Perchlorate Incidence in Oregon and Human Health Considerations

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1 Background and Objectives

This report was prepared under a Memorandum of Agreement with the Oregon Department of Agriculture (“Perchlorate in Oregon Surface and Groundwater, Agricultural Crops, and Processed Foods”). The objective of this report was to prepare a review and summary of current knowledge of perchlorate occurrence in Oregon, including environmental fate, opportunities for exposure, and risks to human health. The preparation of this document included the following procedures:

1. Summarize the human health risks associated with exposure to perchlorate
2. Summarize the risk based standards for perchlorate adopted by individual states and the National Academy of Sciences
3. Summarize potential sources of perchlorate in Oregon; compare to other regions.
4. Summarize perchlorate ground and surface water monitoring data for Morrow and Umatilla Counties
5. Assess the potential for perchlorate to contaminate food and feed crops, livestock, dairy milk, and processed foods in Oregon
6. Recommend a sampling strategy to identify perchlorate presence, uptake, and bioaccumulation in livestock, food and feed crops, dairy milk, and processed food.

2 Executive Summary

2.1 Perchlorate Incidence in Oregon

Perchlorate ($\text{ClO}_4^-$) occurrence in surface and ground water has garnered increasing concern in the United States since the late 1990s when new analytical methods became available allowing detection at low ppb levels. Perchlorate occurrence is widely distributed in the United States and has been detected in 39 states and Puerto Rico. Perchlorate is both a naturally occurring and man-made chemical. The most common uses for perchlorate are in aerospace programs, military operations and by defense contractors. Perchlorate is also an impurity and degradate in household bleach. Perchlorate anion is commonly associated with the solid salts of potassium, and sodium. Ammonium perchlorate is the most widely used perchlorate compound. Perchlorate has also been found to occur naturally in arid environments. Perchlorate is highly soluble and very stable in most aqueous environments. Perchlorate’s persistence and mobility is of concern for both ground and surface water quality. At sites across the United States the pattern
of perchlorate contamination of ground and surface water is highly variable. In addition, while many sites are associated with known sources, for some sites the source(s) of contamination is unclear. To date, perchlorate has been detected in two areas of Oregon: the lower Willamette Superfund Site and the northern parts of Morrow and Umatilla counties. The results of perchlorate ground and surface water monitoring in Morrow and Umatilla Counties can be generally described as widespread, spatially variable, low-level contamination, with the possible exception of a point source associated with the Boeing Jet Engine Test Facility near Sixmile Creek. Based on monitoring conducted from 2000-2005, across the northern parts of these counties low concentrations of perchlorate were detected in less than half of the wells tested, and most contained 4 μg/L or less. In addition to human exposure to perchlorate in drinking water, when contaminated water is used for irrigation or livestock there is an additional concern regarding the food supply. Residue data for produce from different regions worldwide suggests that the perchlorate originated in the water or the soil (possibly enriched with perchlorate-containing fertilizer) in which they were grown. Consequently, monitoring for perchlorate in water used for irrigation, food processing, and livestock in northern Morrow and Umatilla counties should reduce the likelihood of contamination of the food supply at unacceptable levels.

2.2 Perchlorate and Human Health

The mechanism of effect of perchlorate has been well-studied in humans. Perchlorate inhibits the uptake of iodide by the thyroid gland. The administration of high and sustained doses of perchlorate results in decreased secretion of active thyroid hormones. This effect is magnified when there is insufficient intake of iodine in the diet. Iodine nutrition is an important factor that may modulate the effects of perchlorate on the thyroid gland.
The human body has normal physiological mechanisms to compensate for decreases in thyroid hormone production, but when thyroid hormone function is deficient this can result in the clinical diagnosis of hypothyroidism. The developing fetus, neonate, and pregnant women are considered to be sensitive populations at higher risk of adverse outcomes from deficient thyroid gland function (hypothyroidism), because maternal thyroid hormones play an important role in normal fetal brain development during the first trimester of pregnancy. Hypothyroidism that occurs in early development or later stages of pregnancy (congenital hypothyroidism) can have adverse impacts on fetal brain development and cognitive function after birth.

Advances in analytical chemistry have enabled scientists to measure perchlorate at very low concentrations in the environment. These advances have enabled scientists to measure the prevalence and magnitude of perchlorate residues in agricultural commodities and foods intended for human consumption. Data are accumulating from investigations of the prevalence and magnitude of perchlorate residues in agricultural commodities and foods intended for human consumption. In one recent study of leafy vegetables cultivated in multiple states throughout North America, estimates of dietary exposure were less than 4% of the reference dose (0.7 μg/kg/day), as recommended by the National Academy of Sciences (NAS). The reference dose (RfD) is an estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects during a lifetime. In addition to green leafy vegetables, milk has been identified as a potential source of dietary exposure to perchlorate.

Much of the scientific data on human exposure to perchlorate has been derived from investigations of drinking water. There have been several epidemiological studies investigating whether there is evidence of adverse effects on thyroid function in populations living in
communities where perchlorate has been detected in drinking water. The majority of these studies have not found evidence of an association between perchlorate in drinking water and adverse effects on thyroid function in neonates, children, and adults. A longitudinal study of pregnant women and their newborns was conducted in Chile, involving three different cities with varying concentrations of perchlorate in their drinking water (ranging from <4 μg/L to 120 μg/L). No significant adverse effect on thyroid hormone levels was observed in association with exposure to perchlorate in drinking water during early and late pregnancy, or among neonates born in the different cities.

In 2005, the NAS issued a report that summarized the human health risks of perchlorate ingestion. The NAS reviewed the epidemiological data on perchlorate in drinking water, and concluded that the available evidence did not support a causal association between perchlorate exposure in drinking water and congenital hypothyroidism, or changes in thyroid function in newborns (at drinking water levels up to 120 μg/L). The NAS recommended using the inhibition of iodide uptake as an upstream, nonadverse effect which would represent a conservative and health protective approach towards deriving a reference dose. The NAS agreed that human data collected in a controlled environment provided a more reliable basis for the risk assessment than animal data.

