform, normal, and point estimates
  - User input file: Log_{10}uniform distribution for raw wastewater adenovirus concentration
- Failure framework
  - Comparison of short-duration (15-min) vs. long-duration (3-hr) failures to duplicate published data

Final Notes: “Management Barriers”







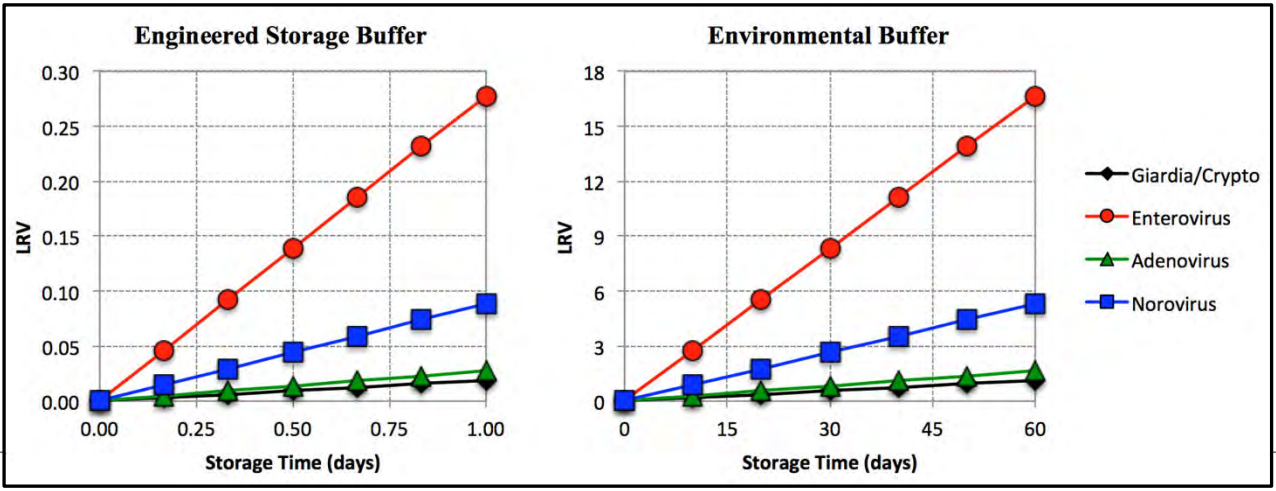
1. How can an ideal ‘CSTR’ (tank) be used to model dilution in small reservoirs or engineered storage buffers?

2. How can response retention time (RRT) be integrated into the management barrier?

Final Notes: "Management Barriers"

Pathogen	N	Base *e* Mean[1] (d^{-1})	Lognormal Dist. (d^{-1})		Source
			μ	σ	
Giardia	14	0.044	-3.132	2.211	Boehm et al. (2018)
Cryptosporidium	22	0.041	-3.201	1.842	Boehm et al. (2018)
Virus (all)	8	0.155	-1.865	1.152	Boehm et al. (2018)
Enterovirus[2,3]	96	0.640	-0.446	1.054	Boehm et al. (2019)
Pathogen	**N**	**Base *e* Median (d^{-1})**	**Range (d^{-1})**		**Source**
			Min	**Max**	
Adenovirus[2]	8	0.063	0.021	0.288	Boehm et al. (2019)
Norovirus[2,4]	5	0.205	0.020	0.368	Boehm et al. (2019)

[1]Calculated as e^{μ} with μ from reported lognormal distribution; [2]Includes reported values for experiments performed with culture methods and in freshwater (no distinction for temperature); [3]Determined from maximum likelihood estimation in Matlab; [4]Based on experiments with murine norovirus.



$$LRV = \frac{k\ (days^{-1}) \times time\ (days)}{2.303}$$

Implications of including or excluding pathogen die-off?

Dependent on the application, specifically the amount of storage or travel time and the environmental conditions.

Location: Teleconference
Date: August 4, 2020
Time: 9:00am – 1:00pm PDT

DPR-1 QMRA/PATTP Workshop Agenda

Join the Meeting: https://global.gotomeeting.com/join/927704405
Call-in: +1 (646) 749-3112
Access Code: 927-704-405

Time	Topic	Speaker(s)
9:00 am – 9:05 am	Welcome & Introductions	Brian Pecson
9:05 am – 9:25 am	Case Study 1	Edmund Seto
9:25 am – 9:45 am	Case Study 2	Edmund Seto
9:45 am – 10:05 am	Case Study 3	Edmund Seto
10:05 am – 10:50 am	Expanded Investigations • Impact of raw wastewater pathogen concentration assumptions • Impact of treatment redundancy	TWG and Research Team
10:50 am – 11:00 am	10-min Break	
11:00 am – 12:00 pm	Expanded Investigations • Impact of treatment variability • Impact of failure assumptions • Sensitivity analysis	TWG and Research Team
12:00 pm – 12:50 pm	Ask the Experts – Q&A	All
12:50 pm – 1:00 pm	Next Steps	Brian Pecson

DPR-1 QMRA/PATTP WORKSHOP

August 4, 2020

INTRODUCTIONS

- Technical Working Group
  - Brian Pecson, Trussell Technologies (Chair)
  - Nick Ashbolt, University of Alberta
  - Charles Haas, Drexel University
  - Theresa Slifko, Metropolitan Water District
- Research Team
  - Dan Gerrity, Southern Nevada Water Authority
  - Edmund Seto, University of Washington
- Additional Staff
  - Anya Kaufmann, Trussell Technologies
- WRF/State Board Coordination
  - Adam Olivieri
- State Water Board
  - Faraz Asad
  - Randy Barnard
  - Brian Bernados
  - Steven Book
  - Jing Chao
  - Candida Granillo-Dodds
  - Saeedreza Hafeznezami
  - Bob Hultquist
  - Eugene Leung
  - Aide Ortiz
  - Sherly Rosilela
  - Dave Spath
  - Kurt Souza
  - Mark Bartson
  - Robert Brownwood
  - Tricia Lee
  - Laura McLellan
  - Claire Waggoner
- Water Research Foundation
  - Julie Minton
  - Erin Partlan

AGENDA

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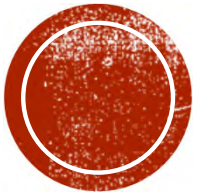
12:50 pm – 1:00 pm	Next Steps	Brian Pecson



CASE STUDIES

Edmund Seto

DPRisk Tutorial

Edmund Seto

August 4, 2020

Case Study 1:
QMRA for Enterovirus in a Default DPR Scenario

This case study demonstrates a quantitative microbial risk assessment for Enterovirus, using virus data from DPR-2.

The case study also demonstrates a sensitivity analysis on the the dose response model and also differential performance between AWPFs, including differences in overall redundancy and facilities with tight tolerances on critical control points vs. facilities with less stringent monitoring of operational performance.

Learning objectives

1. Take a "walk through" of the different sections of the tool
2. Understand how to specify raw wastewater concentrations
3. See how default settings provided with the tool can make it easier to setup model scenarios
4. Become familiar with providing user-specified input files to expand the features of the tool

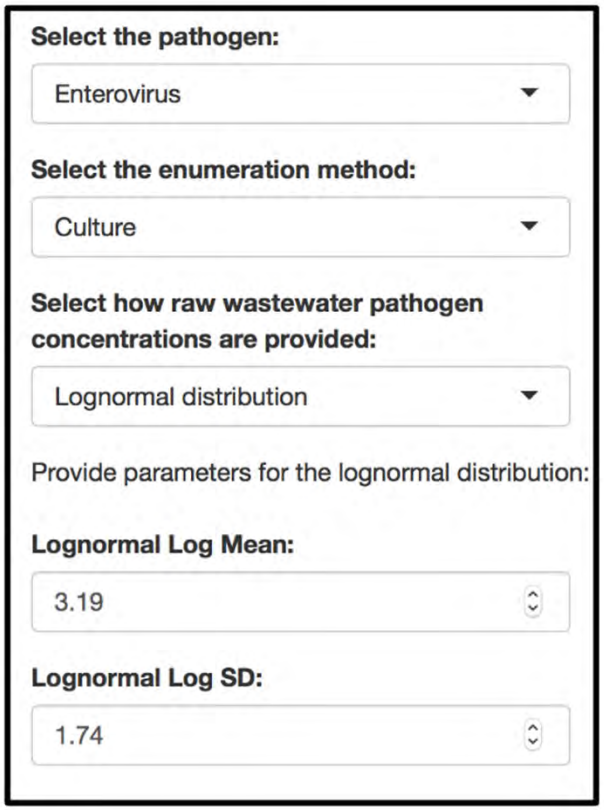
Let's get started…

Step 1: Specify Raw Wastewater Concentrations

- Select from the left side of the tool, "Raw Wastewater Pathogen Concentrations"

- Select enterovirus as our pathogen, and culture as the enumeration method.
- Enter in the statistical distribution for enterovirus raw wastewater concentration based on DPR-2.

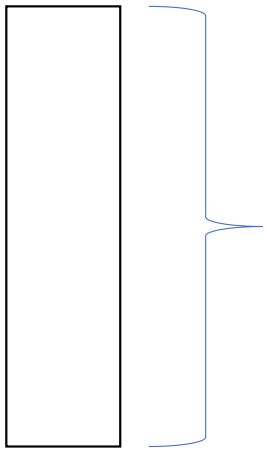
  A lognormal distribution with
  log mean of 3.19
  log SD of 1.74



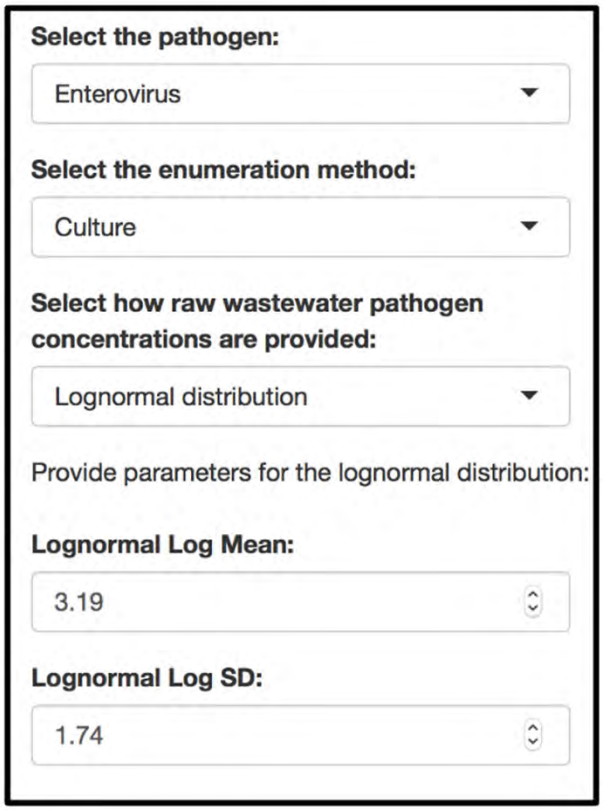
Step 1: Specify Raw Wastewater Concentrations

- What happens in the background in DPRisk is a parameter set starts to be created for the model…

Input raw virus concentrations (MPN/L)

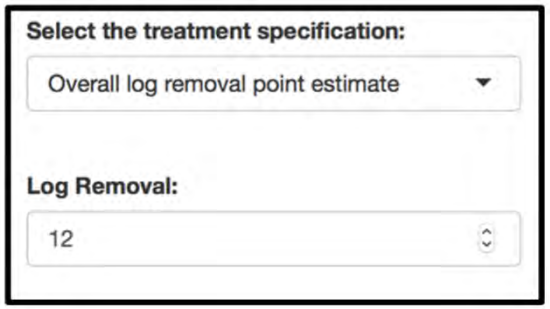


10,000 values.
Each one represents a 15-min conc



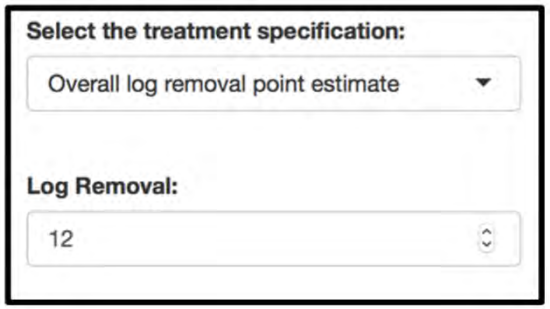
Step 2: Specify Treatment Train

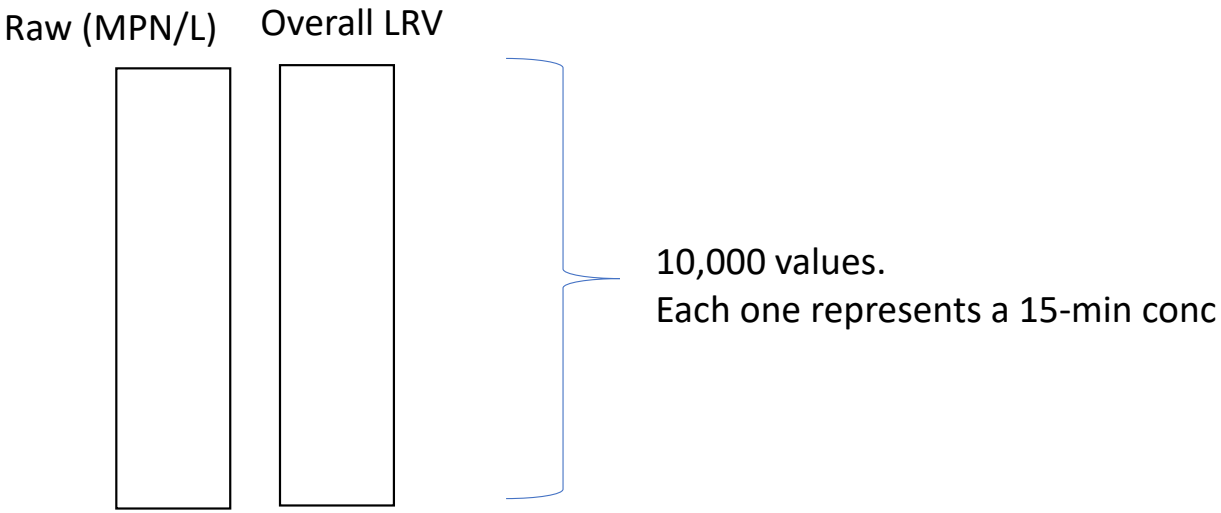
- Select from the left side of the tool, "Treatment Train"
- For this case study, we'll specify a single LRV for the entire treatment train.
- This is provided as an "Overall log removal point estimate"
- The LRV will be specified as 12 which is consistent with the California potable reuse regulatory framework for groundwater replenishment when targeting viruses.



Step 2: Specify Treatment Train

- Again, more calculations are performed in the background by the tool…

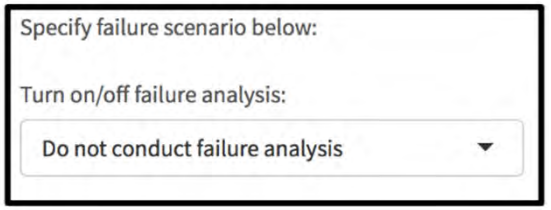




Step 3. Treatment Failure Specification

- Select from the left side of the tool, "Treatment Failure"

- In this case study, we will not incorporate treatment failures, so leave this set to "Do not conduct failure analysis"



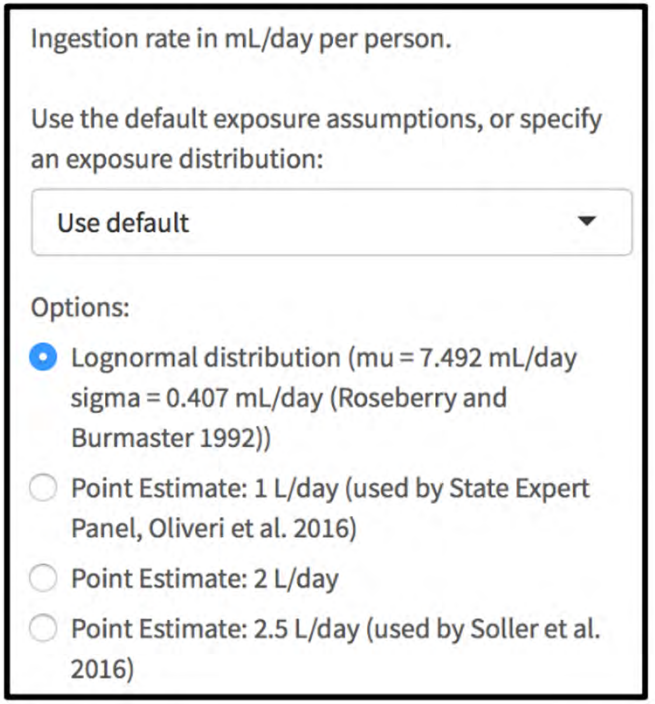
Step 4. Management Barriers

- Select from the left side of the tool, "Management Barriers"

- In this case study, we will not incorporate management barriers, such as blending, dilution, or die-off, so keep the default LRV values of 0.

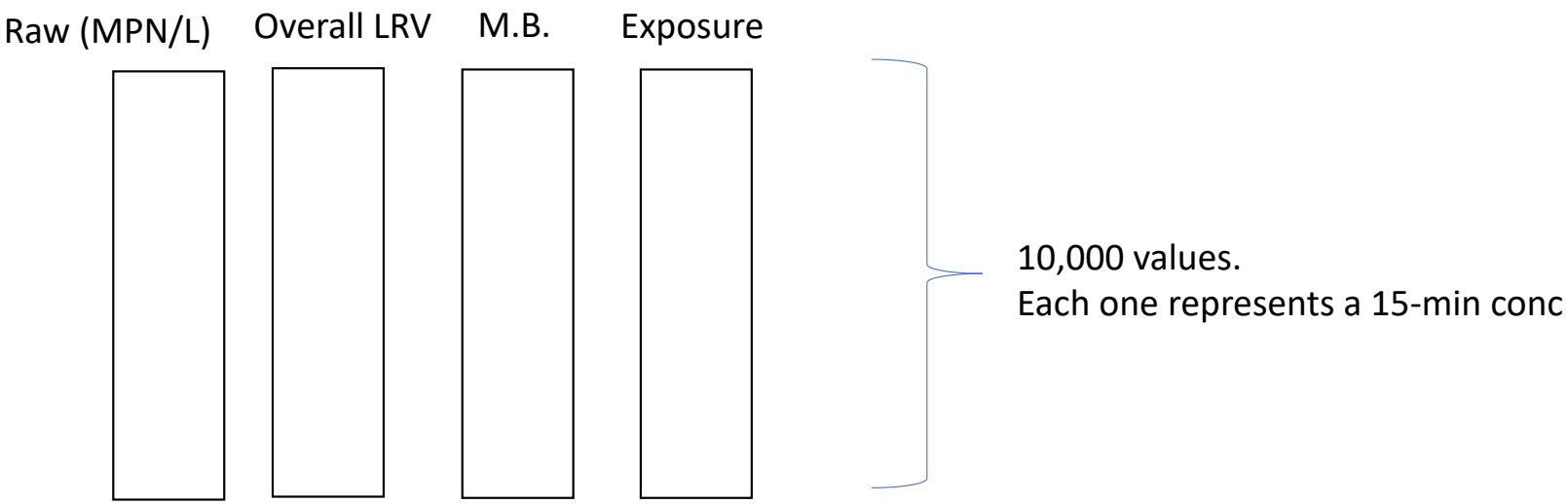
Step 5. Exposure

- Select from the left side of the tool, "Exposure"
- Notice various default assumptions are provided, and be easily selected.
- We'll use the default "Lognormal distribution from Roseberry and Burmaster, 1992", which corresponds to median of 1,798 mL/day.
- The 1,798 mL is divided by 96, so that each 15-min period in the day gets an equal amount of exposure.



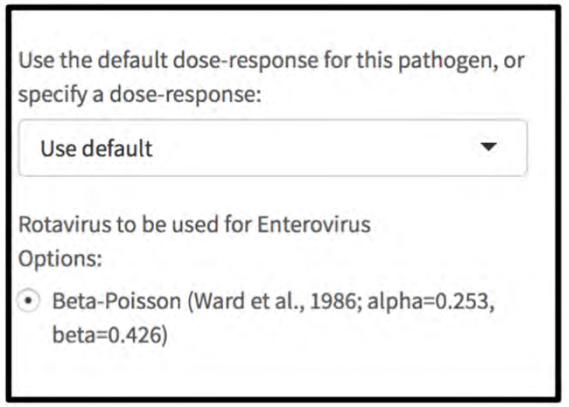
Step 5: Exposure

- Again, more calculations are performed in the background by the tool…



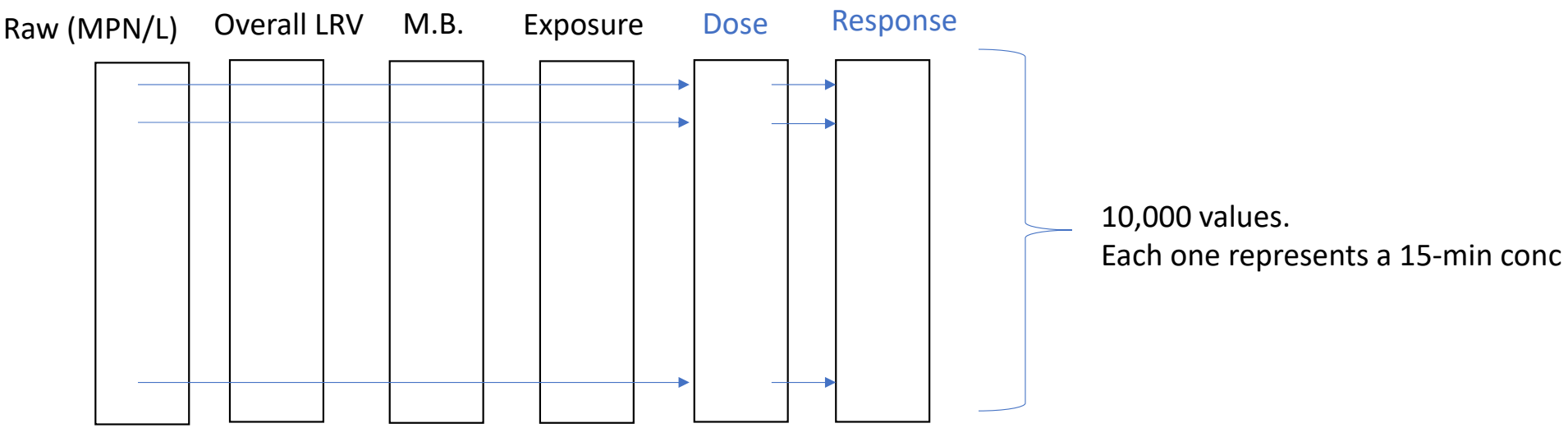
Step 6: Dose-Response

- Select from the left side of the tool, "Dose-Response"
- Notice various default assumptions are provided, and be easily selected.
- We'll use the default "Beta=Poisson from Ward et al., 1986".



