PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE
Building responsible supply chains

PSCI PIE&AMR TEAM

Guidance for calculating dilution factors considering mixing zones

The following document provides guidance on potential techniques, methodologies, and available data sources. The correct approach to follow is dependent on specific aspects of the risk assessment to be conducted. The PSCI does not advocate a single correct approach or data source, but aims to provide information to help risk assessors design assessments suitable for their requirements.

Appendix A3: Guidance for calculating dilution factors considering mixing zones

There are many local situations where a receiving water body is only a narrow channel or is subject to low flows. In these situations, there is a risk that the mixing zone will occupy a major part of the cross-section which can have adverse consequences for the passage of aquatic life and could impact a large percentage of sessile organisms downstream of a discharge. To prevent such problems, some local regulators may place a limit on the proportion of the channel width occupied by the mixing zone. For example, the Netherlands limits the mixing zone to 25% of the cross-section of the water body. Therefore, it is important for a facility to understand if there is local guidance on assumed mixing. Also, where shellfisheries, drinking water abstractions, or other areas of special ecological significance are the discharge point, it is important to consider these features when determining the mixing zone. The distance between such features and the discharge point can be of great importance, especially when the distance is less than 10 times the width of the water body.

Several of the modelling and estimating principles used for rivers can be used for lakes. However, the definition of the dimensions of the mixing zone can significantly differ from the definition used for rivers. A major difference between lakes and rivers is the streaming velocity. In general, lakes are much less free-flowing than rivers. The mixing zone can be represented by a half a circle. In most cases the width of a lake is large. Making the length of the mixing zone proportional to the dimensions of the water body, i.e. the area of the water body, length and width of the water body, seems to be logic used by the Water Frame Directive implementation procedures. However, the European Chemicals Agency and U.S. EPA implementation procedures recommend more conservative ways of estimating dilutions for lake discharges. More information on the procedures can be found in Table 6.

Table 6 provides a comparison of the assumptions and inputs for calculating appropriate dilution factors while considering mixing zones in rivers, lakes and ocean receiving waters as recommended by the European Commission (Water Framework Directive), the European Chemicals Agency (REACH), and the US and Canadian EPAs. Assumptions and inputs useful for comparison of PECs to chronic, acute and drinking water PNEC values are included. The choice of which calculation methods are used may be driven in part by local regulator expectations. Table 6 does not include any calculation factors for estuary/tidal waters as they are case specific.

An overview for selecting the appropriate hydraulics for meeting PNEC values was also presented by the Pharmaceutical Supply Chain Initiative (PSCI) in the course of the PIE/AMR Deep Dive training seminar held on 17th September 2019 in Hyderabad, India (https://pscinitiative.org/resource?resource=482).

Table 6 Comparison of European Commission, European Chemicals Agency and United States Environmental Protection Agency surface water quality assessment factors used to assess compliance with Environmental Quality Standards

Guidance	**WFD**	**REACH**	**US EPA / Canada**
Agency	*European Commission*	*European Chemicals Agency*	*US Environmental Protection Agency / Environment Canada*
Guidance Reference	*Water Framework Directive's Technical Background Document on Identification of Mixing Zones (2010) (**Error! Reference source not found. Error! Reference source not found.**)*	*REACH Guidance on information requirements and Chemical Safety Assessment Chapter R.16: Environmental exposure assessment Version 3.0 (2016) **Error! Reference source not found.***	*Technical Support Document for Water Quality-based Toxics Control (1991) (**Error! Reference source not found. Error! Reference source not found. Error! Reference source not found. Error! Reference source not found.**)*
RIVERS - Chronic			
Default dilution factor for chronic PNEC values	Assume no dilution (i.e. no mixing)	A standard dilution of 10 is used when releasing to a freshwater environment.	Not provided. However, you could assume no dilution (i.e. no mixing)
Stream flow used for dilution analysis to meet chronic PNEC values	Q90 (The flow which is exceeded during 90% of the time. Sometimes also called a 10th percentile flow)	When carrying out a site-specific assessment, specific data on the receiving water may be used with regard to the dilution capacity of the environment (site-specific data should be justified and explained). However, it should be noted that a dilution factor higher than 1000 should not be used in any case.	7Q10 (The lowest 7 consecutive day flow that occurs once every 10 years)