The NAS recommended a study by Greer, et al. as the point of departure for the determination of a reference dose for perchlorate. The no observed effect level (NOEL) for iodide uptake inhibition from perchlorate that was determined in that study (7 μg/kg/day) was consistent with other clinical studies that had assessed the same endpoint. An uncertainty factor of 10 was recommended to account for sensitive populations (defined as pregnant women who may have hypothyroidism or iodide deficiency). This resulted in a recommendation for a
perchlorate RfD of 0.7 μg/kg/day. The NAS recommendations for the perchlorate RfD have been accepted by the US EPA. Some states have chosen more protective public health recommendations. These recommendations have been based upon alternative interpretations and the application of different uncertainty factors to the same scientific study by Greer, et al., which was relied upon by the NAS.

There are several other important chemicals in the diet and drinking water that share a similar mechanism of effect as perchlorate. Examples of such chemicals include nitrate and thiocyanate. There is relatively little information in the scientific literature assessing concurrent exposure to these chemicals, but the results of some recent reviews and scientific studies suggest that exposure to nitrate and thiocyanate from drinking water or food accounts for a more significant proportion of iodine uptake inhibition in comparison to perchlorate. As information accumulates to assess human exposure to perchlorate and other chemicals with similar mechanisms of effect, these types of data will be useful to scientists in assessing cumulative risks associated with environmental chemicals that can have adverse effects on human thyroid function.

3 Perchlorate Incidence in Oregon

3.1 Introduction

Perchlorate (ClO₄⁻) occurrence in surface and ground water has garnered increasing concern in the United States since the late 1990s when new analytical methods became available allowing detection at low ppb levels. Perchlorate occurrence is widely distributed in the United States (United States Environmental Protection Agency, 2002) and has been detected in 39 states and Puerto Rico (See Figure 1). Perchlorate is both a naturally occurring and man-made chemical. The most common uses for perchlorate are in aerospace programs, military operations
and by defense contractors. Perchlorate is also an impurity and degradate in household bleach. Perchlorate anion is commonly associated with the solid salts of potassium, and sodium. Ammonium perchlorate is the most widely used perchlorate compound. Perchlorate has also been found to occur naturally in certain highly arid environments. Perchlorate is highly soluble and very stable in most aqueous environments. Perchlorate’s persistence and mobility is of concern for both ground and surface water quality.

At sites across the United States the pattern of perchlorate contamination of ground and surface water is highly variable. In addition, while many sites are associated with known sources, for some sites the source(s) of contamination is unclear. For example, in Henderson, Nevada, where wells near the former Pacific Engineering & Production Company of Nevada (PEPCON) rocket fuel plant, which exploded in 1988, show concentrations ranging from 51.4 to 630 ppm (parts-per-million). Fifty wells near ammonium perchlorate manufacturer Kerr-McGee Chemical Corporation, located near the abandoned PEPCON site, also showed significant perchlorate contamination with levels as high as 3,700 ppm. Water from these sites drains into Lake Mead and the Colorado River, and has resulted in extensive monitoring of downstream water used for drinking and irrigation in both Arizona and California (Urbansky, 1998). By contrast, a 2002 survey of drinking-water wells in western Texas (Jackson, et al., 2004) found perchlorate in >80% of the wells tested over an area of ~60,000 square miles. The levels of perchlorate varied with ~25% greater than 4 μg/L. With no identified anthropogenic sources, the presence of perchlorate can be generally described as widespread, spatially variable, low-level contamination.
Figure 1. EPA National Map of Perchlorate Detections as of September 23, 2004

Disclaimer: The detections shown do not represent the entire universe of perchlorate releases in the United States. Rather this site represents the extent of perchlorate detection data currently known to the EPA as reported from various sources (http://www.epa.gov/fedfac/documents/perchlorate_map/nationalmap.htm)
Although anthropogenic sources have been identified, monitoring for perchlorate in the northern Morrow and Umatilla Counties of Oregon (~550 square miles) showed a similar pattern as reported in the west Texas study, with the possible exception of a point source associated with the Boeing Jet Engine Test Facility near Sixmile Creek. Based on monitoring conducted from 2000-2005, across the northern parts of these counties low concentrations of perchlorate were detected in less than half of the wells tested, and most contained 4 μg/L or less.

In addition to human exposure to perchlorate in drinking water, when contaminated water is used for irrigation or livestock there is an additional concern regarding the food supply. Recent studies conducted by the U.S. Food and Drug Administration (2004), the Environmental Working Group (2003), and others (Jackson, et al., 2005; Sanchez, et al., 2005, Capuco, et al., 2005, Snyder et al., 2005, Krynitsky et al., 2006, Snyder et. al., 2006) have detected perchlorate in samples of leafy vegetables, vegetables, fruits, and infant food (includes processed fruits, vegetables, meats, pastas, infant formula, and dry products), lemon pulp, milk, bottled water, wine, beer, and dietary supplements. For domestic produce, the highest perchlorate levels were 136 μg/L in lettuce. Worldwide the highest level measured was 463 μg/L for a cantaloupe from Guatemala. Domestic perchlorate concentrations in milk ranged from <3 μg/L to 11 μg/L. Perchlorate in United States wine and beer ranged from 0.2 to 4.5 μg/L. Bottled water perchlorate levels ranged from <0.05 to 0.74 μg/L. Perchlorate in dietary supplements (i.e., vitamins and vitamin/mineral supplements) was measured as high as 2,420 μg/L; however, over half the detections were < 30 μg/L.
3.2 Anthropogenic Sources of Perchlorate

Production of ammonium perchlorate first began in the United States in the mid-1940s, primarily for use by the U.S. military. The most common uses for ammonium perchlorate are in explosives and rocket propellants, which have been used widely in military munitions items, such as mortars, grenades and flares and solid fuel rockets. Based on production data from two perchlorate manufacturers, it is estimated that 90 percent of perchlorate compounds are manufactured for use in defense activities and the aerospace industry. While occurring most frequently at domestic Air Force installations, ammonium perchlorate has been detected at Army and Navy sites too. The National Aeronautics and Space Administration (NASA) and Department of Energy (DOE) also have a small number of facilities with perchlorate. In addition, ammonium perchlorate and the other perchlorate salts have been or are used in a wide range of applications, including pyrotechnics and fireworks, blasting agents, solid rocket fuel, matches, lubricating oils, nuclear reactors, air bags and certain types of fertilizers. Improper storage and/or disposal related to the uses mentioned above are the most typical route for perchlorate to enter into the environment (U.S. Environmental Protection Agency, 2006). Another source of perchlorate may be hypochlorite products (bleach) (MassDep, 2005). Sodium hypochlorite is somewhat unstable and will decompose to chlorate. Chlorate can self-oxidize to perchlorate. These processes are accelerated with increasing temperature.