Step 7. Generate Outputs

- Tool computes dose for each 15-min period.
- Then it computes the probability of infection based on the dose-response function.

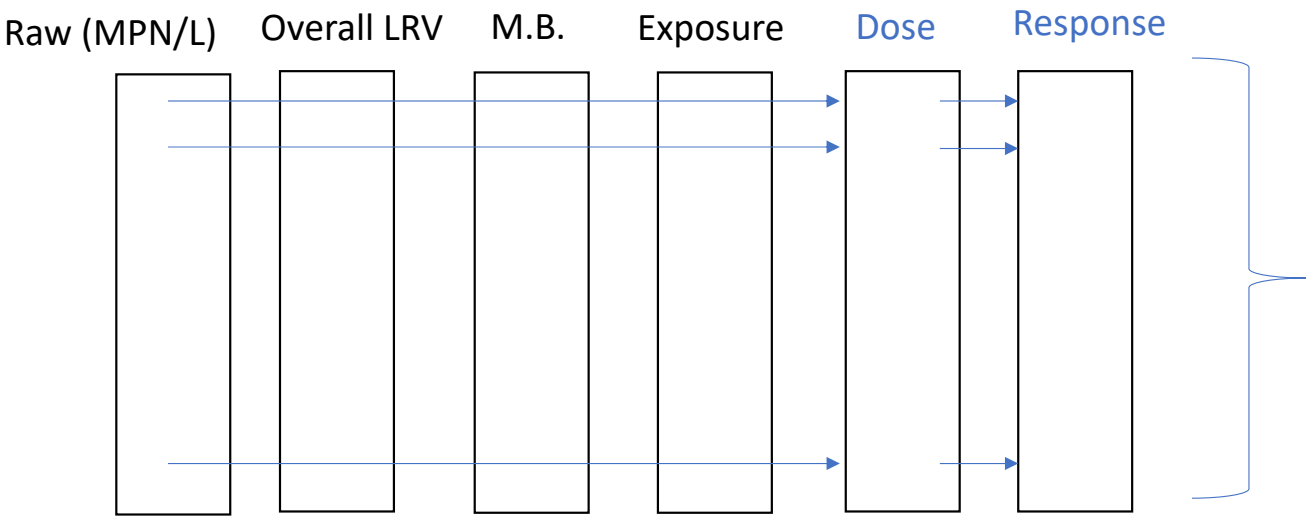


Step 7. Generate Outputs

- Performs the Benchmark PATTP calculation:
  i.e., what is the LRV that meets

Acceptable risk = dose-response ([rawWW] x [exposure] x 10^{-LRV})

This is solved for all 10,000 rows of data from below. (it assumes the risk is constant, i.e., the rawWW and exposure combo occurs every 15-min in the year).



10,000 values.
Each one represents a 15-min conc

Step 7. Generate Outputs

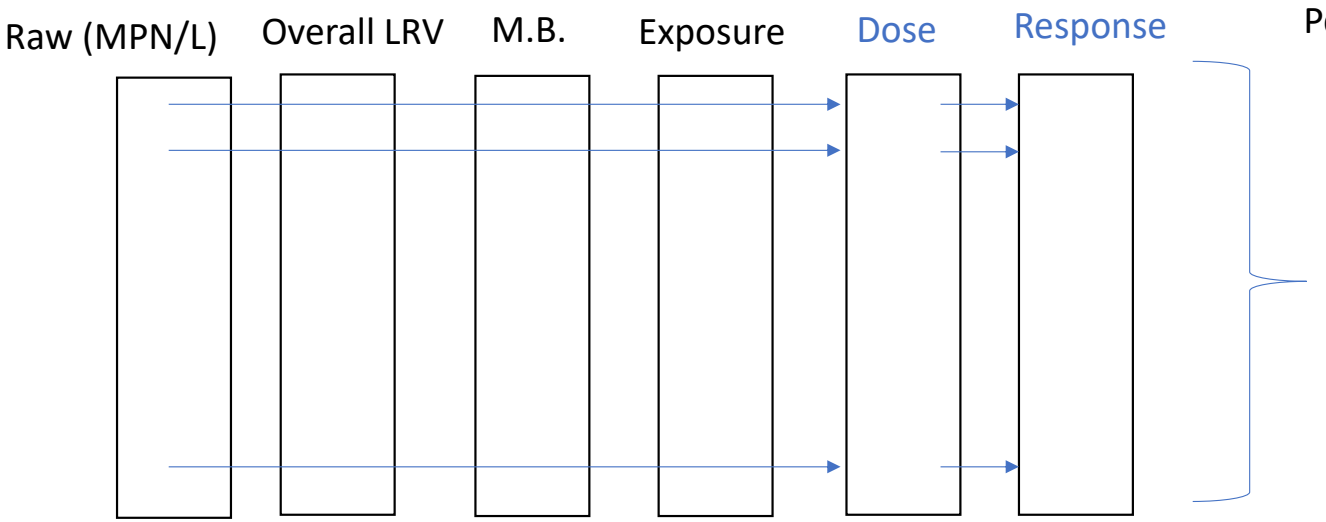
- Performs the Daily and Annualized Risk calculations

$$P_{daily} = 1 - \prod_{n=1}^{96} (1 - P_{15})$$

$$P_{annual} = 1 - \prod_{n=1}^{35,040} (1 - P_{15})$$

The P_{15} correspond to randomly sampled 15-min risks of infection drawn from the "responses" below.

The Pdaily and Pannual calculations are Monte Carlo simulated 10,000 times to generate distributions on Pdaily and Pannual.

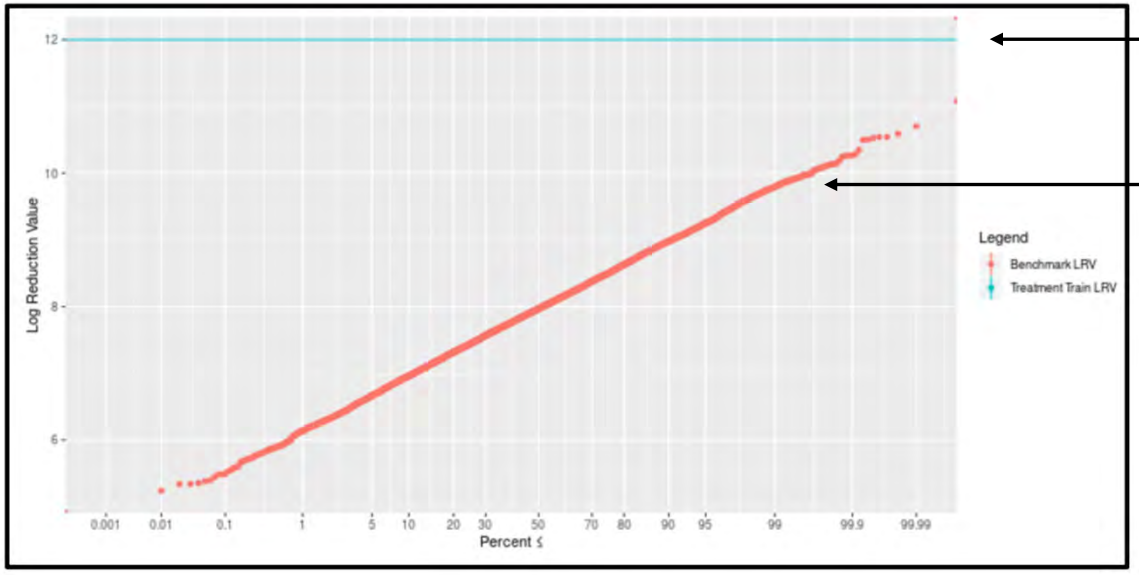


10,000 values.
Each one represents a 15-min conc

Step 8. PATTP Output

- Select from the left side of the tool, "PATTP Output"

- It will take a few seconds for the plots to generate.



The actual specified LRV in this case study was 12.

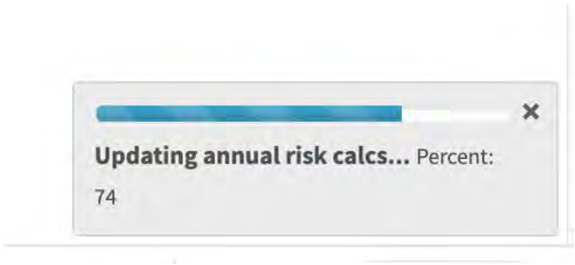
The set of points, or "curve" represents the LRV needed for each of the 15-min periods to exactly achieve an annualized risk of infection of 10^{-4}

Notice how the blue curve is under the red curve for all 10,000 values in the parameter set ➔ LRV of 12 *exceeds* the annualized risk goal 99.99% of the time for this given set of model assumptions.

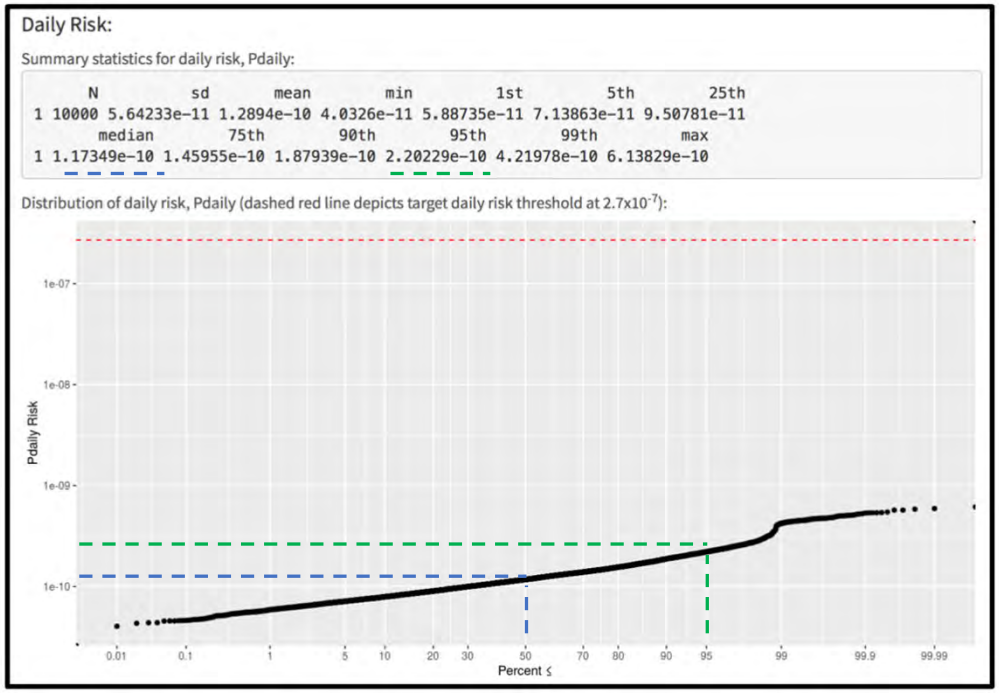
Step 9. QMRA Output

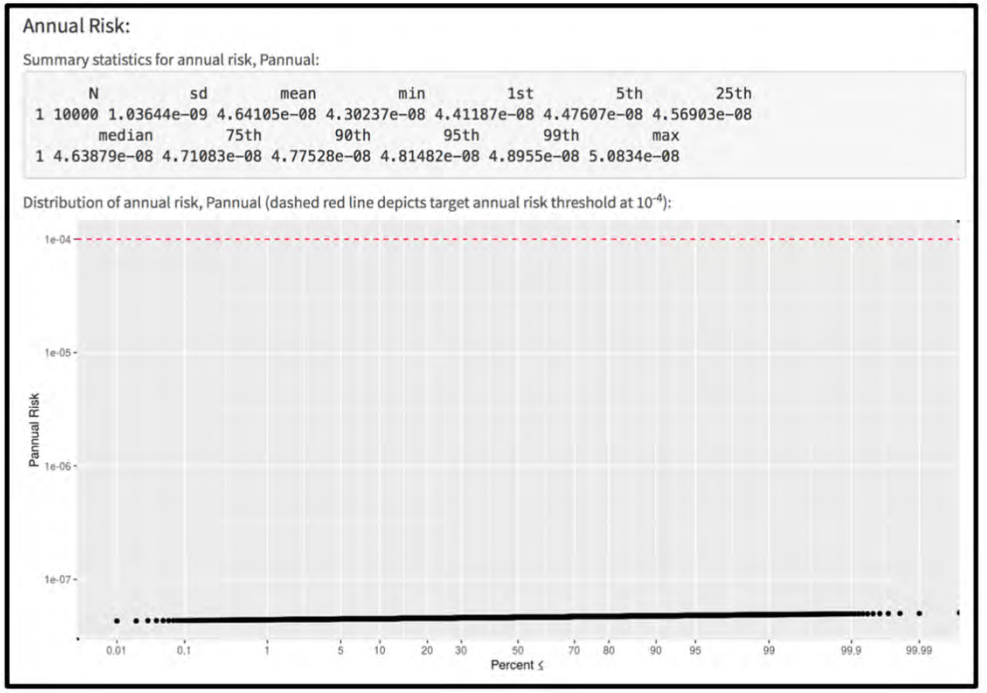
- Select from the left side of the tool, "QMRA Output"

- It will take a few seconds for the risk calculations to complete and the plots to generate.



Step 9. QMRA Output





Pause for Questions

- We'll cover some of the other steps in Case Study 1 later.

Case Study 2

Case Study 2: QMRA for *Cryptosporidium* in a FAT-based DPR Scenario

This case study is based on Pecson et al., 2017, evaluating the reliability of pathogen control at San Diego's Pure Water Demonstration Facility.

The QMRA used actual performance data collected over 1 year. This case study will demonstrate the analysis of the Pecson et al. study for Cryptosporidium.

<u>Learning objectives</u>

1. Specify individual LRVs for treatment train for each process
2. Analyze failure scenarios

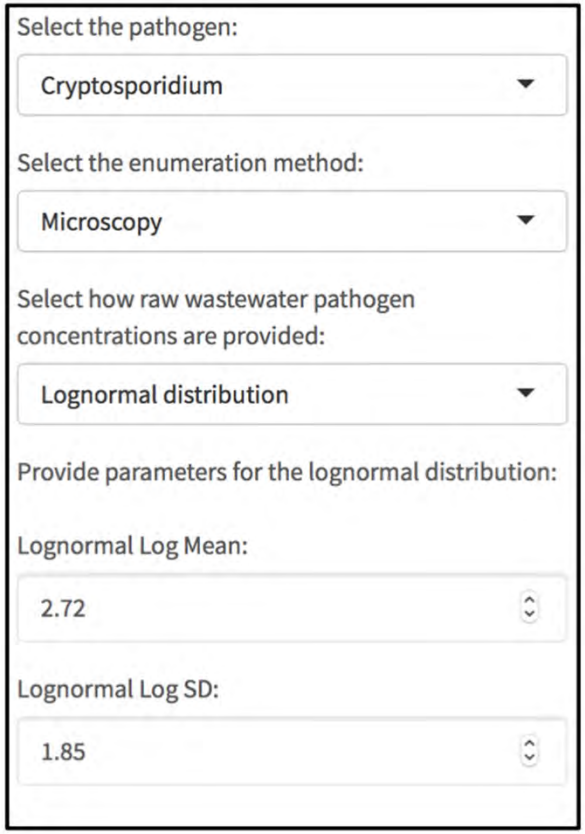
Let's get started…

Step 1: Specify Raw Wastewater Concentrations

- Select from the left side of the tool, "Raw Wastewater Pathogen Concentrations"

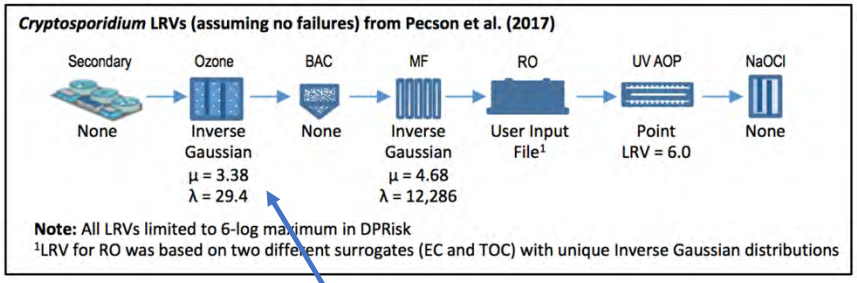
- Select Cryptosporidium as our pathogen, and Microscopy as the enumeration method.
- Enter in the statistical distribution for enterovirus raw wastewater concentration based on DPR-2.

  A lognormal distribution with
  log mean of 2.72
  log SD of 1.85

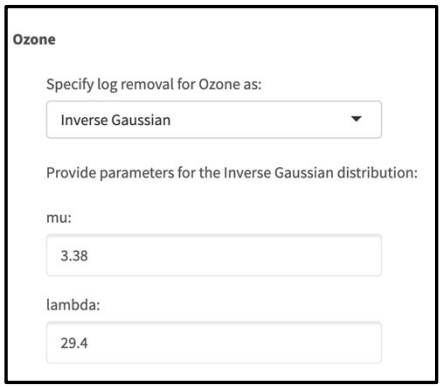


Step 2: Specify Treatment Train

- Select from the left side of the tool, "Treatment Train"



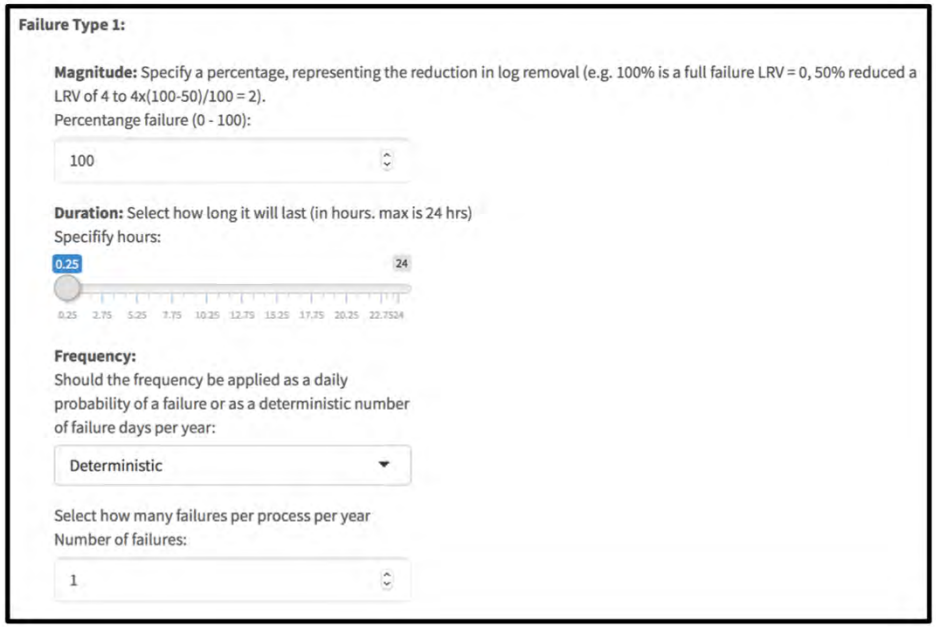
- For this case study, we'll specify a individual LRVs for each treatment train process.
- This is provided as an "Log removal for each process"
- Specify the LRV for processes according to diagram.
- Note that RO is based on a user-provided file of LRV values.



Step 3. Treatment Failure Specification

- In this case study, we will assess the potential effect of treatment failures on risk.
- Select from the left side of the tool, "Treatment Failure"

- Choose "Failure analysis with global settings"
- We will assess the impact of…
  1 failure per year…
  in which the failure magnitude is 100% (i.e., LRV goes to 0)…
  for a duration of 0.25 hours (i.e., 15 minutes).



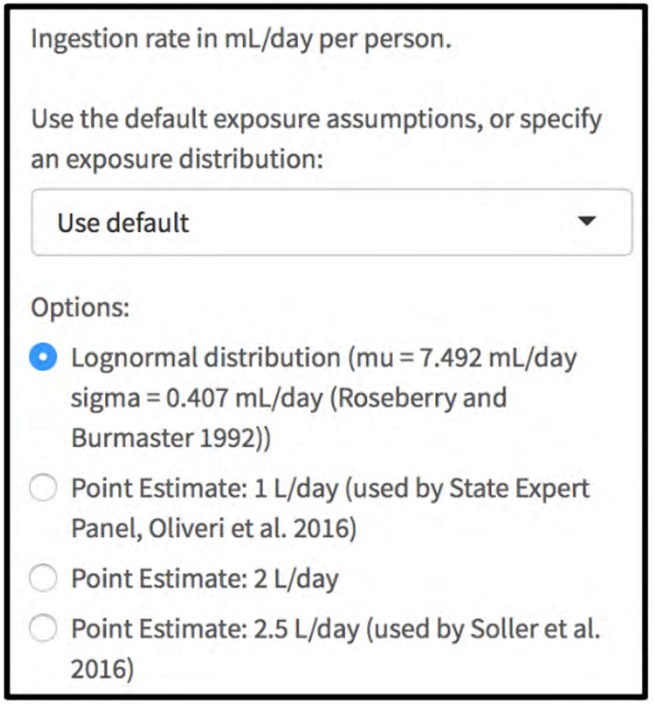
Step 4. Management Barriers

- Select from the left side of the tool, "Management Barriers"

- In this case study, we will not incorporate management barriers, such as blending, dilution, or die-off, so keep the default LRV values of 0.

