

# Air Exposure Durations

APRIL 2020

Air Guidance Values represent air concentrations that are likely to pose little or no health risk to humans, including vulnerable subpopulations. How large or small the value is depends on two factors: 1) how toxic a chemical is (e.g., the minimum amount that will cause health effects) and 2) the duration of the exposure.

Chemical toxicity also varies depending on when exposure occurs during the human lifecycle and for how long (duration) that exposure occurs. When evaluating toxicity, MDH scientists assess the relationship between exposure and resulting health effects. A key objective of the toxicity evaluation is to identify the lowest dose at which adverse effects are observed (the “lowest observable adverse effect level,” LOAEL) and the highest dose at which no adverse effects are observed (the “no observed adverse effect level,” NOAEL). When sufficient information is available, statistical modeling may be conducted to identify a minimal level of adverse effect (known as the lower confidence limit of a benchmark dose, BMDL). The NOAEL, LOAEL or BMDL is adjusted downward through the application of uncertainty (safety) factors to derive a reference concentration (RfC) for noncancer health effects. The RfC is then adopted as an air guidance value representing a concentration that is unlikely to pose a health risk for the specified time duration. An RfC may be derived for shorter and longer exposure durations depending on available and appropriate data from toxicity studies. For chemicals identified as linear carcinogens (i.e., those where a threshold exposure below which cancer is not a concern has not been demonstrated), an inhalation unit risk (IUR) is identified. An IUR represents an upper-bound estimate of cancer risk from exposure to 1 µg/m<sup>3</sup> for a lifetime. An excess cancer risk of 1 in 100,000 is divided by the IUR to derive an air guidance value associated with a negligible cancer risk over a lifetime. For nonlinear carcinogens (i.e., those where a threshold exposure below which cancer is not a concern has been demonstrated), a cancer health-based value may or may not be derived based on a threshold response approach or the non-cancer value may already be protective of cancer effects.

Understanding the relationship between timing, duration and magnitude of exposure is essential in deriving health-based values that are protective of sensitive life stages (e.g., early life-stages or critical developmental windows) and short periods of high exposure. If sufficient toxicological information is available, EPA recommends evaluation of multiple exposure durations for use in risk assessment (US EPA 2002). As part of their recommendations, EPA provided the following definitions for various exposure durations. The Minnesota Department of Health and the EPA Integrated Risk Information System (IRIS) have adopted these definitions as well.

- **Acute** - dosing duration of 1-day or less;
- **Short-term** - repeated dosing for more than 1-day, up to approximately 30 days;
- **Subchronic** - repeated dosing for more than 30 days, up to approximately 8 years (10 percent of a lifespan in humans) (roughly equivalent to more than 30 days, up to approximately 90 days in typical laboratory rodent species); and

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- **Chronic** - repeated dosing for more than approximately 8 years (10 percent of a life span in humans) (roughly equivalent to more than approximately 90 days in typical laboratory rodent species).

Within each duration, the RfC is calculated to be protective of all types of adverse effects for that exposure duration.

In an assessment of data derived from a toxicity study, the relevant duration is defined as the time of the first exposure until the point when the adverse effect was first observed. Protocols for toxicity testing do not necessarily evaluate or report effects that may have occurred or been observed at interim time points (i.e., before the end of the study); despite the fact that it is unlikely that effects only occurred at the study's end. MDH acknowledges the limitations of many studies that do not measure or report effects at different points in time during the study, which can result in overestimating the effective duration; meaning the time it takes to elicit an effect may be shorter than that which is stated in the study. When sufficient chemical-specific data are available to do so, MDH will assess interim time points during the study and will use any better estimate of the length of exposure required to elicit an adverse effect as the relevant dosing duration for air guidance values.

In general, shorter-duration values will be higher than longer-duration RfCs for a given chemical because the human body can usually tolerate a higher dose when the exposure duration is short, even though that dose may be harmful when it occurs over a longer duration. It is possible, however, that the RfC for a shorter duration is the same as, or in some cases, lower than the RfC for longer durations. This could result if a short duration was sufficient to elicit an adverse effect--such as if a more sensitive endpoint was assessed in the shorter-duration study (e.g., respiratory irritation, developmental, and immune toxicological studies generally involve short exposure durations)--or if a different species or life stage was assessed. When this occurs, the longer-duration RfC is set equal to the lower, shorter-duration RfC as recommended by EPA (US EPA 2002). This ensures that the RfC for longer durations is also protective of sensitive short-term exposures.

MDH does not specify or enforce any application of air guidance values. Other agencies may adopt air guidance values for regulatory purposes as applicable, depending on the situation and program requirements/limitations.

The updated air exposure durations were adopted in April 2020. Previous air guidance value exposure durations vary and may not be consistent with the new air exposure durations. Older air guidance values and durations may be evaluated on a case-by-case basis in consultation with MDH staff.

### References

U.S. Environmental Protection Agency. 2002. A Review of the Reference Dose and Reference Concentration Process. EPA/630/P-02/002F.

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U.S. Environmental Protection Agency Integrated Risk Information System Glossary. Accessed March 2020.

[https://iaspub.epa.gov/sor\\_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary](https://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary)

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