3.3 Perchlorate Chemistry and Environmental Fate

Perchlorate (ClO$_4^-$) consists of four-double covalent bonds between chlorine and oxygen (tetrahedral coordination), making this highly soluble oxyanion very stable and nonreactive in aqueous environments. Chlorine is environmentally abundant, ranking 18$^{\text{th}}$ among the elements and is ubiquitous in the atmosphere, soil and water. The chloride (Cl$^-$) anion is the most stable
form. Chlorine gas (Cl₂) dissolves in water to form hypochlorite (OCl⁻). Hypochlorite disproportionates spontaneously to chloride and chlorate (ClO₃⁻). Oum et al. (1998) have suggested that an important source of hypochlorite is the photolysis of ozone in the presence of sea salt. In the atmosphere the various chlorine oxides form free radical intermediates and ClO₃⁻ can react with hydroperoxy (·OOH) or hydroxyl (·OH) free radicals to form perchlorate. To investigate atmospheric lightning as an energy source for the formation of perchlorate, Dasgupta et al. (2005) exposed NaCl/NaOCl aerosol to an electrical discharge in the laboratory and analyzed for Cl⁻ and ClO₄⁻. They also simulated desertification conditions with UV light and UV/high level ozone (O₃) exposure. While the electrical discharge experiments demonstrated the plausibility of electrical storms as an energy source in the formation of atmospheric perchlorate from chloride and/or hypochlorite, the UV/UV-O₃ experiments were less convincing. However, Glen Miller (Miller, et al., 2006) and associates at the University of Nevada, Reno, have demonstrated that perchlorate can be formed when salt solutions are exposed to ozone and UV light in the presence of titanium dioxide, a known photo-sensitizer present in desert soils - suggesting that photochemical oxidation on these soils may form perchlorate.

As perchlorate does not adsorb onto inorganic surfaces, particularly those characterized by net-negative surface charges, it should move freely with soil water. Physical processes including mixing and dispersion control the distribution of perchlorate in groundwater. In arid and aerobic environments perchlorate is very stable. When present in the soil, perchlorate’s persistence and mobility make it a likely ground and surface water contaminant.

The overall reduction of perchlorate to chloride is given by the following half reaction:

\[ \text{ClO}_4^- + 8\text{H}^+ + 8e^- = \text{Cl}^- + 4\text{H}_2\text{O}, \]

with an \( E^0 \) of 1.39 volts (V) and an \( Eh \) (pH7) of 0.98 V. This reaction suggests that perchlorate may be reduced in natural systems such as wetlands that are
partially anaerobic and other microbially-active environments with plentiful and diverse electron donors. Perchlorate is reduced to intermediate compounds - chlorate and chlorite - and eventually to chloride in these environments by serving as a terminal electron acceptor during oxidation of reactive organic carbon. Perchlorate reduction is both thermodynamically and microbially enhanced under denitrifying conditions. Over the last decade researchers (Chaudhuri, et al., 2002; Coates, et al., 1999; Logan, 2001; Coates and Achenbach, 2004) have investigated the specialized perchlorate-respiring microorganisms (PRMs) which have evolved that reduce perchlorate into chloride. PRMs have been isolated from diverse environments both pristine and contaminated. The species Dechloromonas and the Azospira, which are dominant PRMs in the environment, can grow over a broad range of environmental conditions; but generally grow optimally at circumneutral pH values in freshwater. By contrast, their activity is expected to be marginal under arid soil and climatic conditions. These findings suggest that PRMs may not be prevalent in soils of the semi-arid climate of Eastern Oregon.

3.4 Perchlorate in Fertilizer and Natural Sources

The presence of perchlorates in natural nitrate fertilizers from deposits in the Atacama Desert of northern Chile was first reported in the 1880’s (Orris, et al., 2003). One hundred years later the USGS scientists also identified perchlorate in this material (Ericksen, 1981; Van Moort, 1985). In 1999, the EPA began testing for the presence of perchlorate in other fertilizers that did not contain Chilean nitrate. USGS scientists, interested in the relationship between geology and the geochemistry of nitrate sources and the presence of perchlorate, also analyzed samples from sources other than Chile. Initially EPA found that nitrate fertilizers from sources other than the Atacama Desert of northern Chile did not contain measurable levels of perchlorate (Susarla and others, 1999, 2000; Urbansky, 2000). However, in 2002, the EPA reported finding perchlorate in
three solid nitrate fertilizers used for hydroponics (Collette, et al., 2003). Based, in part, on these findings, USGS scientists concluded that “…the presence of perchlorate in some minerals and other evaporite materials other than Chilean nitrates indicates that natural geochemical processes can produce perchlorate.” (Orris, et al. (2003). They also suggest “Some of the factors related to the natural formation of nitrates would also seem to be necessary for the formation of natural perchlorates. These factors include aridity and the presence of salines and related minerals.” In addition, Ericksen (1983) suggests that most nitrates in the Chilean deposits have a biogenic origin and that leaching and redeposition of the saline materials by infrequent rainwater led to concentration of the nitrates. Ericksen also suggested that the perchlorate may have formed by photochemical reactions between chlorine and ozone and that the perchlorate was concentrated by the same mechanism that concentrated the nitrates.