Step 5. Exposure

- Select from the left side of the tool, "Exposure"
- Notice various default assumptions are provided, and be easily selected.
- We'll use the default "Lognormal distribution from Roseberry and Burmaster, 1992", which corresponds to median of 1,798 mL/day.
- The 1,798 mL is divided by 96, so that each 15-min period in the day gets an equal amount of exposure.



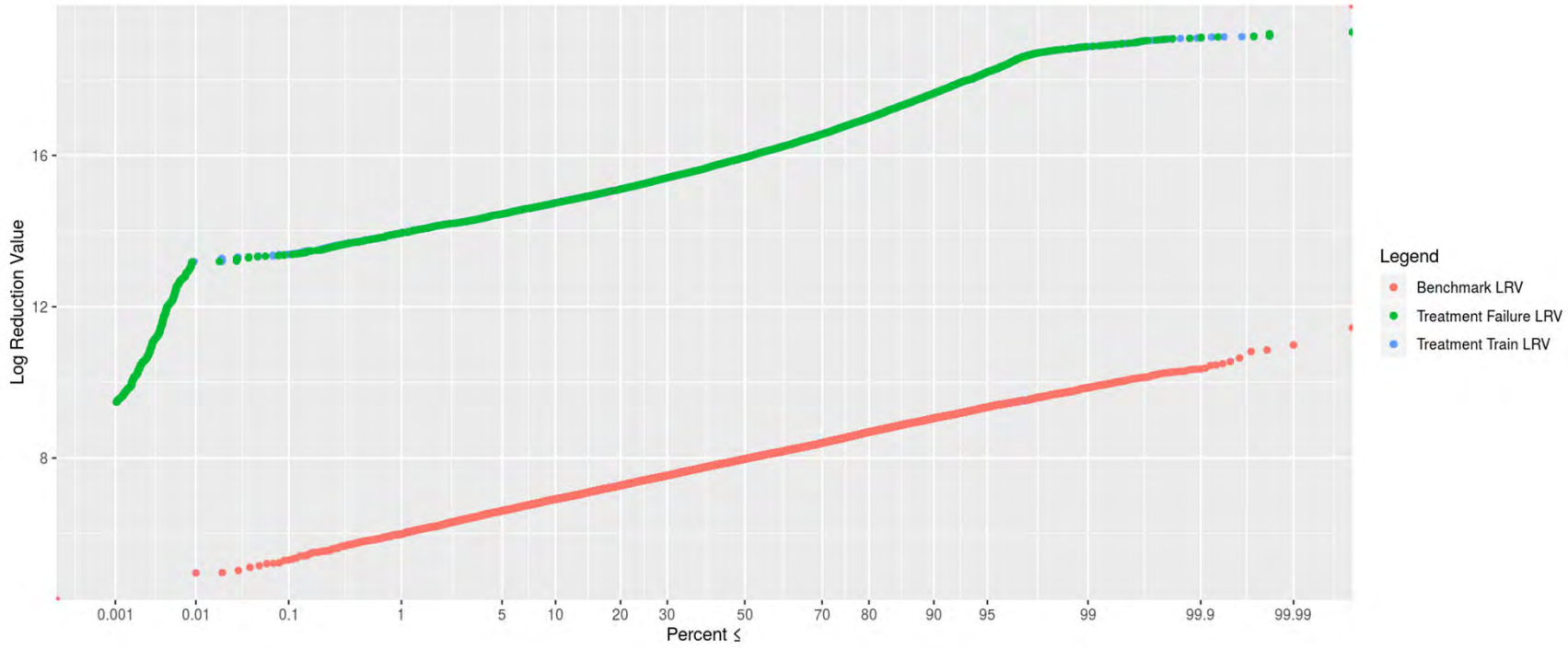
Step 6: Dose-Response

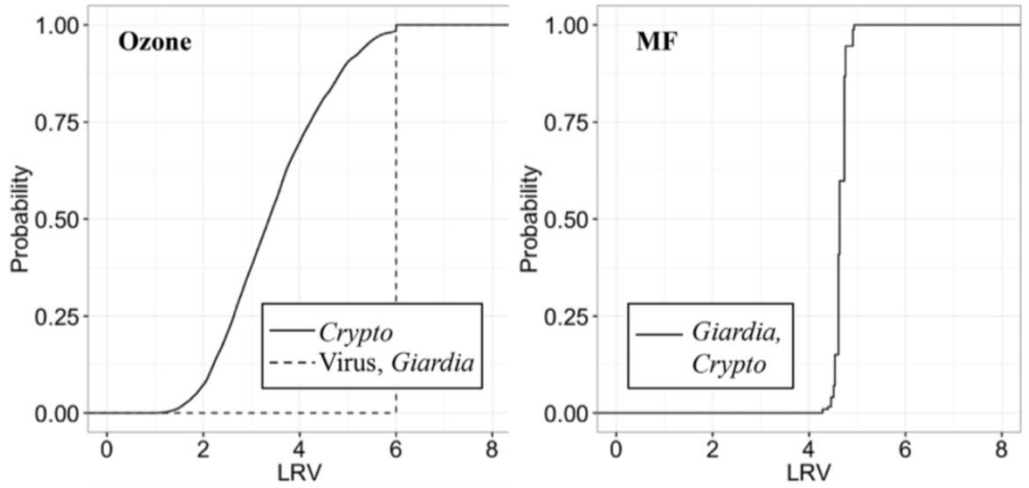
- Select from the left side of the tool, "Dose-Response"

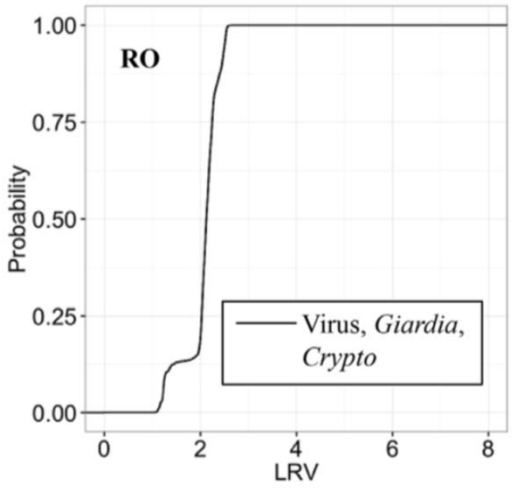
- Notice various default assumptions are provided, and be easily selected.

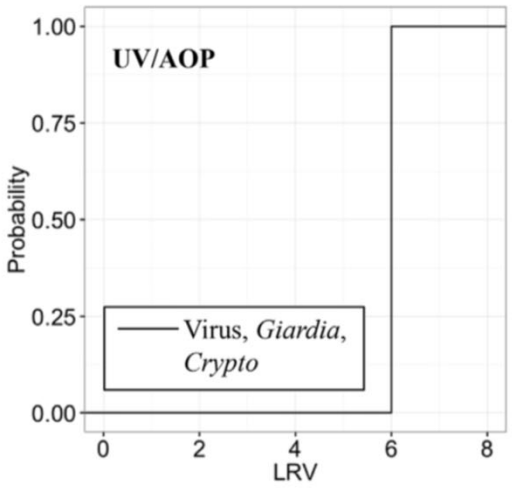
- We'll use one of the defaults "Beta-Poisson from Messner and Berger, 2016", with $\alpha = 0.116$ and $\beta = 0.121$

Step 7: PATTP Output

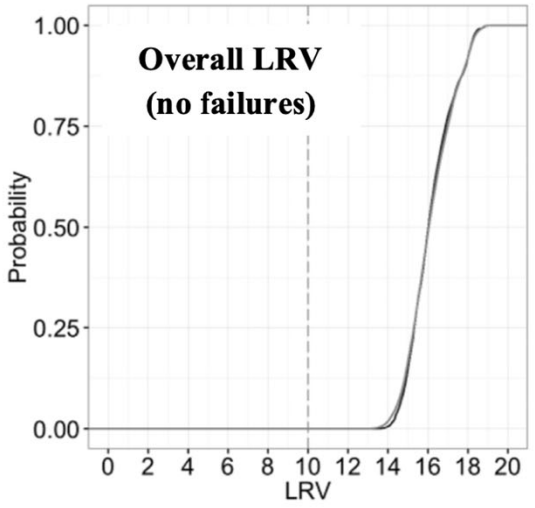




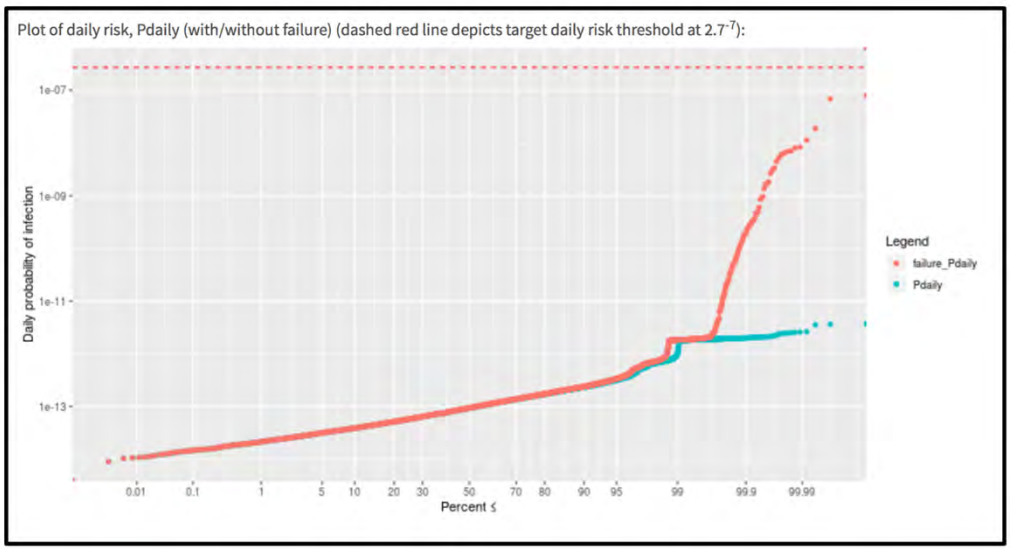


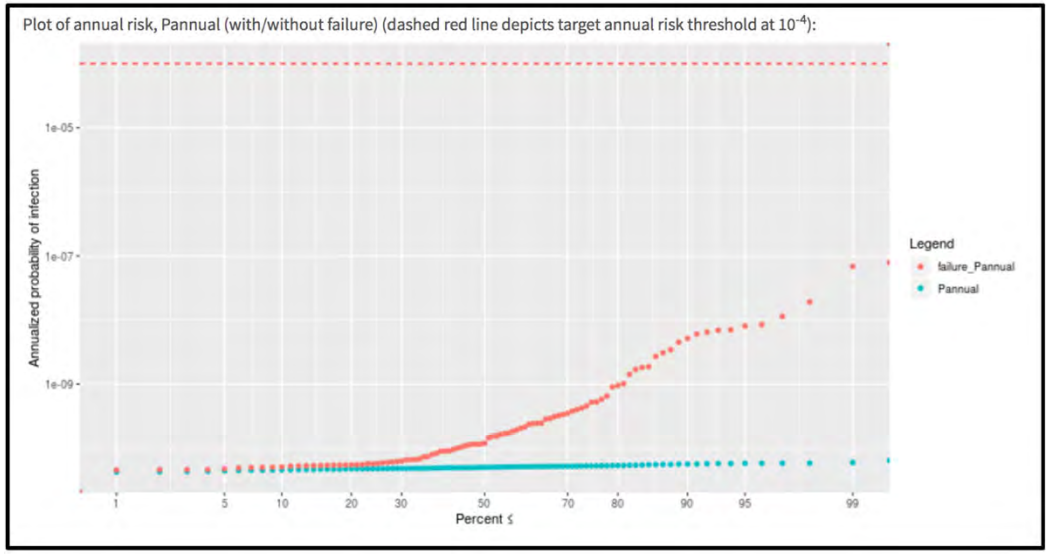


Summary of treatment LRVs from Pecson et al. (2017)



Step 8: QMRA Output





Pause for Questions

Case Study 3

Case Study 3:
QMRA for Adenovirus in a FAT-based DPR Scenario

This case study is based on Soller et al., 2018, evaluating the reliability of pathogen control in hypothetical treatment trains experiencing short-duration, off-spec conditions.

This case study will demonstrate the analysis of the study for Adenovirus.

Learning objectives

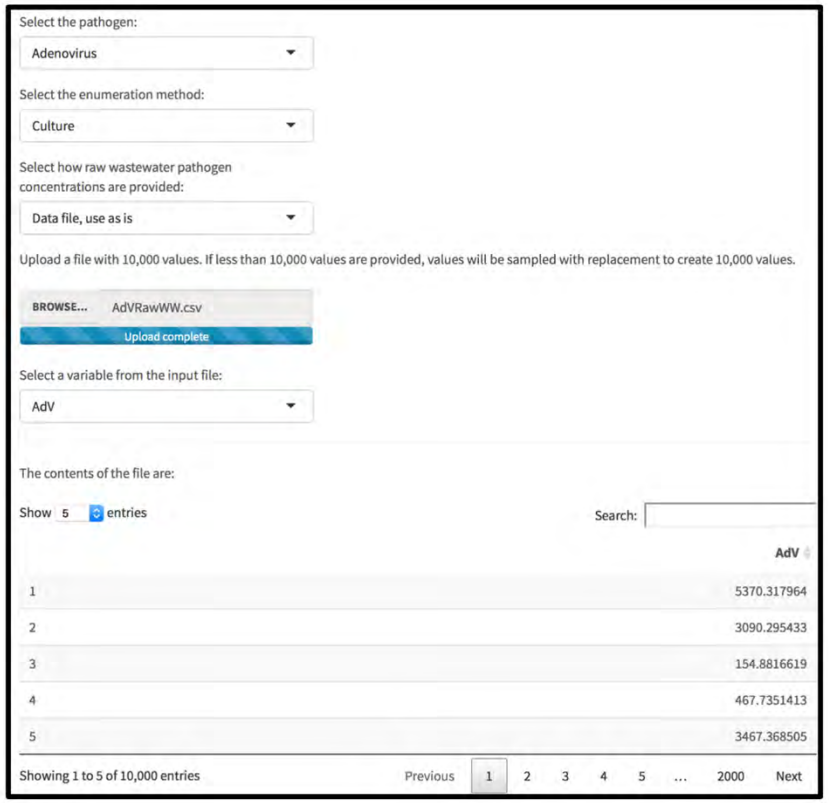
1. Specify individual LRVs for treatment train for each process
2. Specify a failure analysis scenario
3. Specify LRVs for treatment processes that are not to be included in the failure analysis

Let's get started…

Step 1: Specify Raw Wastewater Concentrations

- Select from the left side of the tool, "Raw Wastewater Pathogen Concentrations"

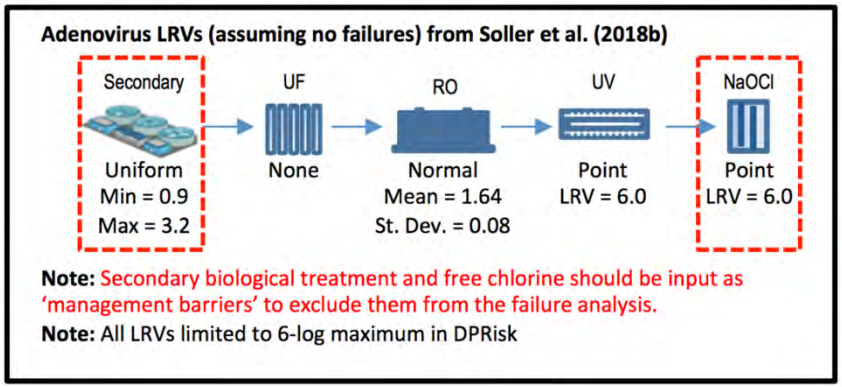
- Select Adenovirus as our pathogen, and Culture as the enumeration method.
- We'll provide a data file with a column of 10,000 raw wastewater concentrations. The file corresponds to a distribution with a min of 1.8 log and max of 3.8 log virus. The file is called "AdVRawWW.csv"

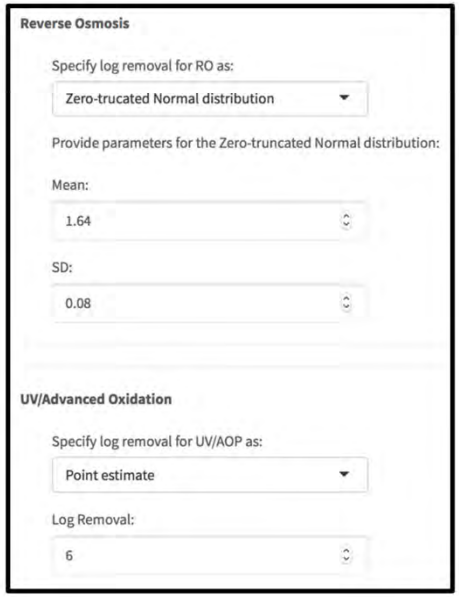


Step 2: Specify Treatment Train

- Select from the left side of the tool, "Treatment Train"

- For this case study, we'll specify a individual LRVs for each treatment train process.
- This is provided as an "Log removal for each process"
- Specify the LRV for processes according to diagram for RO and UV.
- **However:** in this model, we want to modify the specification, so that Secondary Biological Treatment and Free Chlorine are NOT subject to failures. So do NOT enter them in this section of the tool.

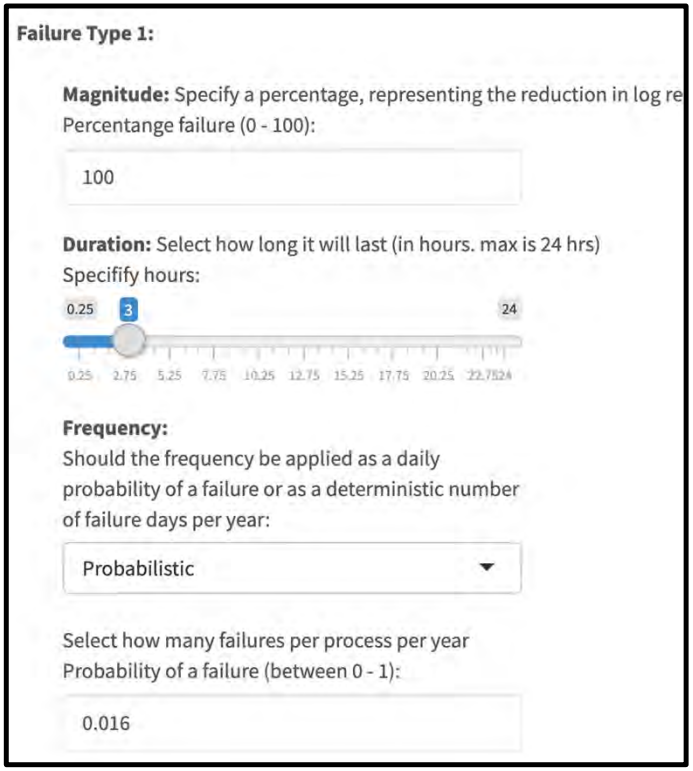




Step 3. Treatment Failure Specification

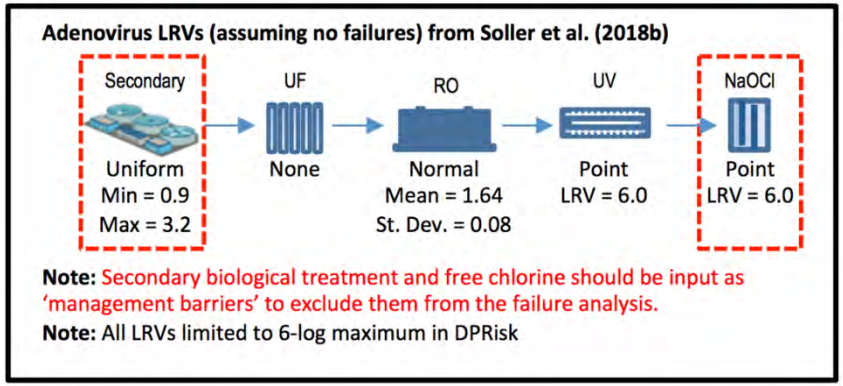
- In this case study, we will assess the potential effect of treatment failures on risk.
- Select from the left side of the tool, "Treatment Failure"

- Choose "Failure analysis with global settings"
- Note: the Soller, et al study used different failure probabilities for different processes. In our case, we'll focus on the worst-case failure scenario.
- We will assess the impact of…
  daily failure probability of 0.016…
  in which the failure magnitude is 100% (i.e., LRV goes to 0)…
  for a duration of 3 hours.



Step 4. Management Barriers

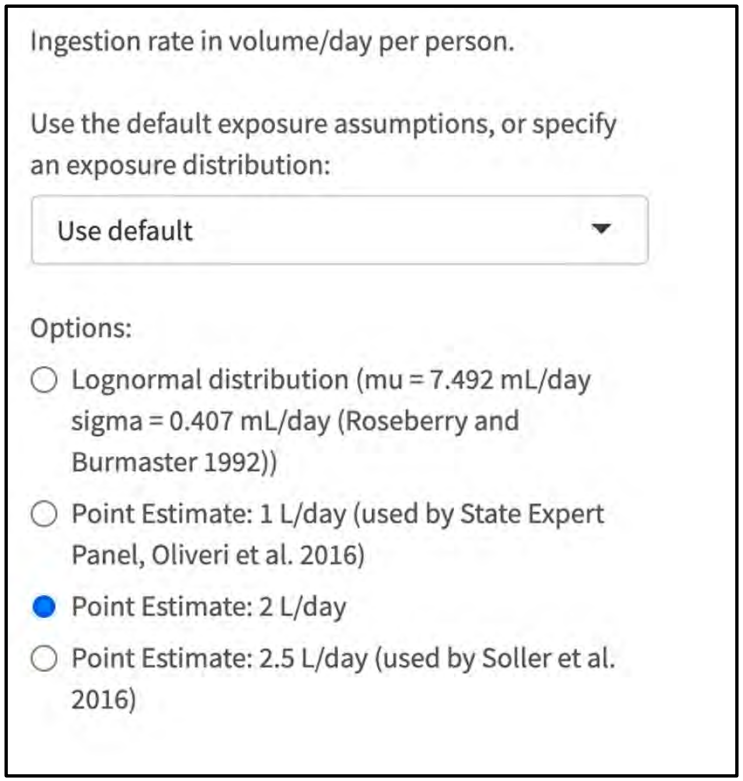
- Select from the left side of the tool, "Management Barriers"
- In the Soller et al. study management barriers were not considered.