Guidance	WFD	REACH	US EPA / Canada
Mixing zone size allowed for chronic PNEC	Up to 100% Q90. The WFD guidance notes that In some countries a limit is placed upon the proportion of the channel width occupied by the mixing zone. For example, in the Netherlands the mixing zone is limited to 25% of the cross-section of the water body. In the discharge test criteria are chosen in such a way that when mixing zone criteria can be met in streaming water bodies at distance (L), the cross section taken by in the mixing zone, bounded by EQS, (in general) will not be greater than 25%.	Based on defaults only unless computer modelled or dye tested	While the TSD does not prescribe mixing zones for chronic PNEC values, EPA regulations require each state to adopt mixing zone rules and EPA approve them. The most common general guideline is that the chronic mixing zone should be limited to no more than ¼ (25%) to ½ (50%) of the cross-sectional area and/or volume of flow of the stream, leaving at least ½ to ¾ (75%) free as a zone of passage for aquatic biota, nor should it extend over ½ of the width of the stream. Higher allowances are allowed if complete mixing can be demonstrated.
Recommended averaging period to meet chronic PNEC values	Not specified. PNEC values appear to be treated as daily maximum values.	Not specified. PNEC values appear to be treated as daily maximum values.	Recommended to not exceed a 4 day average unless basis for PNEC was based on longer term testing (i.e. 7 or 21 days). Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met.
RIVERS - Acute			
Mixing zone allowed to meet acute PNEC values	Q90 (The flow which is exceeded during 90% of the time. Sometimes also called a 10^{th} percentile flow); and the acute PNEC value must be met at 0.25 the stream width and downstream at the edge of mixing zone at distance of 10 times width of the water body of the discharge. The maximum allowed downstream distance is 1000 meters. (CORMIX modelling is usually used to demonstrate dilution factors)	Modelling (such as CORMIX) can be used to demonstrate dilution factors.	1:1 dilution of effluent assumed. 1Q10 (The lowest day flow that occurs once every 10 years). Zones can be expanded if discharge velocity is >3 m/s, limited to 50 times the discharge length scale and must show that the acute PNEC value is met within a distance of 5 times the local water depth in any horizontal directions. (CORMIX modelling is usually used to demonstrate dilution factors)
Recommended averaging period to meet acute PNEC values.	Not specified. PNEC values are treated as daily maximum values.	Not specified. PNEC values are treated as daily maximum values.	1-day maximum. Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met.

Guidance	WFD	REACH	US EPA / Canada
RIVERS Drinking Water			
Default dilution factor for drinking water PNEC values	No default dilution factor specified.	No default dilution factor specified.	30Q5 for non-carcinogens; and harmonic mean flow for carcinogens.
Site specific dilution analysis to meet drinking water PNEC values	Where drinking water is located in the vicinity of the discharge point, it is important to ensure that these form part of the overall appraisal process when determining the mixing zone. The distance between such features and the discharge point can be of great importance, especially when the distance is less then L or 10 times the width of the water body.	Not specified.	Advanced computer simulations may be allowed to refine loading capacity.
Recommended averaging period to meet drinking water PNEC values	Not Specified.	Not Specified.	1-day maximum. Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met.
LAKES – Chronic	WFD	REACH	US EPA/Canada
Default dilution factor for chronic PNEC values	Where there is no flow or rainfall (the ultimate worst-case scenario) the effluent concentration thus has to meet EQS because in theory the concentration reaches EQS due to lack of dilution by other streams, not taking into account processes such as partition, degradation and evaporation.	Not specified.	Discharges to lakes are not entitled to a default mixing zone. Effluents shall meet chronic PNEC values at the point of discharge.