Orris et al. (2003) conclude “The results of our preliminary analyses for perchlorate in natural materials does not negate our initial hypothesis that natural sources of perchlorate (other than Chilean nitrates) are most likely to occur in similar depositional environments, especially in arid climates with strong evaporitic conditions. More importantly, these findings support the notion that natural deposits may be the primary source for the occurrence of low levels of perchlorate (< 4 μg/L) in ground and surface waters in arid climates of the Western United States.”

In the past it is likely that nitrate fertilizer contaminated with perchlorate (of Chilean origin) was used in the northern parts of Morrow and Umatilla counties. Therefore, historic use of Chilean nitrate fertilizer must be considered as a source of perchlorate.

In a more recent USGS study (Plummer, et al., 2006), groundwater was analyzed from remote parts of the Middle Rio Grande and found perchlorate concentrations of 0.12 to 1.8 μg/L.
As there are no known industrial sources in the study area and because the water samples are pre-anthropogenic in age (0-28,000 years), a natural source is likely. They suggest an atmospheric source for perchlorate that over geologic time was concentrated at the surface through evapotranspiration, and transported to groundwater, with some loss to the soil environment (microbial recycling of perchlorate) before aquifer recharge. They estimate that pre-anthropogenic bulk atmospheric deposition had a perchlorate concentration on the order of 0.09 μg/L. Based on this assumption and evaporitic conditions during the late Holocene (last ~10,000 years) in north-central New Mexico, they suggest that perchlorate concentrations as high as 4 μg/L are possible in the groundwater. They also imply, based on groundwater chloride/bromide ratios (Davis, et al., 1998), that stronger evaporitic conditions exist in parts of Arizona, Nevada, California, and New Mexico for which bulk atmospheric deposition could result in perchlorate groundwater concentrations as high as 19 μg/L. These bulk atmospheric deposition estimates are consistent with the recent study by Dasgupta et al. (2005), which measured perchlorate in 17 samples of precipitation from Lubbock, Texas.

Although many sites with perchlorate contamination have known point source(s), in other areas, some vast, point source(s) cannot explain the monitoring results. Point sources usually have a tight, controlled plume produced off some industrial site that used to manufacture or handle perchlorate (Brandhuber and Clark, 2005). In the west Texas study (Jackson, et al., 2004), arguably the most comprehensive to date, no plume-like pattern is discernible; perchlorate’s occurrence is random. The authors report some wells yielding relatively high perchlorate concentrations immediately adjacent to wells with little or no detectable perchlorate. In addition, researchers (Orris, et al., 2003) at the US Geological Survey have found perchlorate in the low-parts-per-billion range in some naturally occurring evaporite materials in scattered locations in
the Western Hemisphere. However, because perchlorate is frequently present in small amounts, it has been difficult to isolate enough to study the source directly and discern natural from manmade.

To further investigate the source of perchlorate in the west Texas study, Dasgupta et al. (2005) measured perchlorate in 17 samples of precipitation from Lubbock, Texas. The concentrations ranged from <0.01 to 1.6 μg/L with an average of 0.33 μg/L. These findings suggest that the background perchlorate levels measured in the 2002 survey of drinking-water wells in west Texas (Jackson, et al., 2004) may result from the natural flux of perchlorate found in rain and snow. The combination of arid climate (that may concentrate the low-level flux) and geologically recent intensive irrigation may explain, in part, the pattern of low levels of natural perchlorate in ground and surface water. Concordantly, the recent advent of center pivot irrigation in Northern Morrow and Umatilla counties may have mobilized naturally-occurring perchlorate in the soil.

3.5 Perchlorate in Food and Feed

As perchlorate has been identified as a contaminant of drinking and irrigation water, there is concern that it may be taken up and concentrated in plants, or expose livestock through consumption of water or feed. Early concern was raised by the Environmental Working Group (Environmental Working Group, 2003) that perchlorate concentrations of 5 to 9 μg/L in Colorado River water below Lake Mead resulted in contamination of crops or livestock. They found detectable perchlorate in four of 22 lettuce samples (highest level 121 μg/L fresh weight) presumably irrigated with water from the Lower Colorado River. The FDA (U.S. Food and Drug Administration, 2004) conducted a National “market basket” survey of perchlorate in lettuce and found an average concentration of 10.4 μg/L and ranging from <1 μg/L to 129 μg/L (n=128).
When perchlorate concentrations are ranked by either lettuce type or production region no trends are evident, with the exception that most of the non-detects (11 of 12) were from the central coast of California. By contrast, when ranked by perchlorate concentration, two of the top ten samples were from this region. Seven of the top ten were from the Lower Colorado River region; however, the sample with the second highest perchlorate concentration was from Florida. A more recent study by Sanchez et al. (2005) found similarly varied results for perchlorate in a number of lettuce varieties, as well as other leafy vegetables. They also conducted a risk assessment based on perchlorate concentrations in the produce sampled and estimates of dietary consumption. They concluded “For all lettuce types in this survey, hypothetical exposures were less than 4% of the reference dose [0.7 μg/kg/day] recommended by the National Academy of Sciences.” Plant uptake studies of both perchlorate and its analog, the gamma emitter pertechnetate (TcO₄⁻), indicate that perchlorate adsorption results in accumulation primarily in the leaves, and to a much lesser extent in the fruit (Cataldo et al. 1986; Echevarria et al. 1997; Yu et al. 2004; Jackson et al. 2005). Accordingly, Sanchez et al. (unpublished data) reported no detectable perchlorate residues (>5 μg/L) in carrots, squash, onions, sweet corn, and snap beans, and residues above 10 μg/L in cantaloupe and honey dew. As with the leafy vegetables, these crops were irrigated with perchlorate contaminated irrigation water. In a study of uptake of perchlorate by citrus, Sanchez et al. (2006) report perchlorate concentrations in the leaves of 1,835 μg/L dry weight (dw) followed by the fruit (128 μg/L dw). Mean perchlorate concentrations in roots, trunk, and branches were all less than 30 μg/L dw. Lemon pulp perchlorate concentrations ranged from below detection limit (1.25 μg/L) to 38 μg/L fresh weight, and were related to the perchlorate concentration of irrigation water. In a comparison of analytical methods for perchlorate, Krynitsky et al. (2006) report preliminary data from the FDA
Total Diet Study Market Basket survey which will be published on-line at http://www.cfsan.fda.gov/~comm/tds-res.html. They report concentration ranges (in μg/L) for selected leafy vegetables, vegetables, fruits, and infant food (includes processed fruits, vegetables, meats, pastas, infant formula, and dry products). Spinach (range = 6.1–768, mean = 46.0, n = 19) had the high perchlorate levels, followed by carrots (range = 1.2–111, mean = 13.8, n = 12), cantaloupe (range = 2.8–115, mean = 13.4, n = 12), lettuce (range = 2.9–136, mean = 12.8, n = 27), and infant foods (range = 0.89–12.0, mean = 3.06, n = 25). The method limit of quantification (LOQ) was 1.0 μg/L in fruits, vegetables, and infant foods, and 3.0 μg/L in dry products.