- **However:** we WILL use the Management Barriers section of the tool in order to implement work-arounds to include treatment processes that are NOT included in the Failure Analysis.
- Use the "Blending" section to specify the LRV distribution for Secondary Biological Treatment.
- Use the "Dilution" section to specify the LRV point estimate for Free Chlorine.

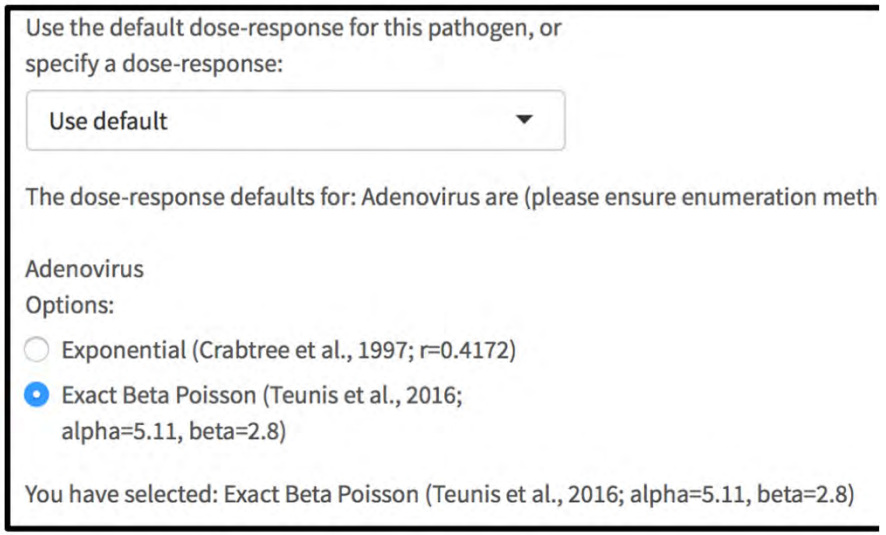
Step 5. Exposure

- Select from the left side of the tool, "Exposure"
- Notice various default assumptions are provided, and be easily selected.
- We'll use the default "2 L/day", which was specified by Soller et al.

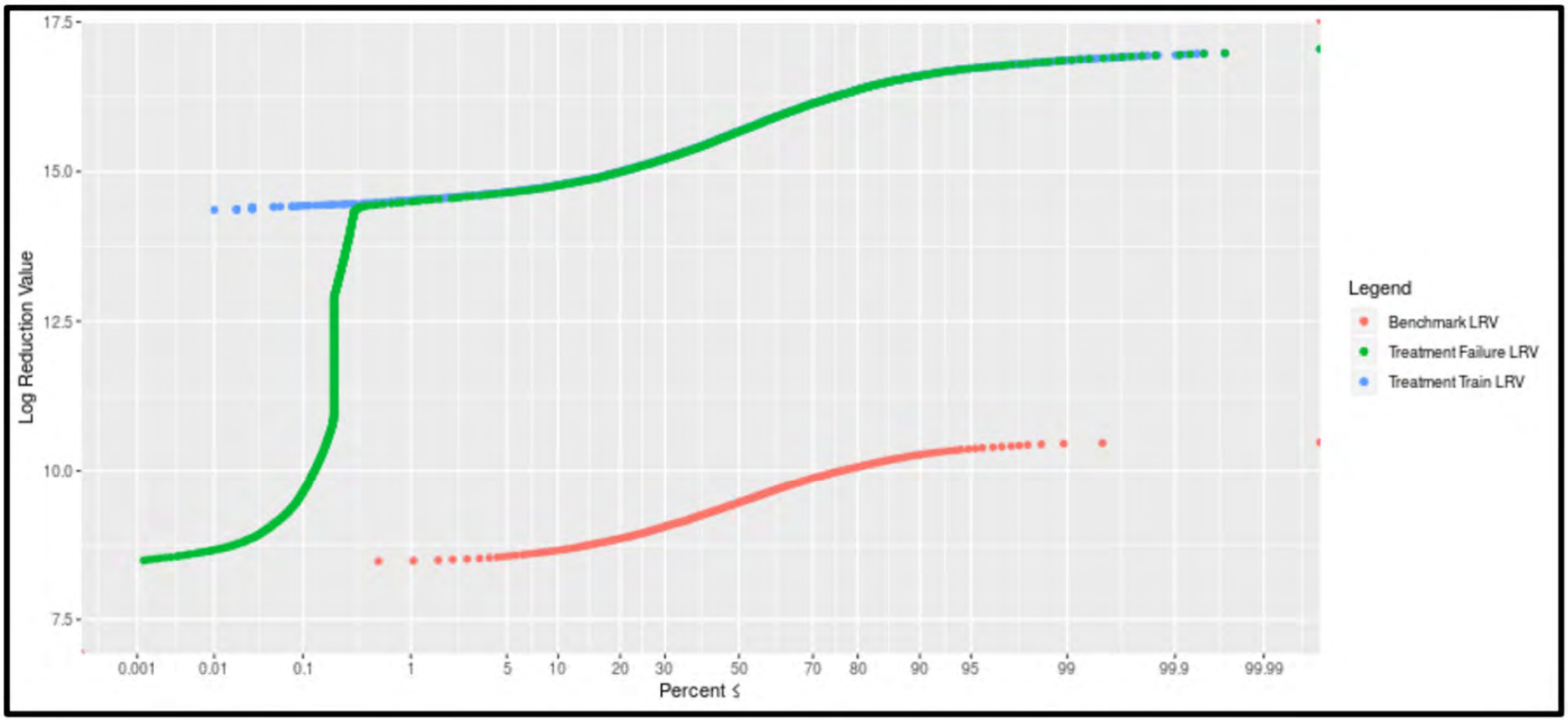


Step 6: Dose-Response

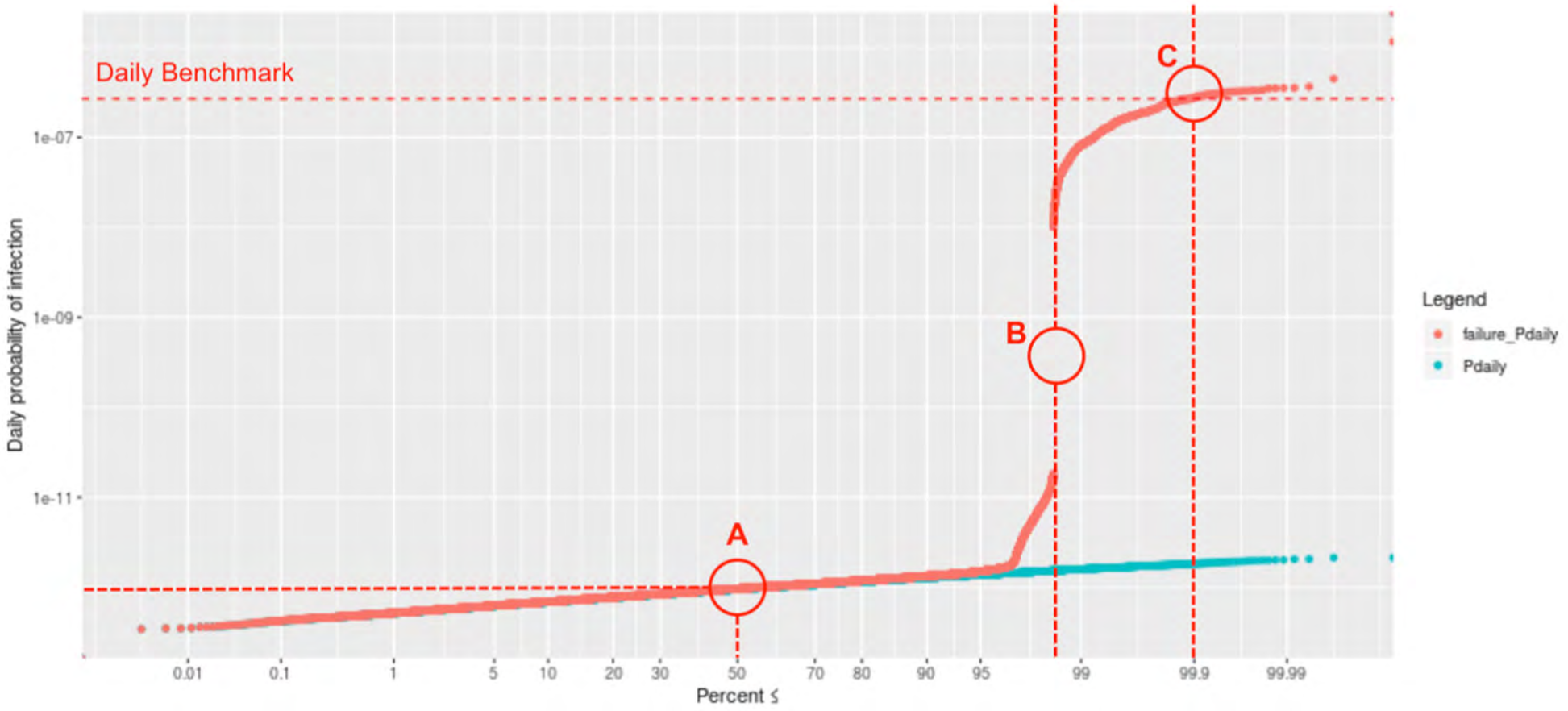
- Select from the left side of the tool, "Dose-Response"
- Notice various default assumptions are provided, and be easily selected.
- We'll use one of the defaults "Exact Beta Poisson", with
  $\alpha = 5.11$ and $\beta = 2.8$



Step 7: PATTP Output



Step 8: QMRA Output


Daily Benchmark
C
B
A
1e-07
1e-09
1e-11
Daily probability of infection
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤
Legend
failure_Pdaily
Pdaily

Pause for Questions

Expanded Investigations

- Impact of raw wastewater pathogen concentration assumptions
  (Case Study 1 – Crypto, Case Study 2 – Crypto variability)
- Impact of treatment redundancy
  (Case Study 2 – ozone variation, Case Study 2 – management barriers)

- Impact of treatment variability
  (Case Study 1 – variation on overall LRV)
- Impact of failure assumptions
  (Case Study 2 – Pecson study curves)
- Sensitivity analysis
  (Case Study 1 – changing dose-response)

DPR-1 WORKSHOP: EXPANDED INVESTIGATIONS

Brian Pecson, Trussell Technologies

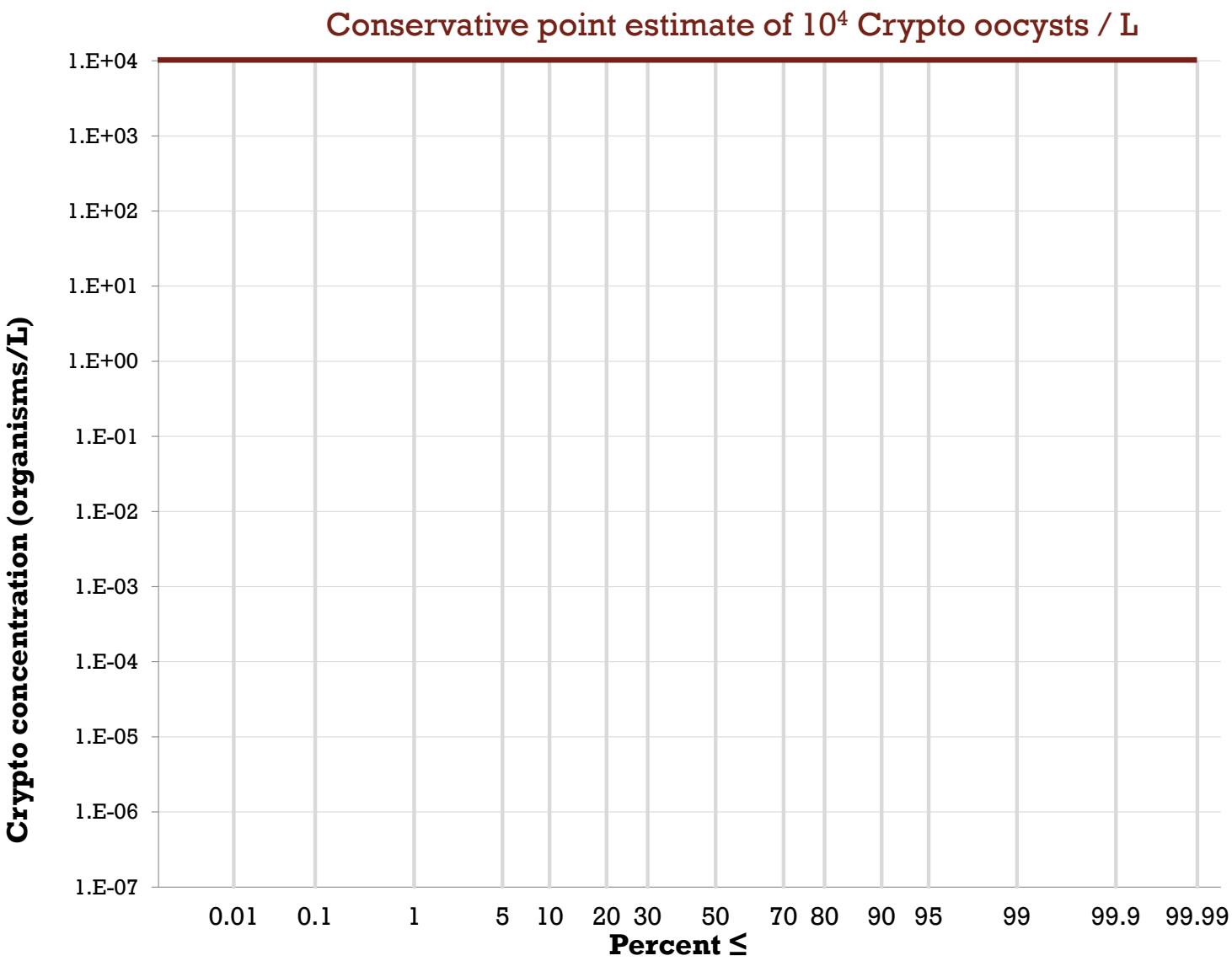
Anya Kaufmann, Trussell Technologies

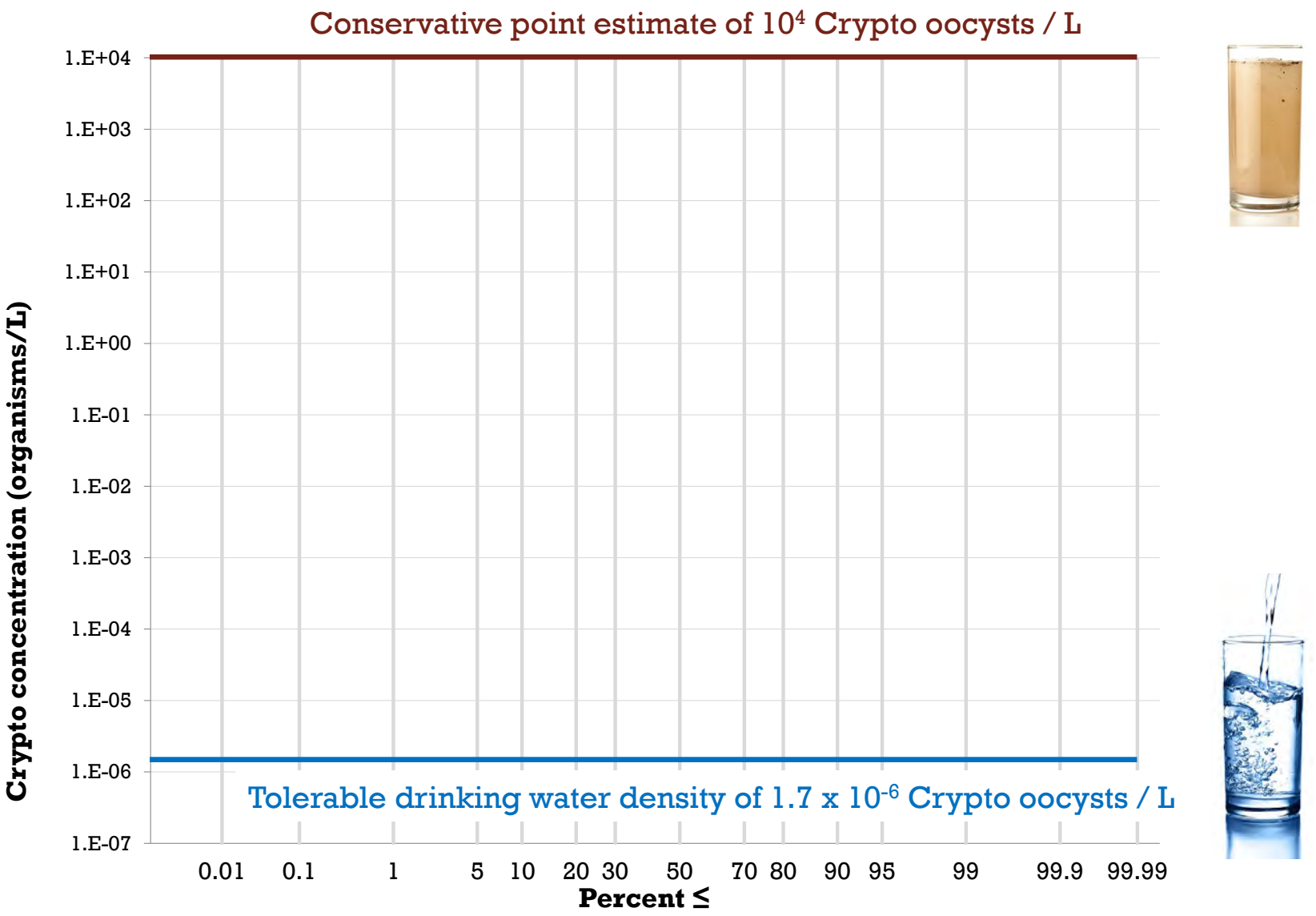
August 4, 2020

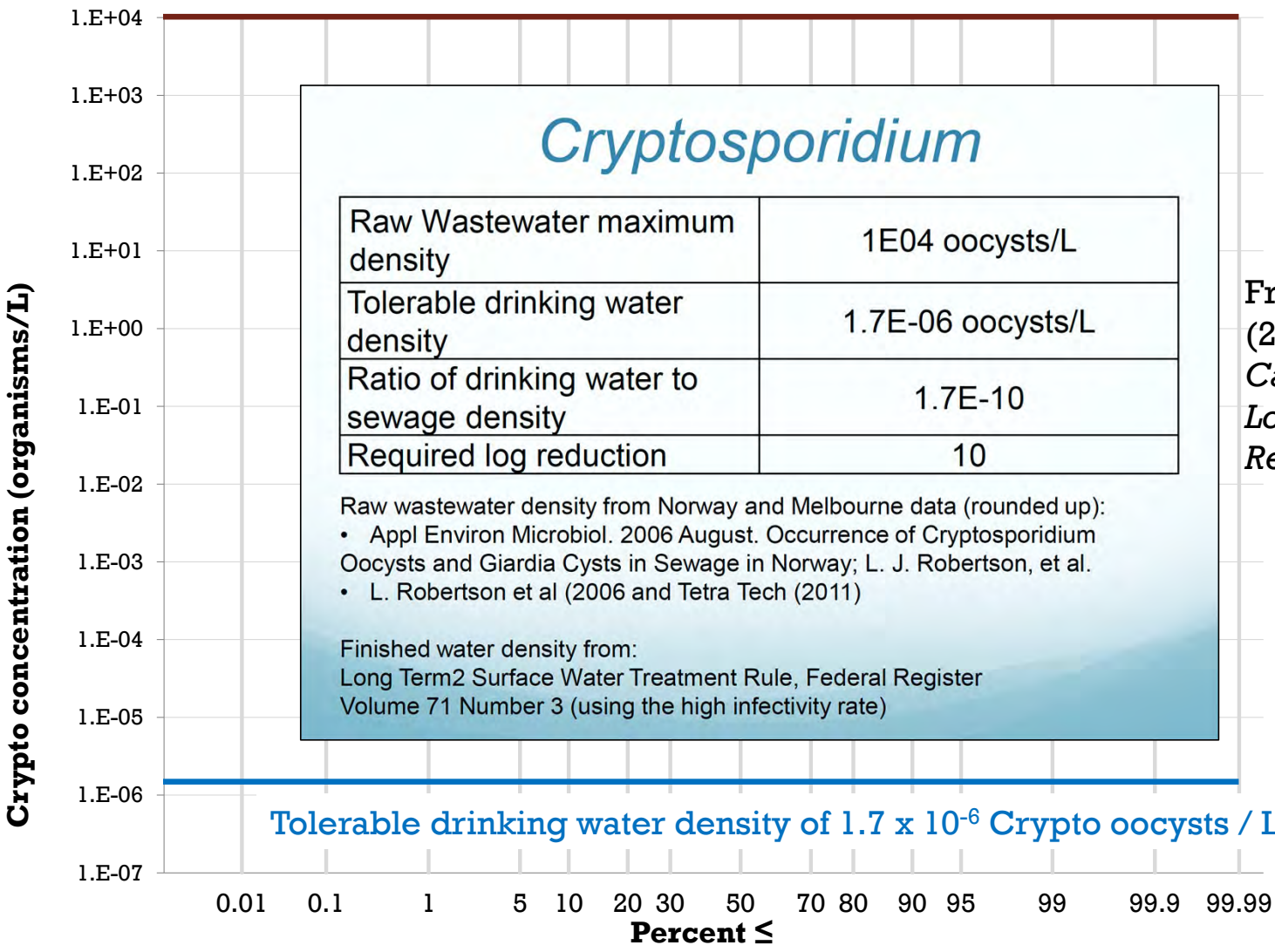
EXPANDED INVESTIGATIONS TOPICS

- Understanding the Benchmark Curve
- Impact of Raw Wastewater Pathogen Concentration Assumptions
- Impact of Treatment Redundancy
- Impact of Treatment Variability and Failure Assumptions
- Sensitivity Analysis