Guidance	WFD	REACH	US EPA / Canada
Site specific dilution analysis to meet chronic PNEC values	Difficult to identify simple criteria for lakes. One of the most determining factors in this context is the type of initial mixing. Two types of mixing can be identified PLUME-mixing and JET-mixing. Mixing in the near vicinity of the point of discharge (the first few meters) can be described by either jet-mixing or plume-mixing. The mixing pattern with the highest calculated mixing-factor is used to describe the mixing in the first few m from the point of discharge. Use of mixing models can produce dilution factors of 10 or greater.	Modelling (such as CORMIX) can be used to demonstrate dilution factors.	Ambient mixing is minor for lakes and reservoirs because flow velocity is assumed to be minimal and mixing is accomplished by means of the discharge momentum and buoyancy. While EPA has not nationally set mixing zones for lakes, it has approved default dilution factors of 10:1 or up to 10% of a lake surface area, whichever is less, in many states.
Recommended averaging period to meet chronic PNEC values	Not specified. PNEC values appear to be treated as daily maximum values.	Not specified. PNEC values appear to be treated as daily maximum values.	Recommended to not exceed a 4 day average unless basis for PNEC was based on longer term testing (i.e. 7 or 21 days). Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met. See TSD for more details
LAKES – Acute	WFD	REACH	US EPA/Canada
Default Mixing zone allowed to meet acute PNEC values	No default mixing zones for acute PNEC values.	No default mixing zones for acute PNEC values.	No default mixing zones for acute PNEC values.
Site Specific Acute mixing zones to meet acute PNEC values	Acute mixing zones shall be sized on a case-by-case basis. Computer modelling or dye testing can be used.	Acute mixing zones shall be sized on a case-by-case basis. Computer modelling or dye testing can be used.	Acute mixing zones shall be sized on a case-by-case basis. Computer modelling or dye testing can be used.
Recommended averaging period to meet acute PNEC values.	Not specified. PNEC values are treated as daily maximum values.	Not specified. PNEC values are treated as daily maximum values.	1-day maximum. Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met. See TSD for more details.
LAKES – Drinking Water	WFD	REACH	US EPA/Canada
Default dilution factor for drinking water PNEC values	No default dilution factor specified.	No default dilution factor specified.	Same as chronic PNEC value default mixing zone (see above).

Guidance	WFD	REACH	US EPA / Canada
Site specific dilution analysis to meet drinking water PNEC values	Where drinking water is located in the vicinity of the discharge point, it is important to ensure that these form part of the overall appraisal process when determining the mixing zone. The distance between such features and the discharge point can be of great importance, especially when the distance is less then L or 10 times the width of the water body.	Not specified.	Same as chronic PNEC value site-specific mixing zone (see above). Advanced computer simulations may be allowed to refine loading capacity.
Recommended averaging period to meet drinking water PNEC values	Not Specified.	Not Specified.	1-day maximum. Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met. See TSD for more details.
OCEAN Chronic	**WFD**	**REACH**	**US EPA/Canada**
Default dilution factor for chronic PNEC values	For emissions along the shoreline or open waters, the total length of the mixing zone is L m. Equation is used that leads to a mixing zone positioned between a point L/2 m downstream and a point L/2 m upstream of the point of discharge. When using a maximum length of 1000 m for the mixing zone this leads to a mixing zone defined as half a circle with a radius of 500 m. For the average depth at the shoreline a value of 5 m is assumed. This results in a maximum volume of the mixing zone: $V_{mixing\ zone} = \pi \div 2 \times (500)^2 \times 5 = 1.96 \times 10^6$ [m³]	A standard dilution of 100 is used when releasing to a marine environment.	No uniform default value from EPA. However, EPA recommends simple single port and multiple port discharge calculations for chronic mixing (i.e. far-field) zones. See Appendix A for calculations and examples.

Guidance	WFD	REACH	US EPA / Canada
Ocean dilution used for site specific dilution analysis to meet chronic PNEC values	For emissions along the shoreline or open waters, the total length of the mixing zone is L m. Equation is used that leads to a mixing zone positioned between a point L/2 m downstream and a point L/2 m upstream of the point of discharge. When using a maximum length of 1000 m for the mixing zone this leads to a mixing zone defined as half a circle with a radius of 500 m. For the average depth at the shoreline a value of 5 m is assumed. This results in a maximum volume of the mixing zone: $V_{mixing\ zone} = \pi \div 2 \times (500)^2 \times D\ [m^3]$ D = specific depth	When carrying out a site-specific assessment, specific data on the receiving water may be used with regard to the dilution capacity of the environment (site-specific data should be justified and explained). However, it should be noted that a dilution factor higher than 1000 should not be used in any case.	Computer modelling or dye testing can be used.
Mixing zone size allowed for chronic PNEC	Computer modelling or dye testing can be used.	Computer modelling or dye testing can be used.	Computer modelling or dye testing can be used.
Recommended averaging period to meet chronic PNEC values	Not specified. PNEC values appear to be treated as daily maximum values.	Not specified. PNEC values appear to be treated as daily maximum values.	Recommended to not exceed a 4 day average unless basis for PNEC was based on longer term testing (i.e. 7 or 21 days). Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met. See TSD for more details.