In a recent study El Aribi et al. (2006) analyzed foods and beverages for perchlorate in individual samples collected worldwide. Produce samples from the United States included plums (0.090 μg/L), blueberries (0.094 μg/L), apples (0.116 μg/L), watermelon (0.243 μg/L), tomatoes (0.260 μg/L), green lettuce (6.63 μg/L), oranges (9.99 μg/L), and green grapes (19.29 μg/L). For other parts of the world, the highest levels were found in produce from Central and South America; cantaloupe from Guatemala measured the highest at 463 μg/L. Perchlorate in United States wine ranged from 0.197 to 4.53 μg/L, whereas a Rose wine from Portugal measured 50.25 μg/L. Perchlorate in United States beer ranged from 0.364 to 2.014 μg/L. The highest level measured in beer worldwide was 8.98 μg/L in a Lager from Chile. In evaluating perchlorate residue data for a subset of produce (tomatoes, oranges, grapes) from different regions worldwide, the authors report that only certain production regions indicate a strong presence of perchlorate. They speculate that the perchlorate originated in the water or the soil (possibly enriched with perchlorate-containing fertilizer) in which they were grown.
Alfalfa is known to accumulate perchlorate, making it and other dietary components (including water) sources of exposure to livestock (Jackson et al. 2005). In a recent study conducted by the FDA (U.S. Food and Drug Administration, 2004), perchlorate was detected in commercial fluid milk in 13 states at concentrations ranging from <3 μg/L to 11 μg/L (mean = 5.8). A study by Capuco et al. (2005) had similar findings for both manually and mechanically collected milk, indicating that perchlorate’s presence cannot be attributed to contamination during automated milking, collection or processing. They also report that up to 80% of ingested perchlorate is metabolized, most likely in the rumen, before reaching meat or milk.

Using liquid-chromatography – tandem triple-quadrupole mass spectrometry (LC-MS/MS) Snyder et al. (2005) analyzed a limited number of bottled water samples (n=21) and found perchlorate levels ranging from <0.05 to 0.74 μg/L in ten samples. Samples were also analyzed for bromate, chlorate, and iodate. For samples with perchlorate detections, the ratio of iodate to perchlorate ranged from 5 to 269, with an average of 48 times more iodate ion than perchlorate.

Using a similar method of analysis, Snyder et al. (2006) analyzed dietary supplements (i.e., vitamins and vitamin/mineral supplements) for perchlorate. Perchlorate was detected in 20 of the 31 dietary supplements tested. The highest level detected was 2420 μg/L; however over half the detections were < 30 μg/L. The majority of these samples also contained iodine. As inhibition of thyroidal iodine by perchlorate is the biochemical event used to infer the potential for a toxic response in humans, co-exposure to perchlorate and iodine should be evaluated when assessing risk.
3.6 Monitoring for Perchlorate in Oregon

To date, perchlorate has been detected in two areas of Oregon: the lower Willamette Superfund Site\(^1\) and the northern parts of Morrow and Umatilla Counties, referred to in this report as the Lower Umatilla Basin Perchlorate Study Area (LUB PSA) (see Figure 2).

In 1990 Oregon Department of Environmental Quality (DEQ) declared the Lower Umatilla Basin (LUB) in the northern parts of Morrow and Umatilla Counties a Groundwater Management Area (GWMA) as required under in Oregon’s Groundwater Protection Act of 1989. The law requires DEQ to declare a GWMA if area-wide groundwater contamination, caused primarily by non-point source pollution, exceeds certain trigger levels. DEQ declared the Lower Umatilla Basin a GWMA because elevated nitrate levels (above the 7 mg/l trigger) were detected in many wells in the basin. Along with continued monitoring for nitrate, starting in 2000 DEQ and Region 10 EPA cooperated in sampling for perchlorate.

3.6.1 Groundwater

Beginning in 2000 there have been 14 sampling events and 391 wells tested in the LUB PSA (see Table 1), with several wells tested multiple times. The results for the individual wells, prepared by DEQ (Oregon DEQ 2006a), are provided in the supporting data (see accompanying data and maps). Events shown in Table 1 include the 2003 synoptic sampling event for perchlorate in the LUB GWMA (Oregon DEQ 2006b) and targeted sampling of potential perchlorate point-sources by Weston Solutions, Inc for Region 10 EPA; these include the Boardman FUDS\(^2\) Site Assessment (Weston 2004), the Cold Springs FUDS Site Assessment

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\(^1\) The lower Willamette Superfund Site perchlorate groundwater contamination originated at the Arkema Facility (former Atofina Chemicals site). Groundwater concentrations in the source area are on the order of 285 mg/L. Clean-up is currently underway (http://yosemite.epa.gov/r10/cleanup.nsf/sites/arkema).

\(^2\) Formerly Used Defense Site
(Weston 2005b), and the North Morrow Study Area Preliminary Assessment/Site Inspection Report & Addendum (Weston 2005a, 2006). To our knowledge, groundwater monitoring data from these studies is inclusive for the LUB PSA. In addition, there is a much smaller data set for surface water and soil.