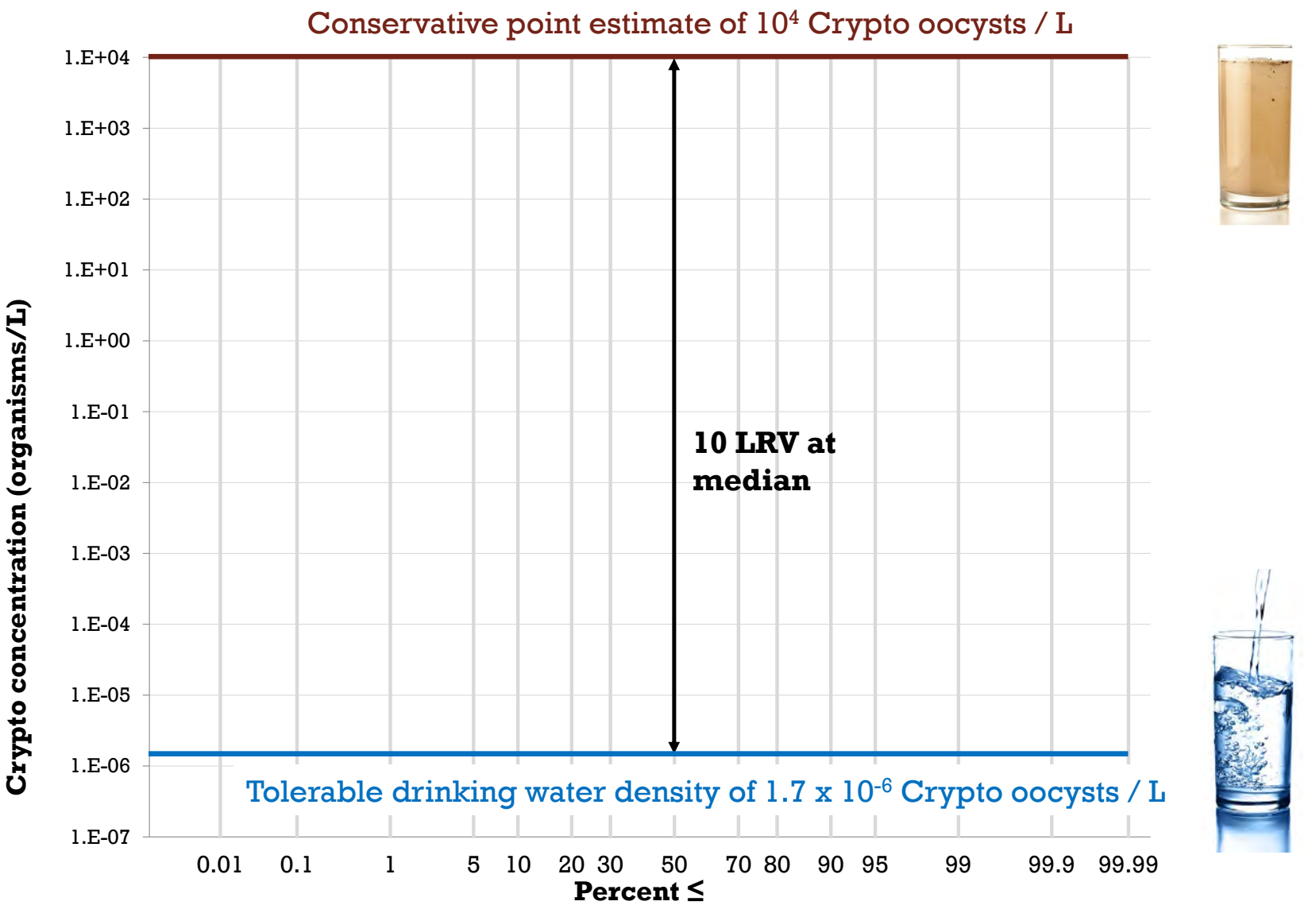
UNDERSTANDING THE BENCHMARK CURVE & IMPACT OF RAW WASTEWATER PATHOGEN CONCENTRATION ASSUMPTIONS

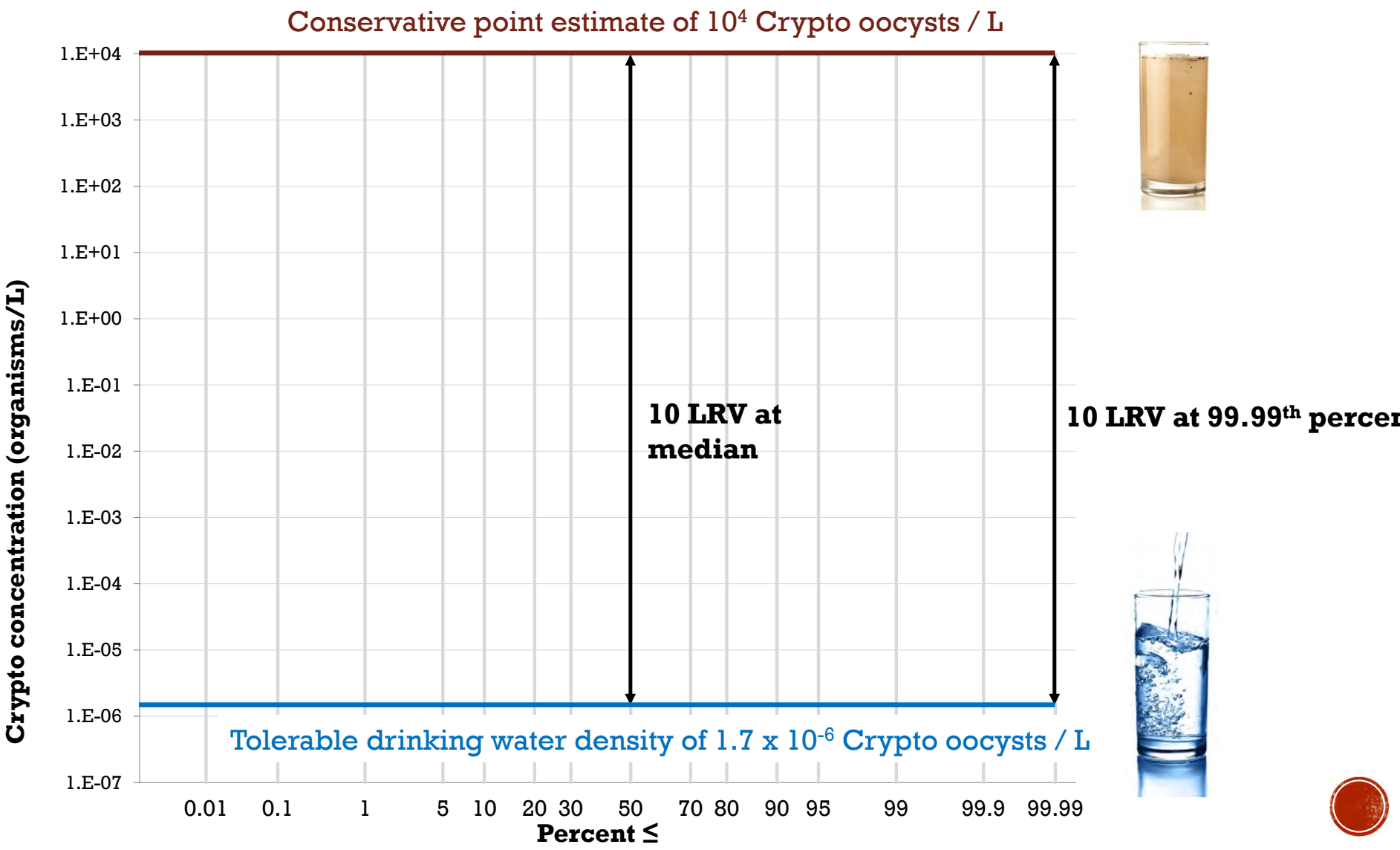

Conservative point estimate of 10⁴ Crypto oocysts / L
Crypto concentration (organisms/L)
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤

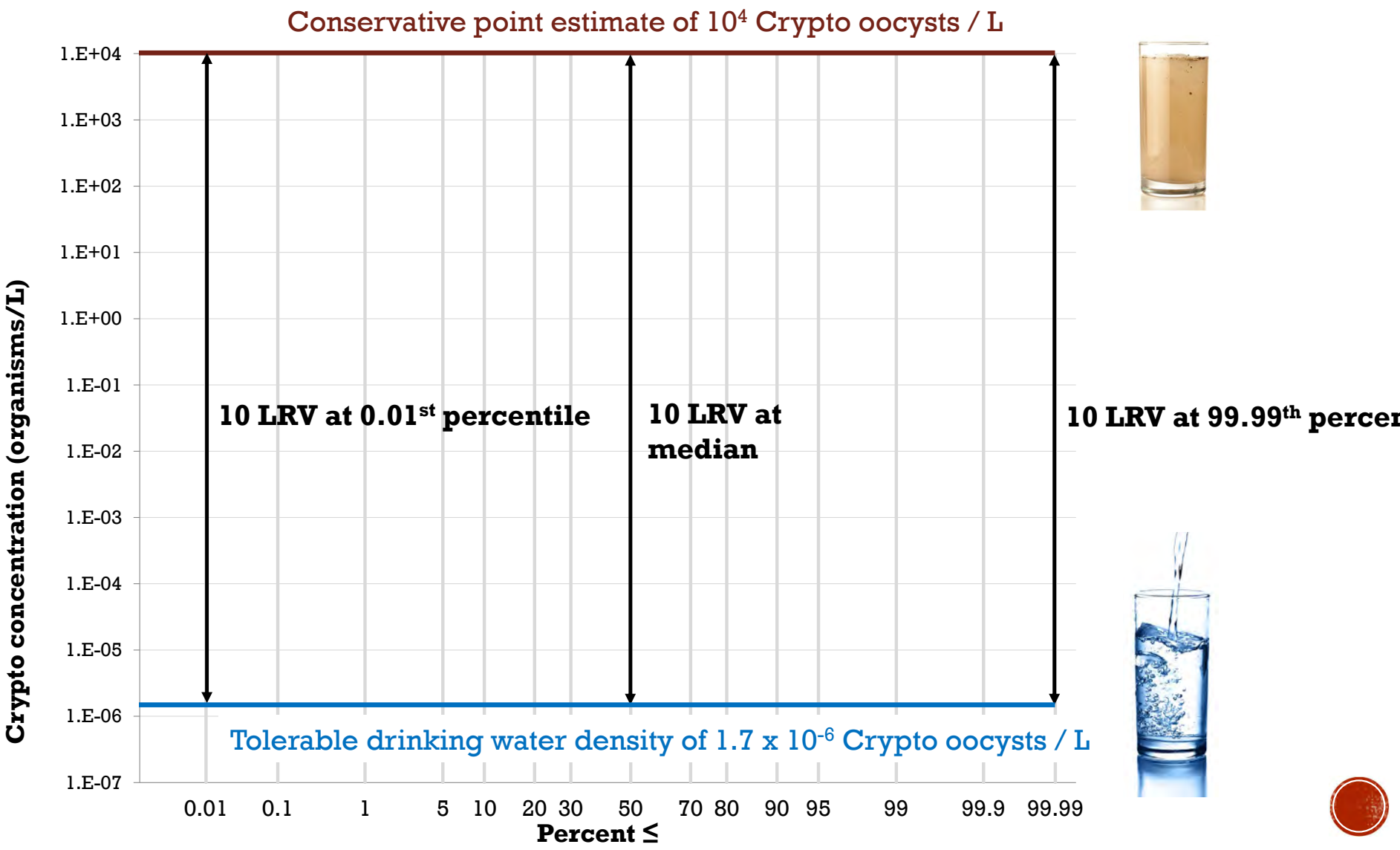

Conservative point estimate of 10^4 Crypto oocysts / L
Crypto concentration (organisms/L)
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤
Tolerable drinking water density of 1.7×10^{-6} Crypto oocysts / L

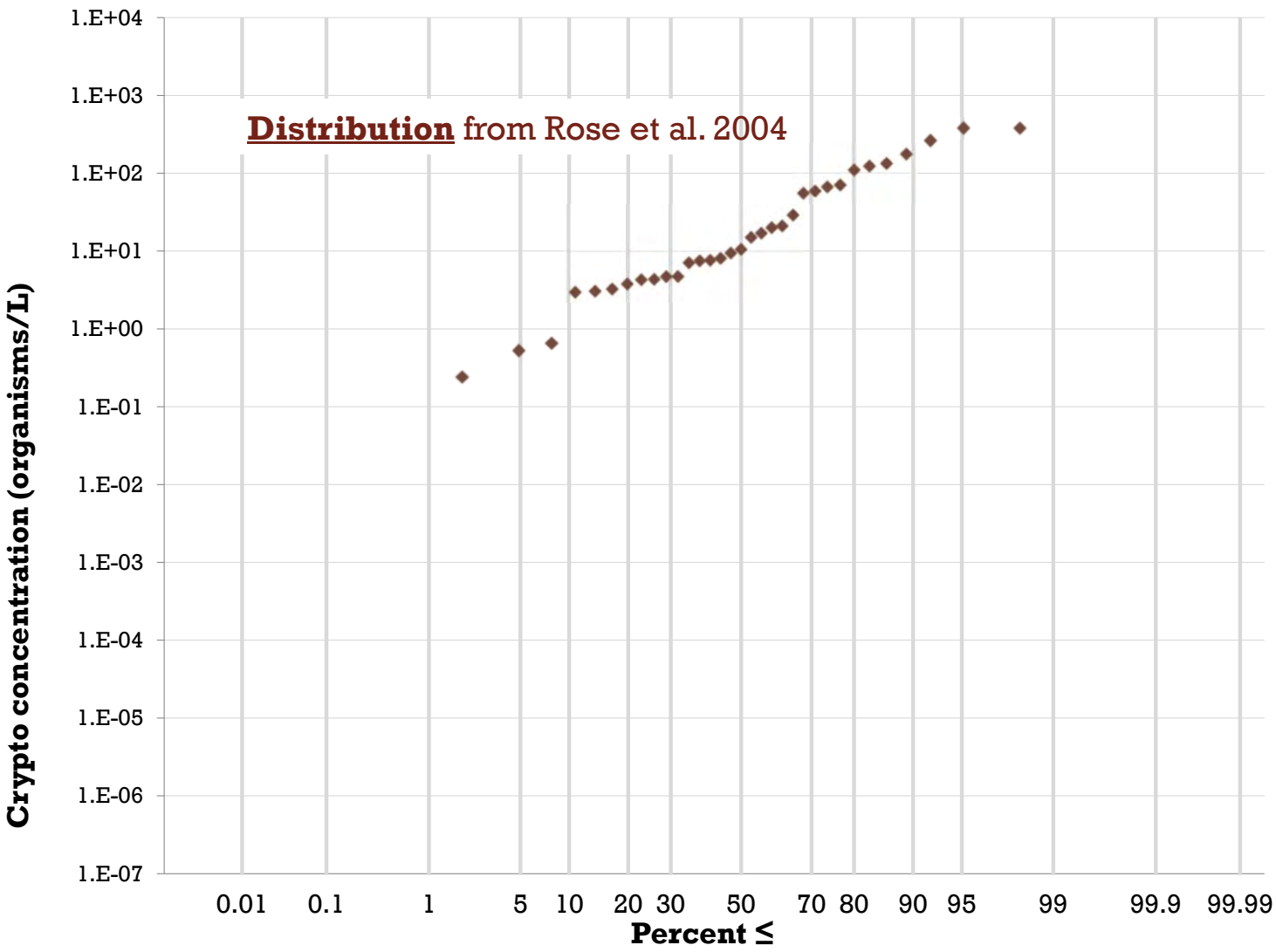


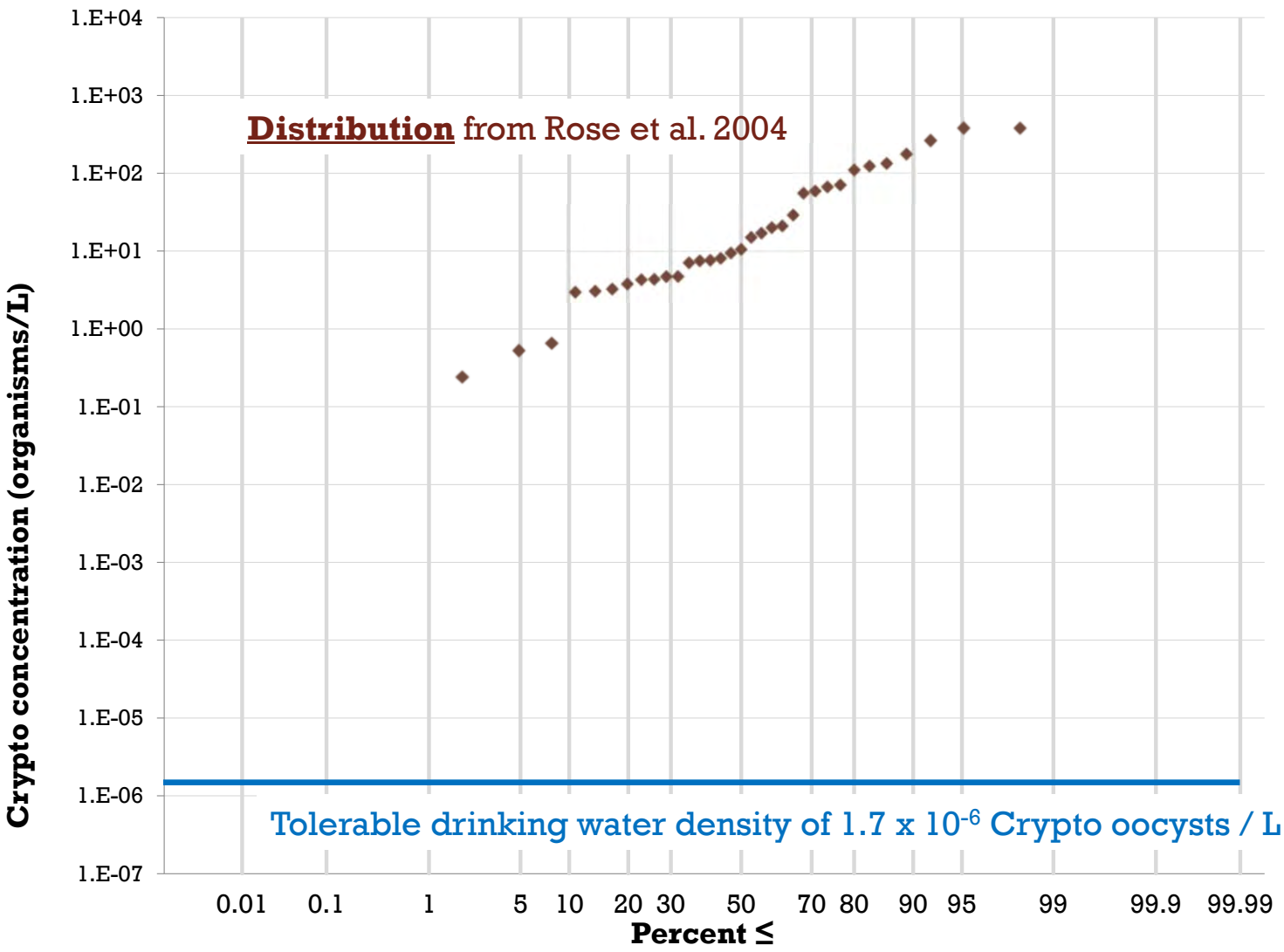
From Hultquist (2016) *Basis for California's 12-10-10 Log Removal Requirements*