Guidance	WFD	REACH	US EPA / Canada
OCEAN Acute	WFD	REACH	US EPA/Canada
Mixing zone allowed to meet acute PNEC values	Initial mixing adjacent to the point of discharge jet-mixing or plume-mixing can be estimated. See pages 17-18 in the		The TSD recommends a simplistic screening equation be used to estimate the initial dilution available in the vicinity of a discharge using the following equation: S = 0.3 (x/d) S = flux-averaged dilution x = distance from outlet d = diameter of discharge outlet The equation provides a minimum estimate of mixing because it is based on the assumptions that outlet velocity is zero and the discharge is neutrally buoyant. See TSD for more details.
Recommended averaging period to meet acute PNEC values	Not specified. PNEC values are treated as daily maximum values.	Not specified. PNEC values are treated as daily maximum values.	1-day maximum. Averaging allowed based on long term average statistical calculation guidance for a monthly average that assures 95% confidence that the daily maximum is met. See TSD for more details.

Example Calculations of Allowable Discharges Based on Receiving Water Body and Guidance Followed

Table 7 demonstrates how the size of the receiving water body (e.g. low, medium, high and very high rivers; shallow, medium, and deep oceans) and guidance followed impacts the calculated allowable mass discharges to meet chronic and acute PNEC values.

The following assumptions were made for the comparisons of the three guidances summarized:

- River Example Calculations used an assumed upstream concentration of 0.
- No high rate effluent diffuser
- The chronic PNEC is 1 µg/L and the acute PNEC is 10 µg/L;
- The upstream flow values used were obtained from gaging station on a river in Spain. The average, Q90 and 7Q10 flow values were calculated from an 11 year data set:

- Average flow = 510,037 m3/day
- Q90 flow = 28,944 m3/day
- 7Q10 flow = 8,220 m3/day

For illustration purposes, the Q90 and 7Q10 values were simply progressively increased by factors of 10, 100 and 1,000 to show medium, large and very large dilution ratios.

<u>Ocean Examples</u>

A single discharge port was assumed for 1,000 m3/day, 10,000 m3/day and 100,000 m3/day discharges into a shallow depth (5 meter), a medium depth (30 meter) and a deep depth (60 meter) in the ocean. Effluent discharge velocity at port equals 1 m3/sec (not a high velocity diffuser – no acute mixing zone).

Table 7 *Results for the different Guidances*

A. WFD Guidance Results

Water type	Effluent Discharge Volume	Upstream Flow	Effluent Discharge to River Dilution Ratio	Chronic PNEC	Acute PNEC	Allowable Mass discharge for Chronic PNEC value (100% stream dilution)	Allowable Mass discharge for Chronic PNEC value (25% stream dilution)	Allowable Mass discharge for Acute PNEC value (25% stream dilution)
River	(m^3/day)	(m^3/day)		(µg/L)	(µg/L)	kg/day	kg/day	kg/day
Small River	10,000	28,944	2.8944	1	10	0.04	0.02	0.17
Medium River	10,000	289,440	28.944	1	10	0.30	0.08	0.82
Large River	10,000	2,894,400	289.44	1	10	2.90	0.73	7.34
Very Large	10,000	28,944,000	2894.4	1	10	28.95	7.25	72.46