There are two methods in general use for testing of perchlorate in environmental samples. EPA Method 314.0 was developed for analysis of drinking water samples and has a reported method detection limit of 2 μg/L. Whereas, EPA Method 8321A-mod is designed for samples with relatively high turbidity or other interferences, such as groundwater collected from monitoring wells and surface water, and has a method detection limit of 0.2 μg/L. With the exception of the different detection limits, the accuracy and precision of the two methods are similar. However, presumably for consistency DEQ reports only groundwater data for analyses using the Method 314.0. Table 1 shows a range of detection limits from 1 to 5 μg/L. For EPA Method 314.0, method detection limits are determined using seven replicates of a standard in reagent water to determine the lowest analyte concentration that, with 99% confidence, is greater than zero. As method detection limit is influenced by interferences, or the presence of common ions other than perchlorate, detection limits greater than the reported method detection limit may be used and detection limits less than the reported method detection limit are possible.

Table 2 shows a summary of perchlorate detections for the LUB PSA. Perchlorate samples were analyzed with both EPA methods. For the majority of samples the results are similar. Consequently, only the results of Method 314 are given in Table 2. Monitoring data in Table 2 are segregated by well water use classes only. Although the depth of the screen for these wells varies greatly, no attempt was made to evaluate this parameter relative to perchlorate detections. However, monitoring wells as a group are “shallow”. The monitoring well category
includes wells that were constructed specifically for groundwater monitoring and are used for no other purpose. A significant number of the monitoring wells are located at food processing facilities (41 wells or about 30% of all monitoring wells). These wells had the greatest percent detections. Both the shallow depth of the screen and their location near possible perchlorate sources associated with land application of food processing wastes should be considered.

The summary data in Table 2 shows that 44% of the wells tested contained perchlorate above the detection limit. Forty-two percent of the irrigation wells contained detectable perchlorate concentrations. No perchlorate was detected in any of the stock watering wells tested, however n=6 is a relatively small sample size.

3.6.2 Surface Water, Sediment, Soil, and Other Data

Surface water, sediment, and soil contamination was investigated alongside groundwater in the studies conducted by Weston Solutions for the USEPA. These studies include the Boardman FUDS Preliminary Assessment/Site Inspection (Weston 2004), the Cold Springs Precision Bombing Range FUDS Preliminary Assessment Site Inspection (Weston 2005b), and the North Morrow Study Area Preliminary Assessment/Site Inspection Report (Weston 2005a; Weston 2006). Examination of surface water data indicated that the majority of surface waters in the NMPS do not have significant perchlorate contamination, with two notable exceptions. The Six-Mile Canyon Creek shows consistent perchlorate contamination ranging from 5-10 μg/L. This creek is located within the Boardman FUDS and is just southwest from the former Boeing Jet Engine Test Site; both of these sites are potential point sources of perchlorate. The only other surface waters with perchlorate detections above 1 μg/L are found in, and to the west and southwest of Cold Springs Reservoir, near the former Cold Springs Precision Bombing Range (Cold Springs Canyon and Despair Gulch). All other surface waters, including the Columbia
River, Butter Creek, Willow Creek, and the Umatilla River, as well as all irrigation canals tested, had results of either “no-detect” or <1 μg/L. In general, contamination was far less common in surface waters than in groundwater.

Soil and sediment samples were also analyzed in the North Morrow Perchlorate Study Area, the Cold Springs FUDS, and the Boardman FUDS reports. None of these soil or sediment samples showed the presence of perchlorate above reliable detection levels (>2 μg/L).

As part of the addendum (Weston 2006) to the original NMPS report prepared for EPA by Weston, testing was conducted on the effluent from reservoir tanks of sodium hypochlorite (bleach) at the Potlatch Pump Station. The sodium hypochlorite is used as a disinfectant and growth inhibitor inside irrigation lines, along with bromide. The effluent tested from the holding container with bleach in it was 570 μg/L (Weston 2006). This high concentration merits more study into the possible contribution of irrigation line disinfectant as another potential source of perchlorate in the region.

3.6.3 Spatial Distribution of Perchlorate Detections

The available information does not allow a rigorous analysis of the spatial relationship between possible sources of perchlorate, land use and well type. However the 2003 DEQ synoptic event, the NMPS report & addendum, the Cold Springs FUDS reports, and the Boardman FUDS report all contain spatially explicit monitoring data. These studies collectively represent more than 2/3 of all available data, and there are no apparent differences in results reported by the other 1/3 of studies for which the spatial information is only approximate. Therefore, the following analysis was developed using the spatially explicit data sets only; we believe this set of data is sufficient to draw general conclusions as to the spatial distribution of perchlorate detections in the NMPS area.
The presence of perchlorate in the LUB PSA can be described as widespread, spatially variable, low-level perchlorate contamination. With the possible exception of a point source associated Boeing Jet Engine Test Facility near Sixmile Creek, the analysis of monitoring data does not appear to indicate any clear source of the perchlorate, as there are no “hot-spots” or plumes of contamination (high concentrations at the center, and gradually decreasing further away from the source). No discernable pattern or specific region of contamination can be identified from the spatial layout of perchlorate detections and “no-detects”. Several sites within 1-2 miles from each other give disparate results, where one site will reliably show 3-8 \( \mu \text{g/L} \) perchlorate, another just a mile or two away reliably tests “no-detect”. In fact, the highest perchlorate detection of 29.2 \( \mu \text{g/L} \) is less than three miles from another well with a “no-detect” result.