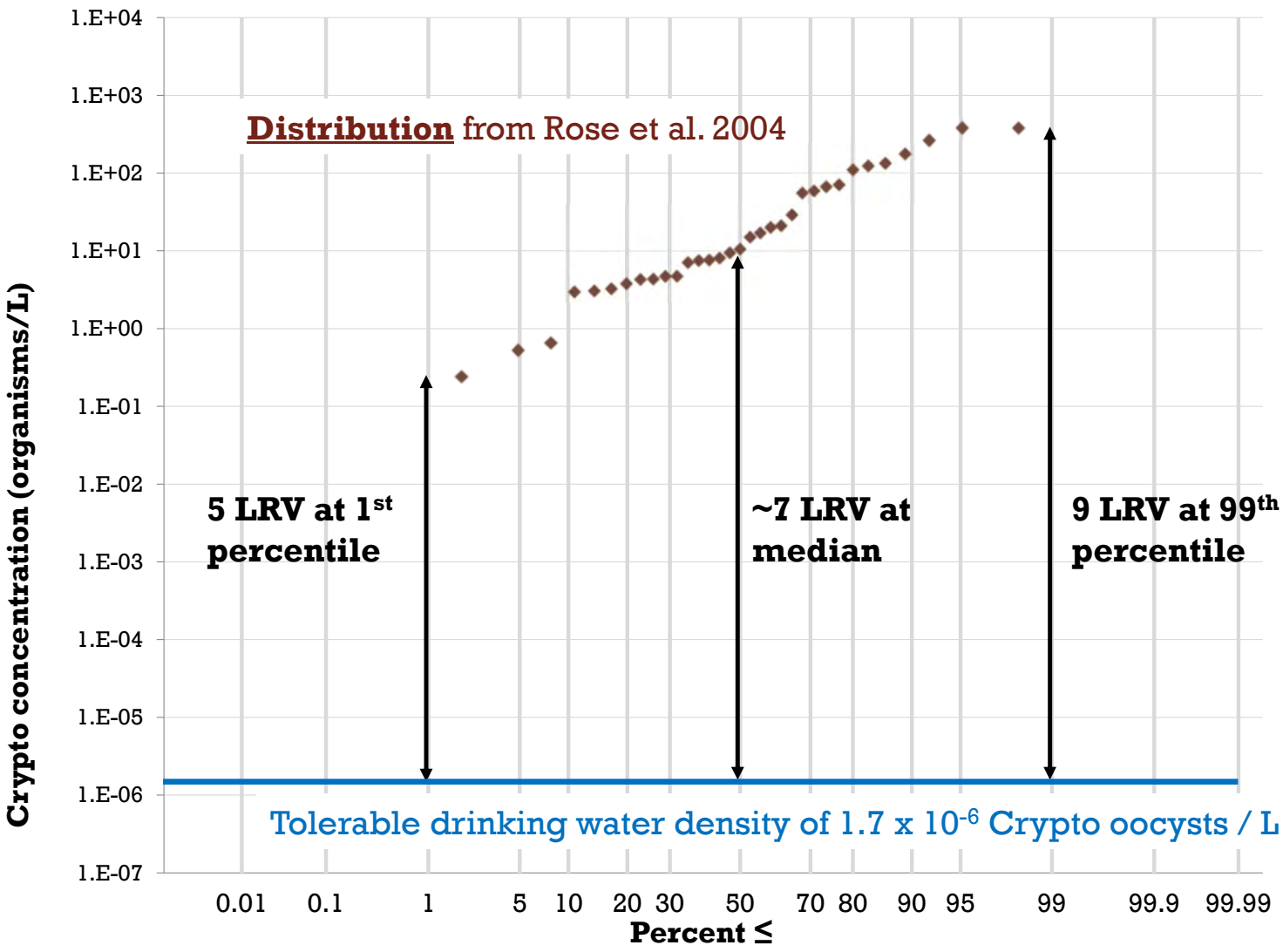

Conservative point estimate of 10^4 Crypto oocysts / L
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
Crypto concentration (organisms/L)
10 LRV at median
Tolerable drinking water density of 1.7 x 10^-6 Crypto oocysts / L
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤


Conservative point estimate of 10^4 Crypto oocysts / L
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
Crypto concentration (organisms/L)
10 LRV at median
10 LRV at 99.99th percenti
Tolerable drinking water density of 1.7 x 10-6 Crypto oocysts / L
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤

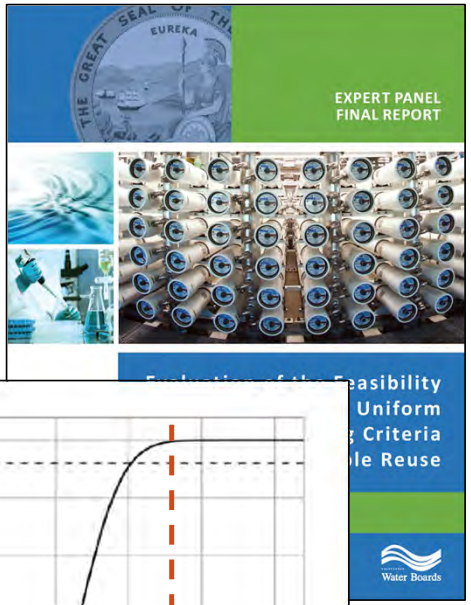

Conservative point estimate of 10^4 Crypto oocysts / L
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
Crypto concentration (organisms/L)
10 LRV at 0.01st percentile
10 LRV at median
10 LRV at 99.99th percenti
Tolerable drinking water density of 1.7 x 10-6 Crypto oocysts / L
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤

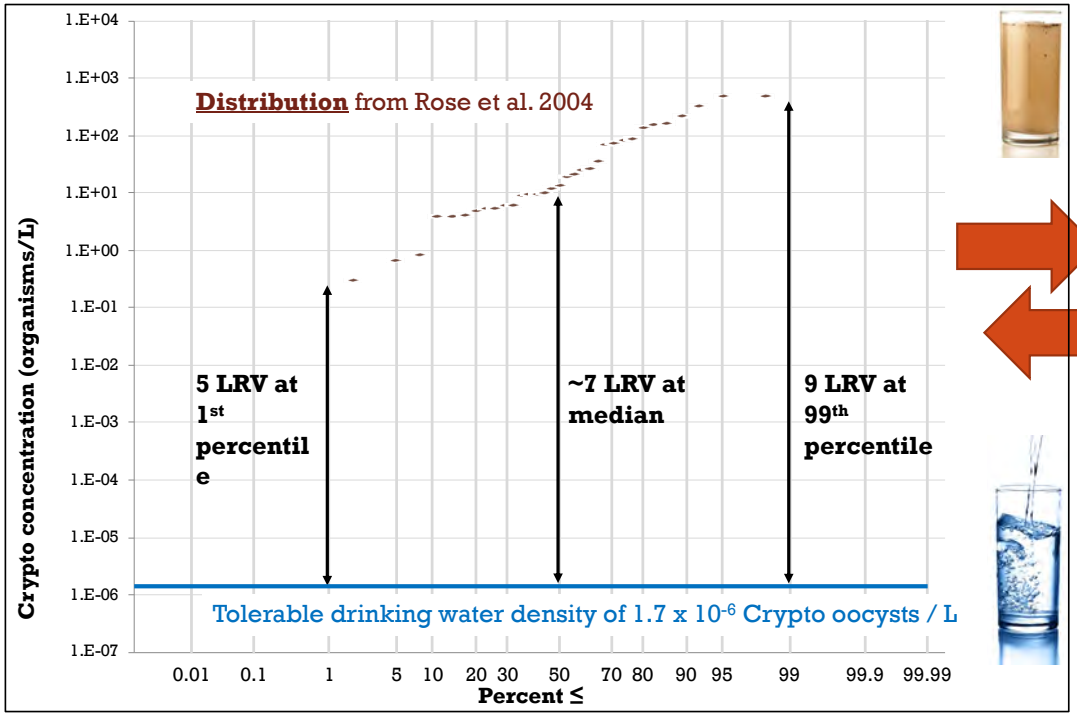

Distribution from Rose et al. 2004
Crypto concentration (organisms/L)
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤

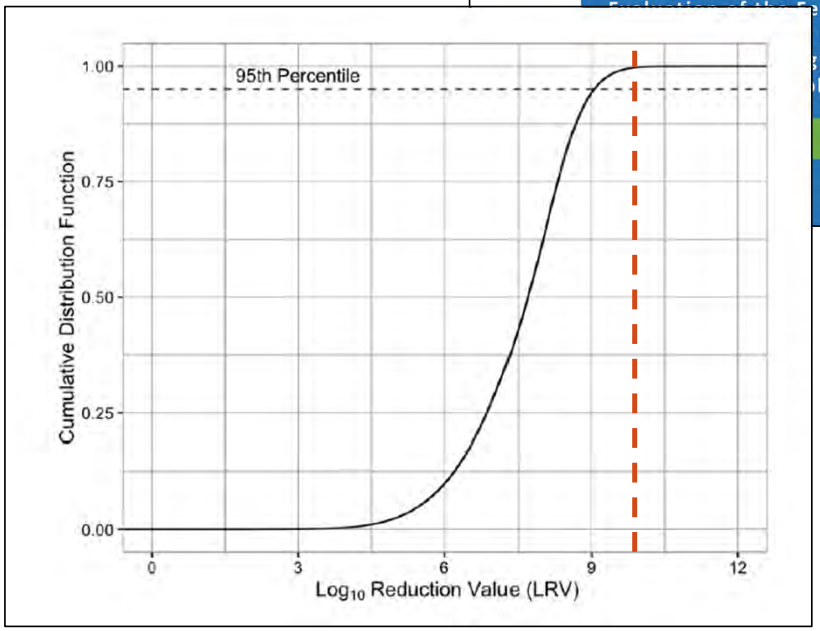

Distribution from Rose et al. 2004
Tolerable drinking water density of 1.7 x 10-6 Crypto oocysts / L
Crypto concentration (organisms/L)
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
0.01
0.1
1
5
10
20
30
50
70
80
90
95
99
99.9
99.99
Percent ≤


Distribution from Rose et al. 2004
Crypto concentration (organisms/L)
1.E+04
1.E+03
1.E+02
1.E+01
1.E+00
1.E-01
1.E-02
1.E-03
1.E-04
1.E-05
1.E-06
1.E-07
5 LRV at 1st percentile
~7 LRV at median
9 LRV at 99th percentile
Tolerable drinking water density of 1.7 x 10-6 Crypto oocysts / L
0.01 0.1 1 5 10 20 30 50 70 80 90 95 99 99.9 99.99
Percent ≤

THE BENCHMARK TREATMENT TRAIN







Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

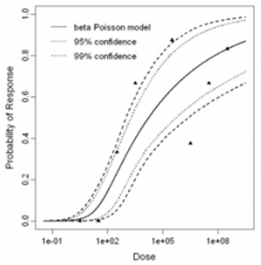
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

1.7 x 10^{-6} Crypto oocysts / L is tolerable because it leads to:

- 10^{-4} infections per person per year

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

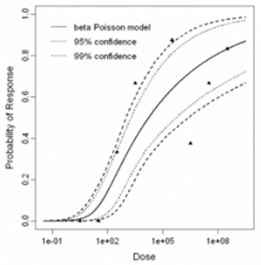
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

1.7 x 10^{-6} Crypto oocysts / L is tolerable because it leads to:

- 10^{-4} infections per person per year
- 2.7x10^{-7} infections per person per day

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

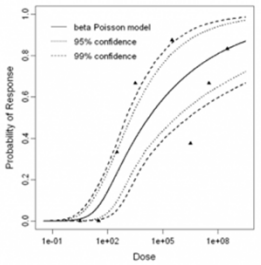
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

1.7 x 10^{-6} Crypto oocysts / L is tolerable because it leads to:

- 10^{-4} infections per person per year
- 2.7x10^{-7} infections per person per day
- **2.9x10^{-9} infections per person per 15 minutes**

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

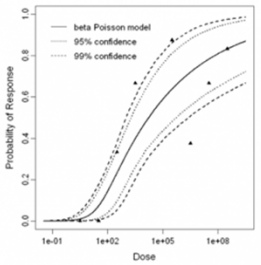
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

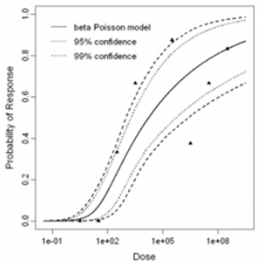
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

10^{-8} oocysts

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

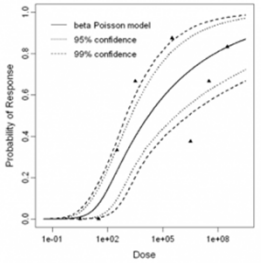
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

10 mL every 15 minutes

10^{-8} oocysts

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

2. Dose-Response

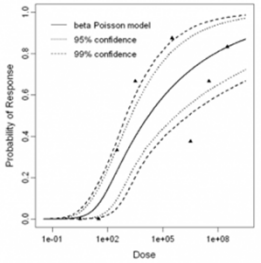
Raw wastewater

Treatment

Drinking water levels

Drinking water consumption

Exposure



Dose-response

Risk

10 mL every 15 minutes

10^{-6} oocysts/ L

10^{-8} oocysts

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

2. Dose-Response

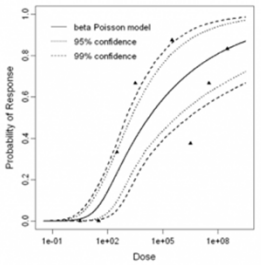
Raw wastewater

Treatment

Drinking water levels

Drinking water consumption

Exposure



Dose-response

Risk

682 oocysts / L

10^{-6} oocysts/ L

10 mL every 15 minutes

10^{-8} oocysts

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

2. Dose-Response

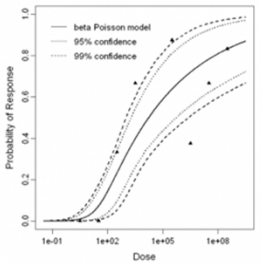
Raw wastewater

Treatment

Drinking water levels

Drinking water consumption

Exposure



Dose-response

Risk

682 oocysts / L

=log (682/10^{-6})

8.8 LRV

10^{-6} oocysts/ L

10 mL every 15 minutes

10^{-8} oocysts

2.9×10^{-9} infections per person per 15 minutes

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

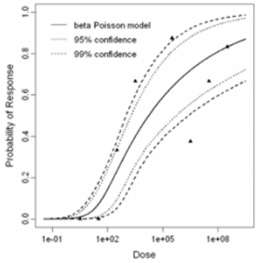
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C)-LRV}\right)^n$$

Calculating the Benchmark Treatment Train

1. Exposure Assessment

Raw wastewater

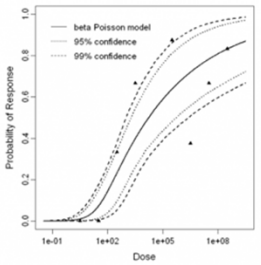
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

Risk

$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C) - LRV}\right)^n$$

Calculating the Benchmark Treatment Train

1. Exposure Assessment

2. Dose-Response

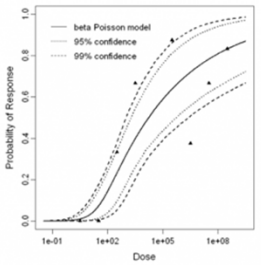
Raw wastewater

Treatment

Drinking water levels

Drinking water consumption

Exposure

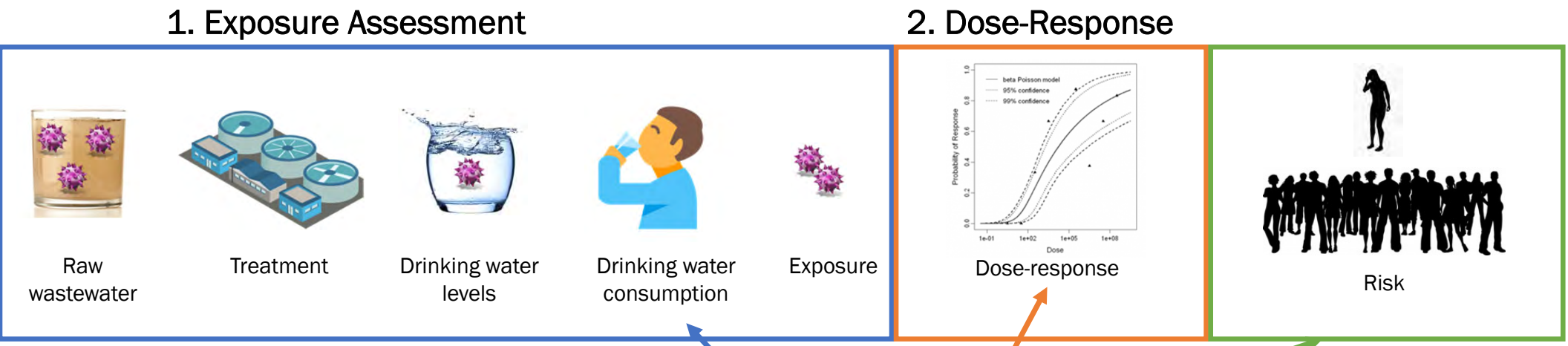


Dose-response

Risk

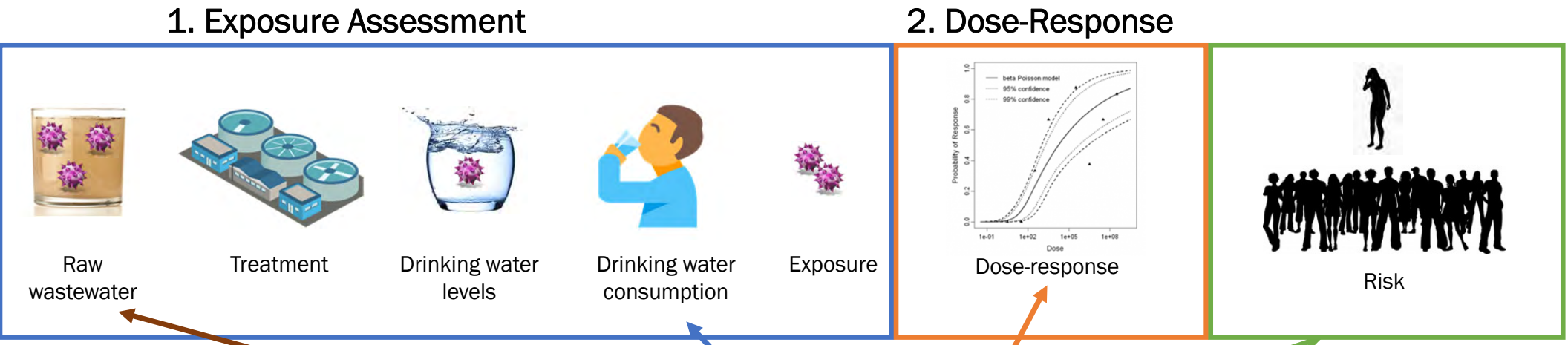
$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C) - LRV}\right)^n$$

Calculating the Benchmark Treatment Train



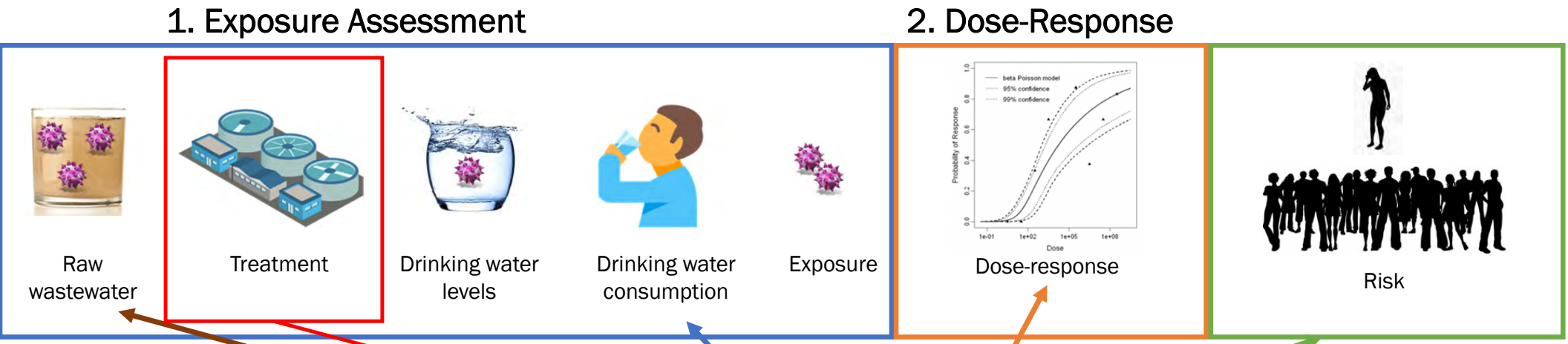
$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C) - LRV}\right)^n$$