Water type	Port Depth	Effluent Discharge Volume	Effluent Discharge Velocity	Effluent Discharge to Ocean Dilution Ratio	Chronic PNEC	Acute PNEC	Allowable Mass discharge for Chronic PNEC value	Allowable Mass discharge for Acute PNEC value
Ocean	m	(m^3/day)	m/sec		(µg/L)	(µg/L)	kg/day	kg/day
Shallow	5	10,000	1.0	196	1	10	1.96	0.10
Medium	25	10,000	1.0	980	1	10	9.80	0.10
Deep	50	10,000	1.0	1,960	1	10	19.60	0.10

B. REACH Guidance Results

Water type	Effluent Dis-charge Volume	Default Dilution of 10:1	Upstream Flow Q90	Effluent Dis-charge to River Dilution Ratio	Chro-nic PNEC	Acute PNEC	Allowable Mass discharge for chronic PNEC value (default stream dilution)	Allowable Mass discharge for chronic PNEC value (100% stream dilution)	Allowable Mass discharge for acute PNEC value (no stream dilution)
River	(m^3/day)	(m^3/day)	(m^3/day)		(µg/L)	(µg/L)	kg/day	kg/day	kg/day
Small River	10,000	100,000	28,944	2.8944	1	10	0.35	0.04	0.10
Medium River	10,000	100,000	289,440	28.944	1	10	0.35	0.30	0.10
Large River	10,000	100,000	2,894,400	289.44	1	10	0.35	2.90	0.10
Very Large River	10,000	100,000	28,944,000	2894.4	1	10	0.35	28.95	0.10

Water type	Port Depth	Effluent Discharge Volume	Effluent Discharge Velocity	Default Mixing Dilution Ratio	Chronic PNEC	Acute PNEC	Allowable Mass discharge for Chronic PNEC value	Allowable Mass discharge for Acute PNEC value
Ocean	m	(m^3/day)	m/sec		(µg/L)	(µg/L)	kg/day	kg/day
Shallow	5	10,000	1	100:1	1	10	1.00	0.10
Medium	25	10,000	1	100:1	1	10	1.00	0.10
Deep	50	10,000	1	!00:1	1	10	1.00	0.10

C. US EPA/Canada Guidance Results

Water type	Effluent Discharge Volume	7Q10 Upstream Flow	Effluent Discharge to River Dilution Ration	Chronic PNEC	Acute PNEC	Allowable Mass discharge for Chronic PNEC value (50% stream dilution)	Allowable Mass discharge for Acute PNEC value (1:1 dilution)
River	(m^3/day)	(m^3/day)		(µg/L)	(µg/L)	kg/day	kg/day
Small River	10,000	8,220	0.822	1	10	0.01	0.20
Medium River	10,000	82,200	8.220	1	10	0.05	0.20
Large River	10,000	822,000	82.200	1	10	0.42	0.20
Very Large	10,000	8,220,000	822.000	1	10	4.12	0.20

Water type	Port Depth	Effluent Discharge Volume	Effluent Discharge Velocity	Effluent Discharge to Ocean Dilution Ratio	Chronic PNEC	Acute PNEC	Allowable Mass discharge for Chronic PNEC value	Allowable Mass discharge for Acute PNEC value
Ocean	m	(m^3/day)	m/sec		(µg/L)	(µg/L)	kg/day	kg/day
Shallow	5	10,000	1	13.6	1	10	0.14	0.10
Medium	25	10,000	1	23.1	1	10	0.23	0.10
Deep	50	10,000	1	61.9	1	10	0.62	0.10

From the results in Table 7A, Table 7B and Table 7C, the following observations can be seen:

- The WFD methods for evaluating chronic and acute toxicity are the least restrictive, especially at higher dilution volumes.
- The ECHA default for chronic mixing will not be protective in situations where there is less than 10 to 1 mixing.
- The ECHA and EPA methods for application of ocean mixing zones for chronic toxicity are more closely aligned than the WFD method. This is because the WFD method relies on a method based a volume of dilution in 500 m radius of the discharge port.

Models such as e.g., the U.S. PhATE or EU GREAT-ER river models may be used to revise the crude PEC values, and to explore the spatial and temporal variability to better understand the risks to humans and biota, to evaluate risk mitigation and management options. References that used the PhATE and GREAT-ER models to refine pharmaceutical risk assessments are amongst others Anderson et al., 2004 [39] and Caldwell et al., 2019 [40]