Noteworthy is the observation that there are very few perchlorate groundwater detections within or near the flood plains of rivers such as the Umatilla River and Butter Creek, suggesting that flood water or subsurface flow percolating through the soil in these areas is able to dilute or wash away perchlorate that would perhaps accumulate in a drier location. Also these areas may contain “reducing environments” were chemical or biological perchlorate degradation may be greater.
<table>
<thead>
<tr>
<th>Sampling Event</th>
<th>Name</th>
<th>Date(s)</th>
<th>Well Type</th>
<th># Wells</th>
<th>Detection Limit (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>Umatilla Depot</td>
<td>8/2001</td>
<td>Monitoring</td>
<td>36</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>Port of Morrow</td>
<td>6/2003</td>
<td>Monitoring</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>DEQ Synoptic</td>
<td>9/2003</td>
<td>Domestic, Irrigation, Industrial, Community well, Stock watering well, Monitoring</td>
<td>85</td>
<td>1, 1, 1, 1, 1</td>
</tr>
<tr>
<td>3</td>
<td>Boeing</td>
<td>8/2000 to 10/2003</td>
<td>Monitoring, Irrigation, Drain, Stock watering well</td>
<td>61</td>
<td>2, 2, 2, 2</td>
</tr>
<tr>
<td>4</td>
<td>Boardman FUDS</td>
<td>6/2004</td>
<td>Domestic, Drinking Water Supply/Community, Monitoring</td>
<td>20</td>
<td>3, 1, 1</td>
</tr>
<tr>
<td>5</td>
<td>DEQ Irrigation</td>
<td>9/2004</td>
<td>Irrigation</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Lamb-Weston</td>
<td>12/2004</td>
<td>Monitoring</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>LUB GWMA Resampling</td>
<td>11/2004</td>
<td>Domestic, Industrial, Irrigation, Monitoring</td>
<td>48</td>
<td>28, 2, 3, 2</td>
</tr>
<tr>
<td>8</td>
<td>Cold Springs FUDS</td>
<td>12/2004</td>
<td>Domestic</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>North Morrow Study Area</td>
<td>12/2004)</td>
<td>Domestic, Community, Industrial, Monitoring</td>
<td>45</td>
<td>34, 4, 1, 2</td>
</tr>
<tr>
<td>10</td>
<td>3 Chowning wells &amp; Before/after Kennedy RO unit</td>
<td>1/2005</td>
<td>Domestic, Before RO Unit, After RO Unit</td>
<td>42</td>
<td>3, 1, 1</td>
</tr>
<tr>
<td>11</td>
<td>UMCD Landfill</td>
<td>4/2005</td>
<td>Monitoring</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Bombing Range Assessment</td>
<td>2005</td>
<td>Domestic, Community, Industrial, Monitoring</td>
<td>51</td>
<td>2, 3, 1, 1</td>
</tr>
<tr>
<td>13</td>
<td>North Morrow Study Area</td>
<td>9/2005</td>
<td>Monitoring</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Monitoring Well</td>
<td>Irrigation Well</td>
<td>Domestic Well</td>
<td>Industrial Well</td>
<td>Community Well</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>---------------</td>
<td>-----------------</td>
<td>----------------</td>
</tr>
<tr>
<td># Samples Analyzed</td>
<td>187</td>
<td>29</td>
<td>131</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td># Locations Sampled</td>
<td>140</td>
<td>26</td>
<td>98</td>
<td>4</td>
<td>10</td>
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<tr>
<td>Wells sampled twice</td>
<td>7</td>
<td>3</td>
<td>27</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Wells sampled ≥3 times</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Minimum Concentration¹</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Average Concentration¹, ², ³</td>
<td>7.6</td>
<td>2.3</td>
<td>3.5</td>
<td>--</td>
<td>2.8</td>
</tr>
<tr>
<td>Maximum Concentration¹</td>
<td>29.2</td>
<td>4.23</td>
<td>13.4</td>
<td>&lt;4.0</td>
<td>4.5</td>
</tr>
<tr>
<td># Wells with Detections</td>
<td>75</td>
<td>11</td>
<td>34</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>% of Wells with Detections</td>
<td>54%</td>
<td>42%</td>
<td>35%</td>
<td>0%</td>
<td>20%</td>
</tr>
</tbody>
</table>

¹ All detections based on EPA Method 314.0
² Average concentration values in the table are the average of DETECTIONS.
³ Average concentrations that include the censored data and substituting one-half the detection limit produces a mean of all 391 samples of 3.3 µg/l.
4 Perchlorate and Human Health

4.1 Perchlorate Pharmacology and Effects on the Thyroid Gland

Perchlorate is one of several environmental chemicals capable of affecting the thyroid gland in humans. The normal function of the human thyroid gland is to take iodine derived from foods, and convert it into thyroid hormones (thyroxine and triiodothyronine). Thyroid hormones are important for human health, because cells throughout the body depend upon these hormones to regulate their metabolism. When thyroid hormone function is abnormally high, this can result in the clinical diagnosis of hyperthyroidism. When thyroid hormone function is abnormally low, this can result in the clinical diagnosis of hypothyroidism.

The developing fetus, neonate, and pregnant women are considered to be sensitive populations at higher risk of adverse outcomes from deficient thyroid gland function (hypothyroidism). The developing fetus is at higher risk because fetal production of thyroid hormones does not develop until later stages of pregnancy (Morreale de Escobar et al., 2004). Hypothyroidism that occurs in early development or later stages of pregnancy can have adverse impacts on fetal brain development and subsequent cognitive function. Congenital hypothyroidism is the term that is used to describe a newborn with abnormally decreased thyroid hormone production. In the State of Oregon, congenital hypothyroidism is a medical condition which is routinely tested for through the Northwest Regional Newborn Screening Program operated by Oregon Department of Human Services.

The effects of perchlorate on human thyroid function have been well-studied in individuals who have hyperthyroidism (Godley and Stanbury, 1954). The effectiveness of potassium perchlorate as a pharmaceutical for hyperthyroid diseases was based upon its mechanism of effect. Perchlorate inhibits the uptake of iodide by the thyroid gland, and
prolonged therapy with high doses of perchlorate results in a decreased secretion of active thyroid hormones in individuals with hyperthyroid conditions (Crooks and Wayne, 1960). This effect is magnified when there is inadequate dietary intake of iodine. Iodine nutrition is an important factor that may modulate the effects of perchlorate on the thyroid gland.