Calculating the Benchmark Treatment Train



$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C)-LRV}\right)^n$$

Calculating the Benchmark Treatment Train



$$Tolerable\ Infection\ Risk = 1 - D_r\left(V\ x\ 10^{\log(C) - LRV}\right)^n$$

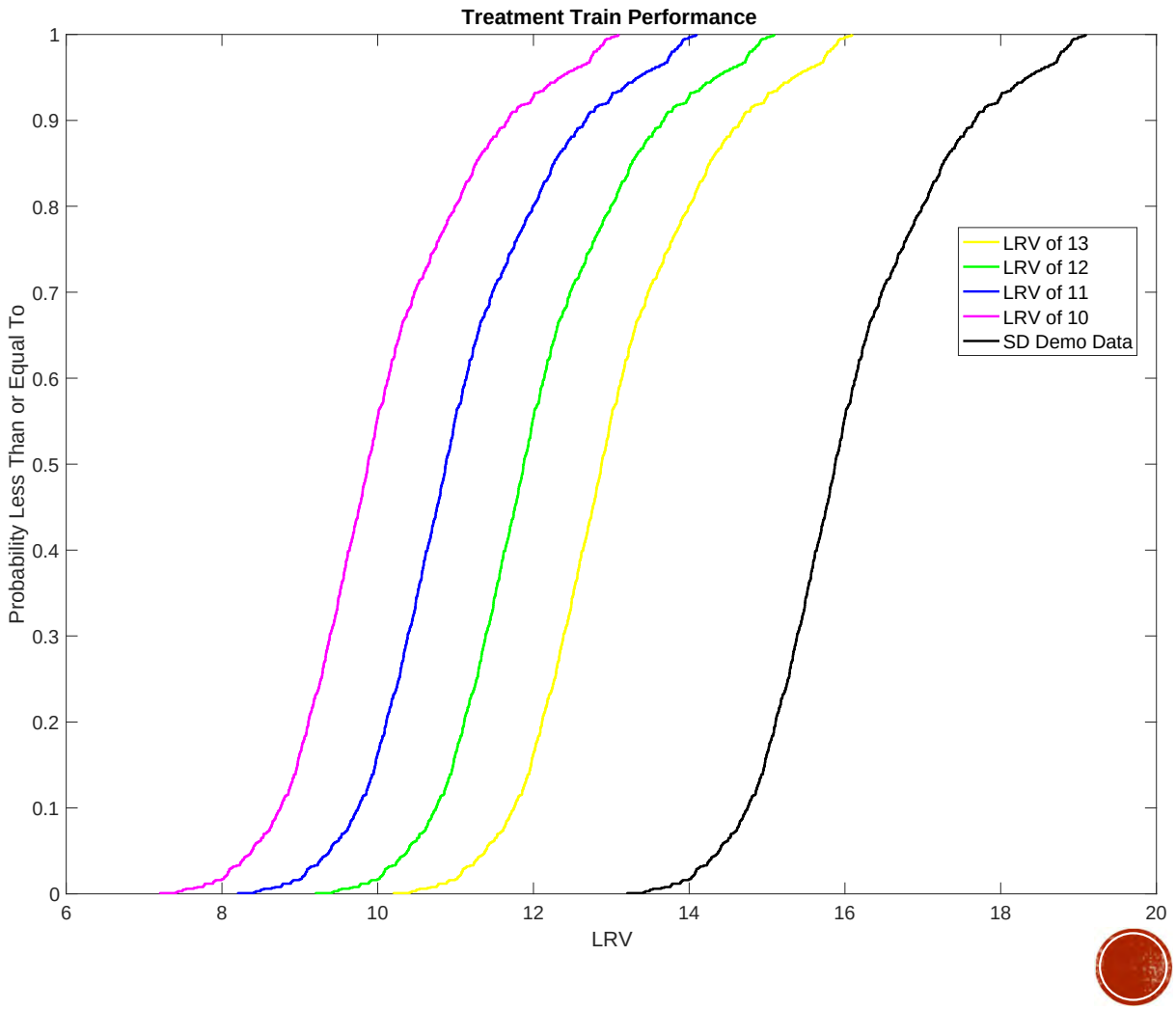
IMPACT OF TREATMENT REDUNDANCY

Treatment Requirements

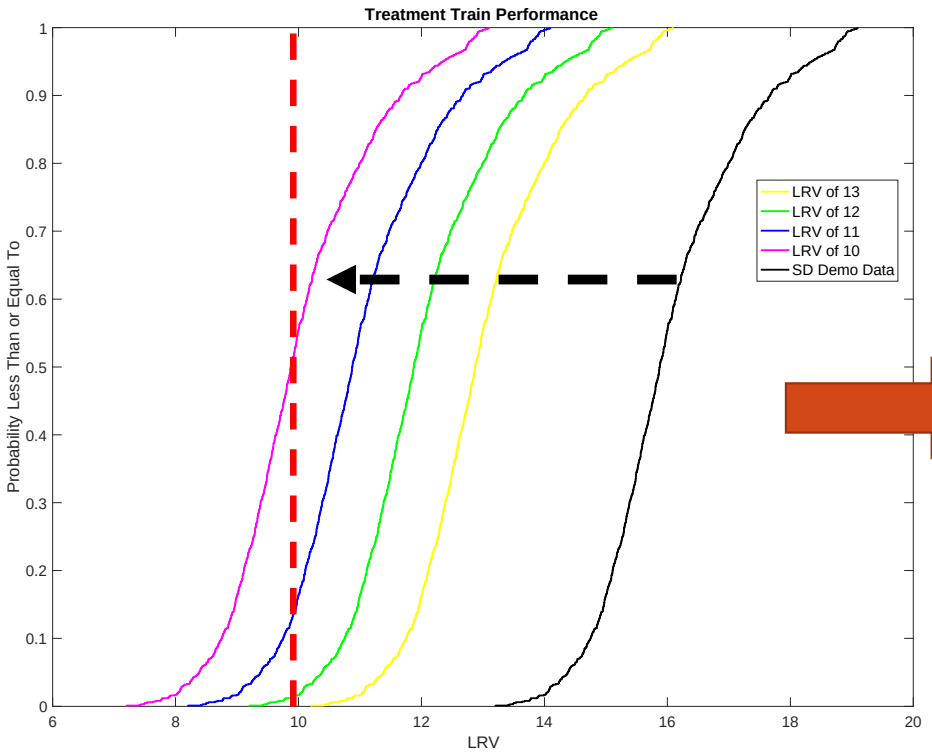
12 / 10 / 10

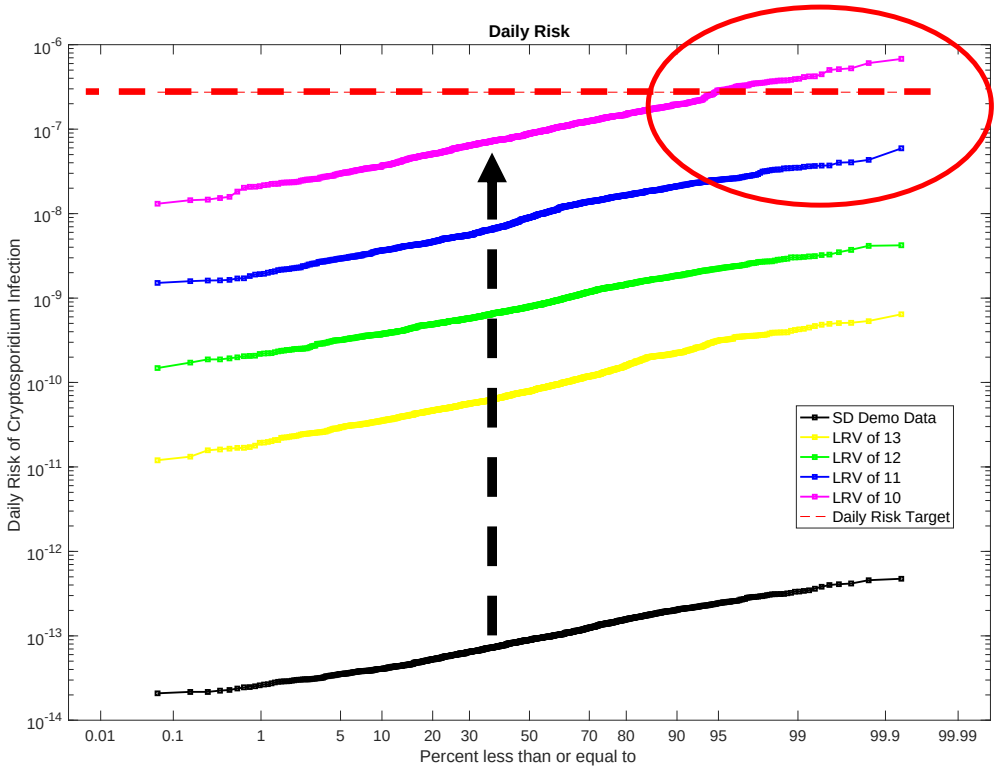
13 / 11 / 11

14 / 12 / 12

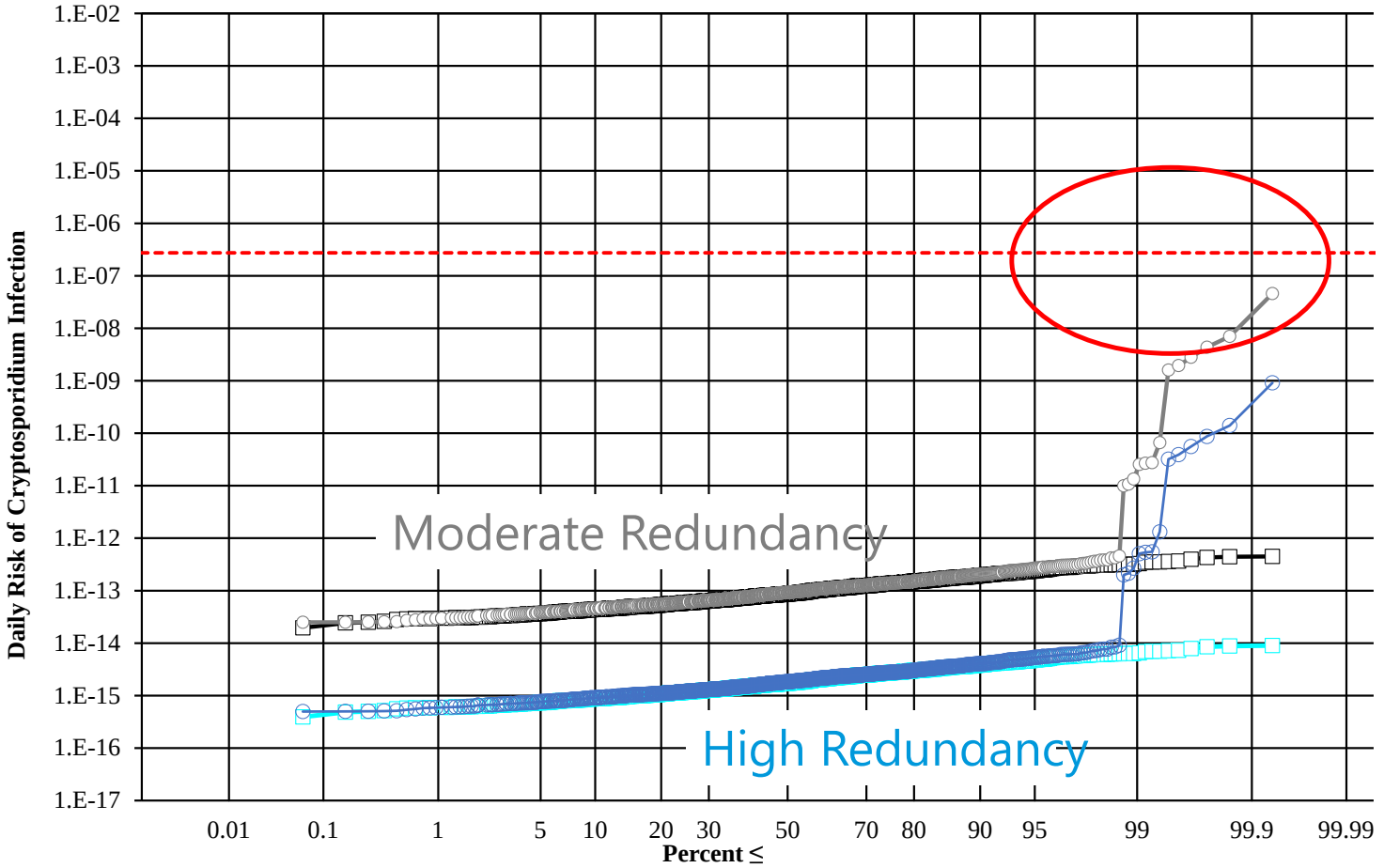


LOWER REDUNDANCY LEADS TO UPWARDS SHIFTS IN RISK



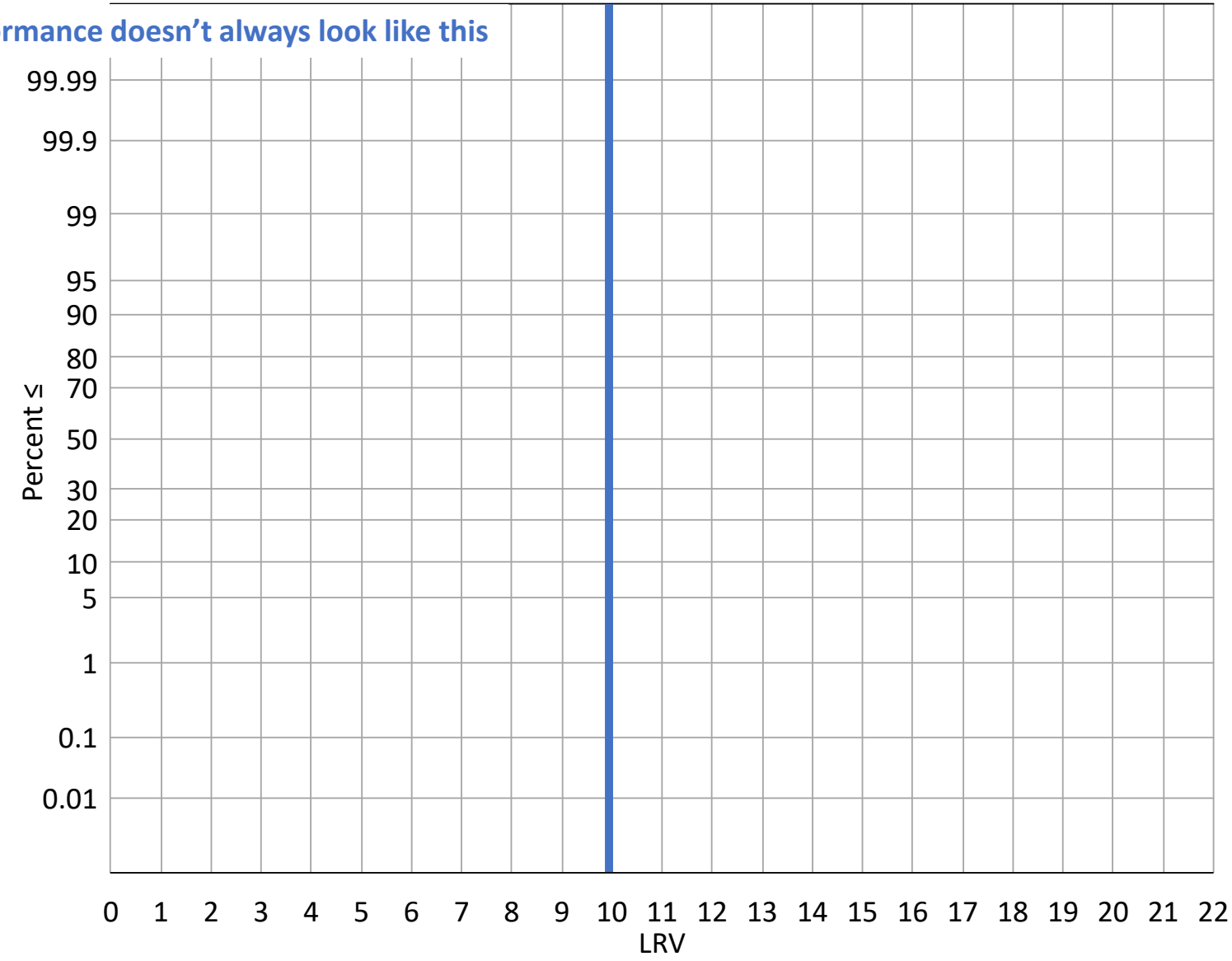


Redundancy is important when considering the impact of low probability failure events

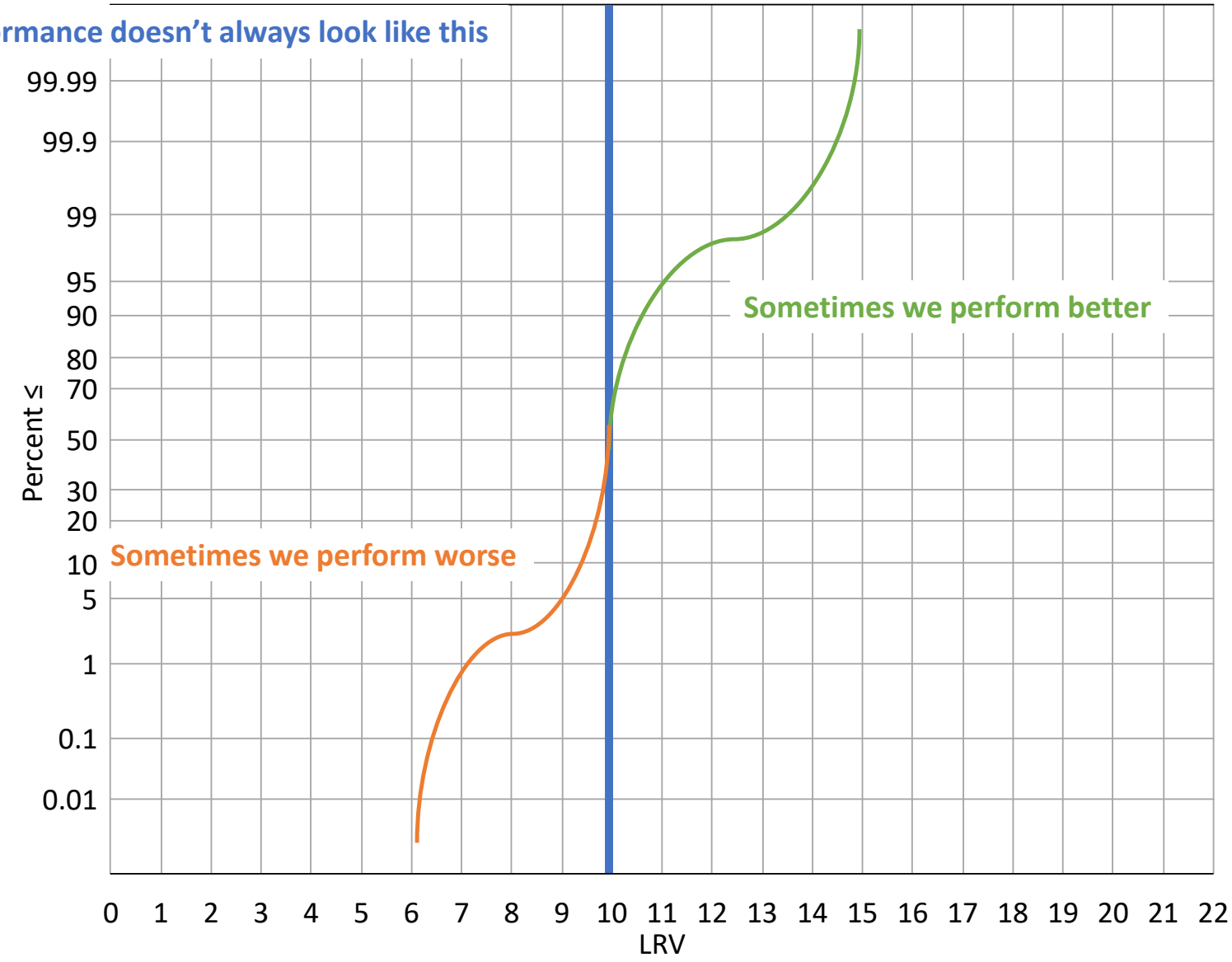


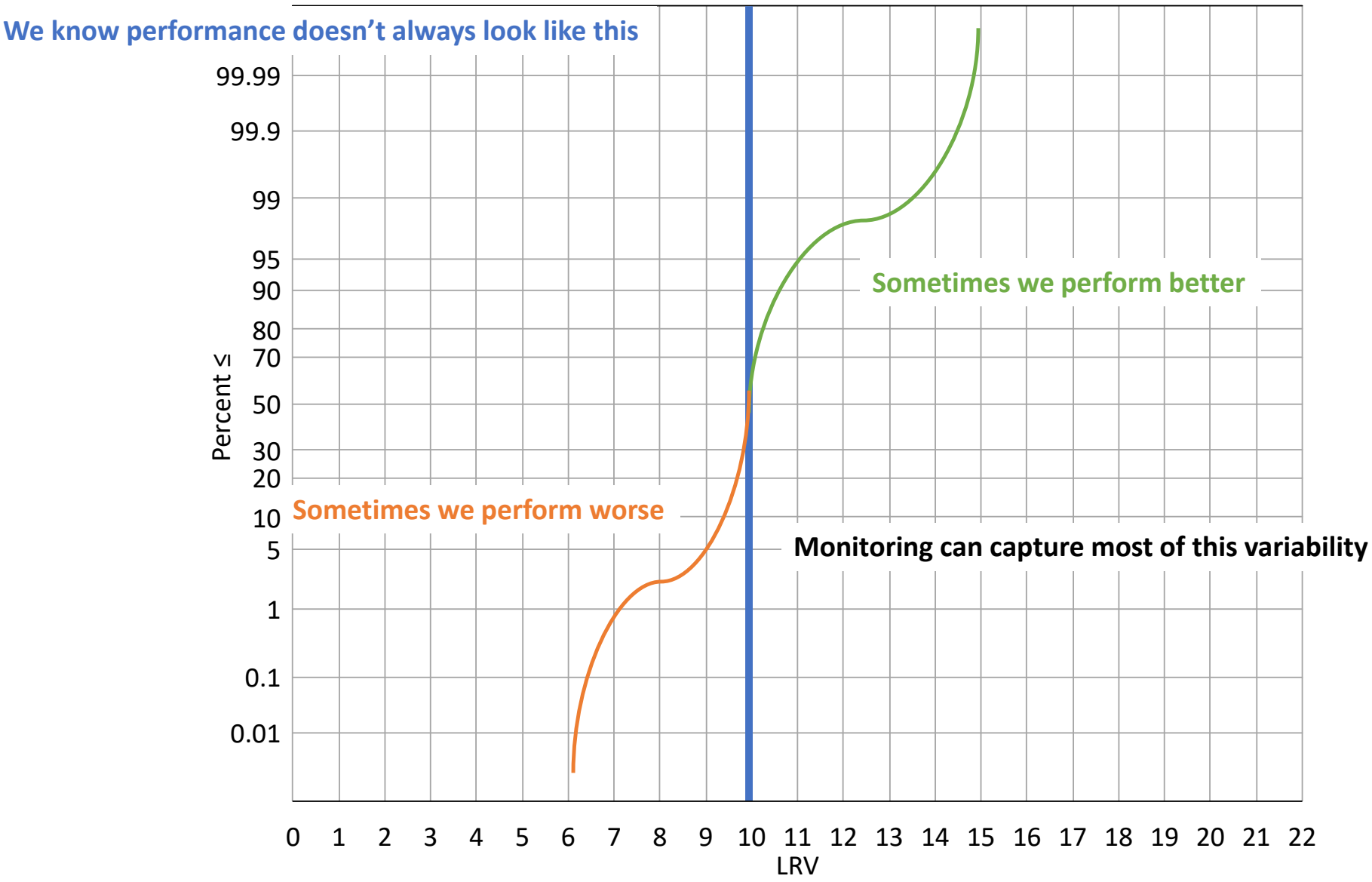
IMPACT OF TREATMENT VARIABILITY AND FAILURES

We know performance doesn't always look like this

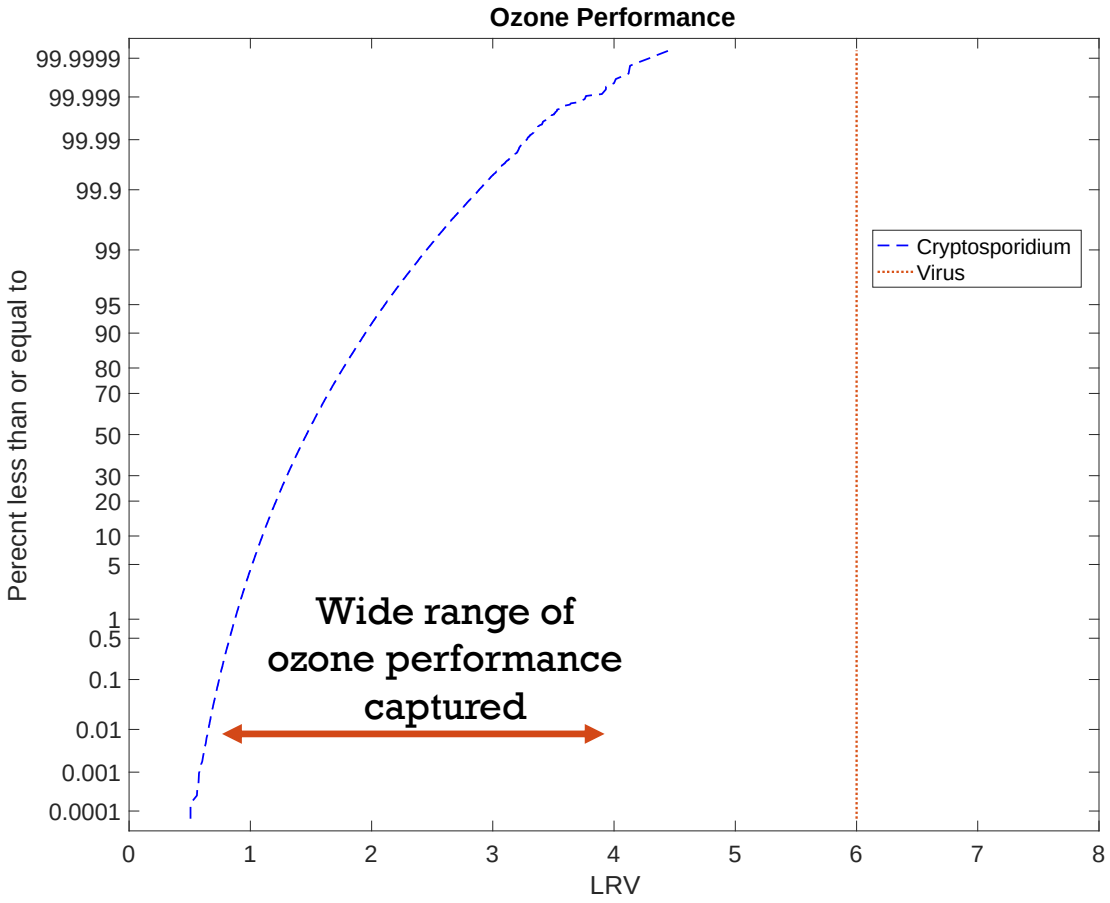


We know performance doesn't always look like this



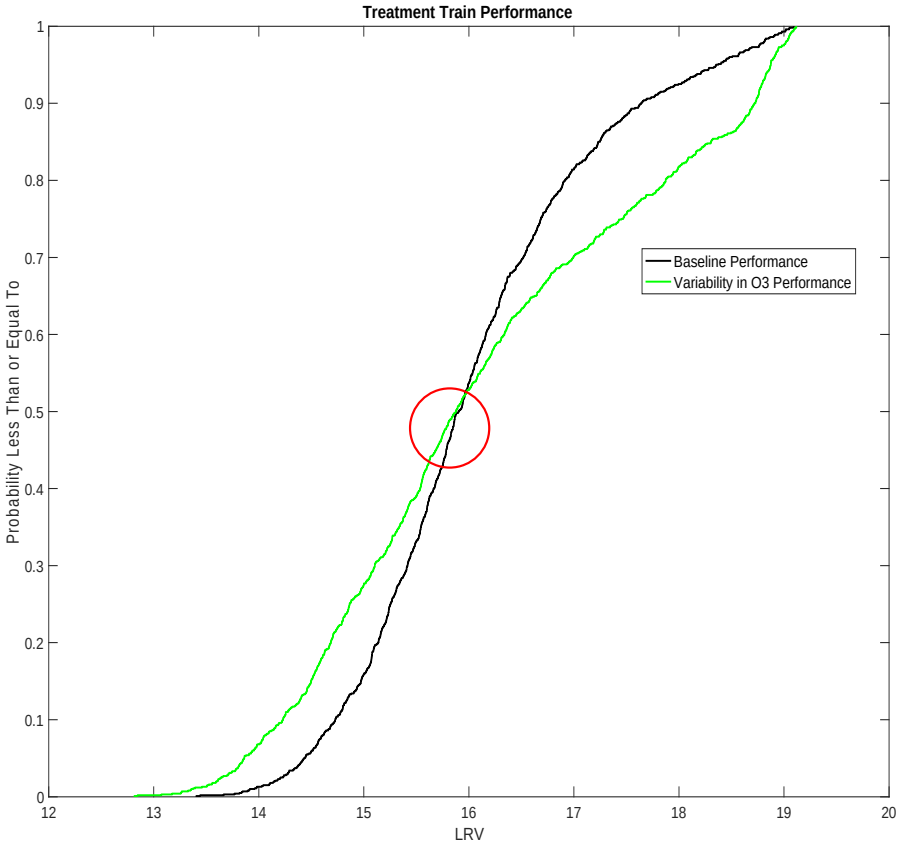

We know performance doesn't always look like this
99.99
99.9
99
95
90
80
70
50
30
20
10
5
1
0.1
0.01
Percent ≤
Sometimes we perform better
Sometimes we perform worse
Monitoring can capture most of this variability
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
LRV

OZONE DISINFECTION EXAMPLE

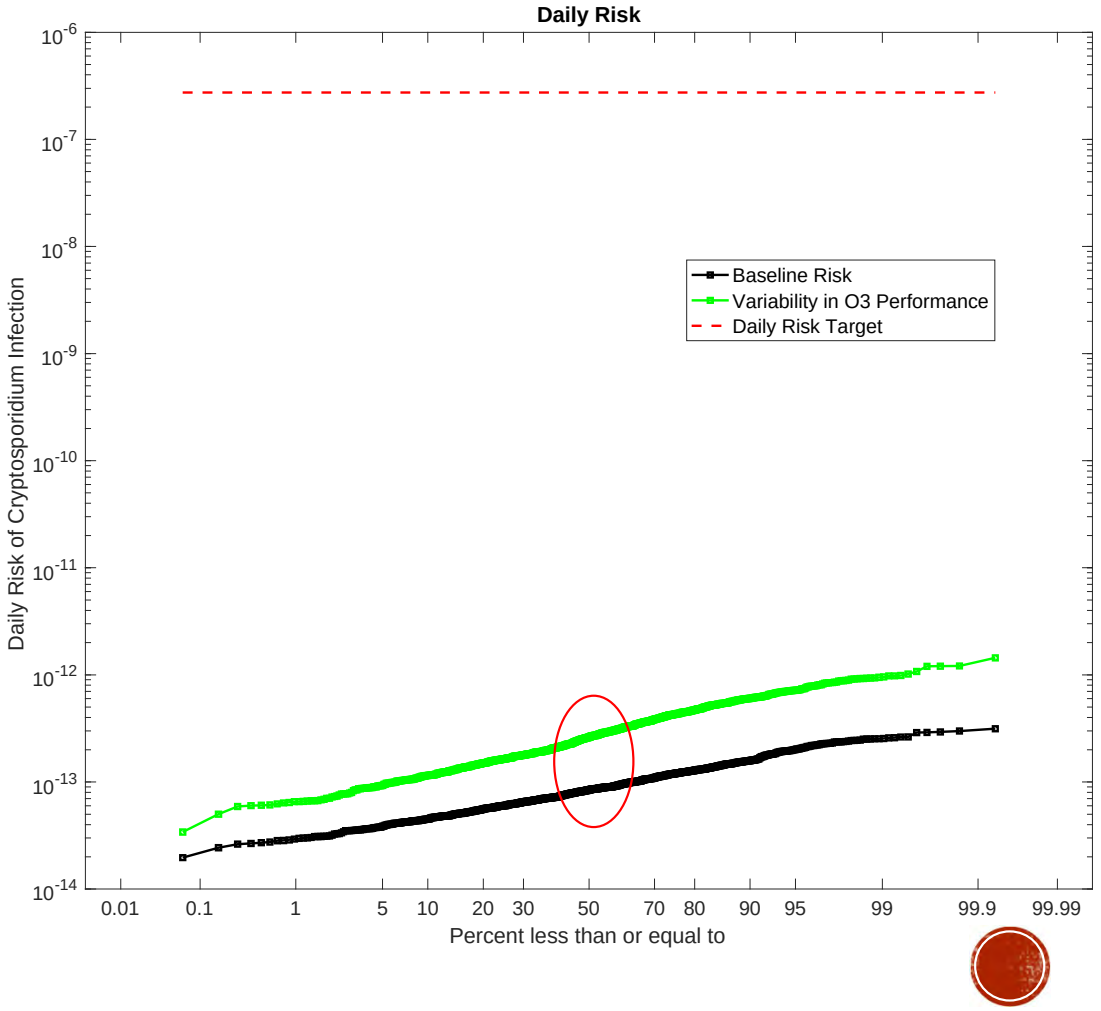


- What causes variation in performance?
  - Water quality
  - Ozone demand
  - Frequency of maintenance
  - Ozone dosing control strategies
- This variability is captured by monitors and shown in the performance curves
- This may vary from site to site

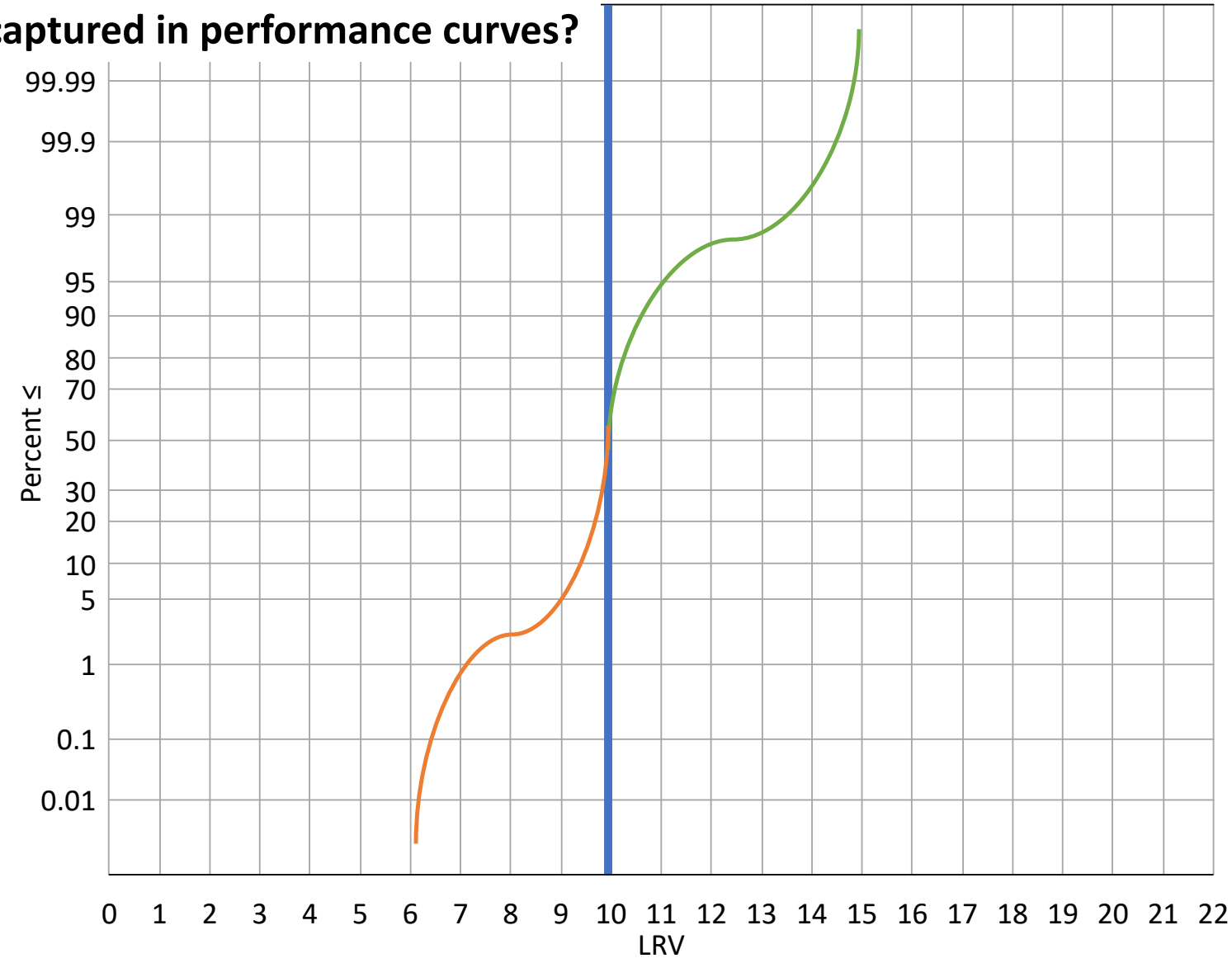
How does this type of variability impact risk?



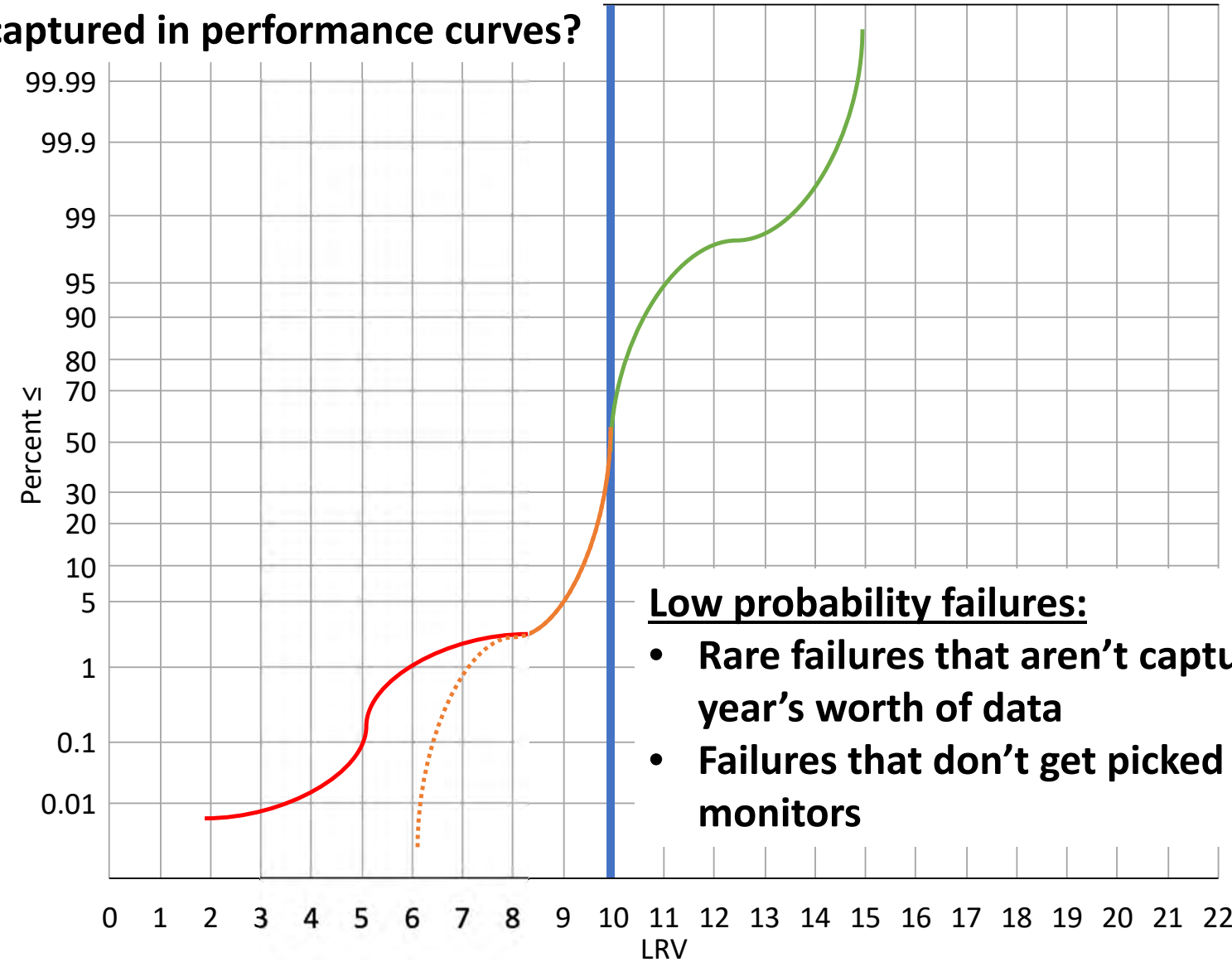
Treatment Train Performance



What isn't captured in performance curves?



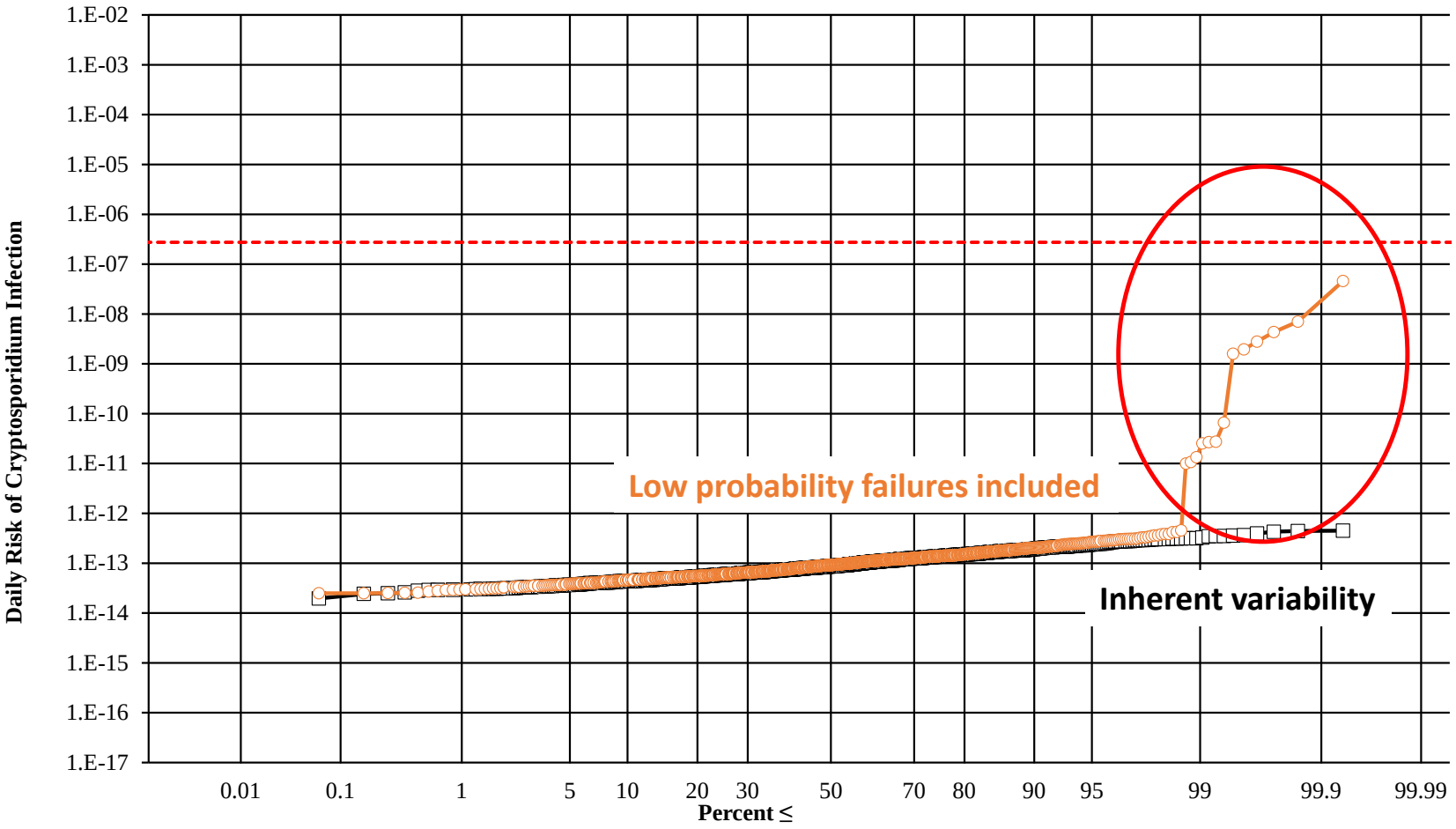
What isn't captured in performance curves?

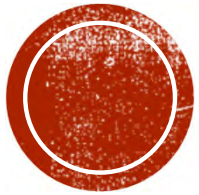


Low probability failures:

- **Rare failures that aren't captured in 1-year's worth of data**
- **Failures that don't get picked up by monitors**

Even low probability failures may impact risk





SENSITIVITY ANALYSIS

Investigate impact on risk by changing assumptions of different steps of QMRA

1. Exposure Assessment

Raw wastewater

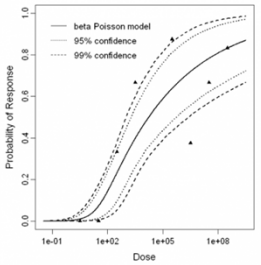
Treatment

Drinking water levels

Drinking water consumption

Exposure

2. Dose-Response



Dose-response

3. Risk Characterization

Risk

Moderate (DPR-2) → Constant point estimate vs. distribution?

High (DPR-1)

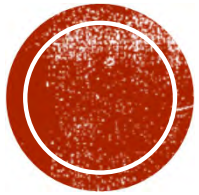
Calculated

Low (Sensitivity Analysis) → Constant point estimate (1.5L) vs. distribution?

Calculated

Low (Sensitivity Analysis) → Beta-Poisson vs. exponential?

Calculated



NEXT STEPS

NEXT STEPS

PRESENT

- Internal QA/QC of PATTP/QMRA with Research Team and Technical Working Group
- "Hands-on" training with PATTP/QMRA Tools: **August 4, 2020**

FUTURE

- Receive feedback from State Water Board on Guidance Document and tools: **August 25, 2020**
- Incorporate raw wastewater concentration data from DPR-2: **Fall/Winter, 2020**

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