High doses of perchlorate have been administered to adults to treat hyperthyroidism (Crooks and Wayne, 1960; Godley and Stanbury, 1954; Stanbury and Wyngaarden, 1952). These doses used to treat adults (ranging from 100 – 1000 mg/day) greatly exceed the amount of perchlorate encountered in food or drinking water. The human body has normal physiological mechanisms to compensate for decreases in thyroid hormone production associated with exposure to perchlorate, which include increasing the production of thyroid secreting hormone (TSH) and increasing the uptake of iodide by the thyroid gland (NAS, 2005).

Potassium perchlorate has been administered at pharmaceutical doses during human pregnancy to treat hyperthyroidism. Twelve pregnant women with hyperthyroidism were effectively treated with potassium perchlorate (Crooks and Wayne, 1960). No adverse effects were reported among the pregnant women in this case series, and infants born to mothers treated with potassium perchlorate did not have adverse outcomes or evidence of significant thyroid disease. Potassium perchlorate has also been administered chronically to individuals with hyperthyroidism whose thyroid function had returned to normal (Wenzel and Lente, 1984). The results of this study provided evidence that moderately high doses of perchlorate given chronically to people with a prior history of hyperthyroidism do not cause hypothyroidism (NAS, 2005). Potassium perchlorate has also been administered to children to treat hyperthyroidism. A case series described the effective use of potassium perchlorate at doses ranging from 200-300 mg/day in children of ages 6-13 years, with no significant side effects (Smellie, 1957).
The use of perchlorate for treating hyperthyroid conditions has declined over time, as more modern pharmaceuticals have been developed. Perchlorate continues to have important medical uses for treating hyperthyroidism caused by the anti-arrhythmic drug amiodarone (Erdogan, et al., 2003; Wolff, 1998). While the pharmaceutical use of perchlorate has generally been well-tolerated in humans with low incidence of side-effects, a rare and serious complication known as agranulocytosis has been described in association with high-dose perchlorate therapy for hyperthyroidism (Hobson, 1961; Johnson and Moore, 1961). Agranulocytosis is a rare and dose-dependent side effect that has been reported to occur with other pharmaceutical drugs (in addition to perchlorate) used in treating hyperthyroidism (Cooper, 2005).

When administered for pharmaceutical uses, potassium perchlorate is readily absorbed after ingestion. The peak concentration of perchlorate in serum is reached in approximately 3 hours. Perchlorate has a relatively short half-life in serum (6-8 hours), and is rapidly eliminated from the body by urinary excretion (NAS, 2005; Greer, et al., 2002). Methods have been developed to detect and quantify perchlorate in urine as a biomarker of human exposure, and one recent study found that perchlorate was present in 100% of urine samples obtained from healthy adults (Valentin-Blasini, et al., 2005).

4.2 Perchlorate: Sources of Exposure in the Environment

As perchlorate is no longer commonly utilized as a pharmaceutical, the main sources for human exposure include the diet as well as drinking water. The recognition of the diet as a source of human exposure to perchlorate is a relatively recent discovery; data is accumulating from investigations of the prevalence and magnitude of perchlorate residues in agricultural commodities and foods intended for human consumption. Perchlorate in foods has been
summarized in a previous section of this document. In the United States leafy vegetables often show the highest perchlorate levels.

In one recent investigation, scientists measured perchlorate in leafy vegetables originating from conventional and organically cultivated produce in multiple states throughout North America. Of 438 vegetable samples analyzed, 16% of the conventionally produced samples and 32% of the organically produced samples had quantifiable levels of perchlorate (Sanchez, et al., 2005). The investigators utilized United States Department of Agriculture statistics on food consumption, and data from the EPA Exposure Factors Handbook to estimate dietary exposure to perchlorate based upon the levels that were measured. The estimated mean dietary perchlorate exposure for adults was approximately 1 μg/day for conventionally produced leafy vegetables, and 2 μg/day for organically produced leafy vegetables. Estimates of mean dietary perchlorate exposure for children ages 2-5 were approximately 0.56 μg/day for conventionally produced leafy vegetables, and 1.18 μg/day for organically produced leafy vegetables. Based upon these measurements, the estimated doses for perchlorate from eating green leafy vegetables in all age and gender groups were less than 10% of the reference dose for perchlorate (0.7 μg/kg/day), as defined by the National Academy of Sciences (NAS, 2005; Sanchez, et al., 2005). The reference dose (RfD) is an estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects during a lifetime.

The national study of perchlorate in green, leafy vegetables also concurrently assessed the presence of nitrate, which shares a similar mechanism of effect to perchlorate, in terms of the ability to competitively inhibit the uptake of iodide into the thyroid gland (Sanchez, et al., 2005). The analyses showed nitrate was generally present at much higher concentrations than
perchlorates in the vegetables sampled. Based upon the data on perchlorate and nitrate in these vegetables, the potential for inhibition of iodide uptake from nitrate was more than 100 times greater than that from perchlorate (Sanchez, et al., 2005).

In addition to green leafy vegetables, milk has been identified as a potential source of human exposure to perchlorate. The US FDA sampled milk collected at retail stores from various regions of the country (US FDA, 2004). Perchlorate was measurable in 101 out of 104 samples, and the mean concentration was 5.76 μg/L (range 3.16-11.3 μg/L). These results were similar to what was reported in another market basket study of milk conducted in Texas (Kirk, et al., 2003). Another recent study has reported the detection of perchlorate in human breast milk, at a mean concentration of 10.5 μg/L (Kirk, et al., 2000). The results of one recent scientific publication suggest that women of reproductive age are not likely to exceed the reference dose when consuming perchlorate in milk and drinking water (Baier-Anderson et al., 2006), but it is also generally acknowledged that data are limited and further research is needed to obtain more accurate information about human exposure to perchlorate from all possible sources.

Most of the scientific data on human exposure to perchlorate has been derived from investigations of groundwater and drinking water. In 2001, the US EPA began to monitor perchlorate in large public water systems, as well as a representative sample of small systems. As of May 2004, the data indicate that perchlorate in public drinking water supplies range from less than 4 μg/L to 200 μg/L, with a median value of 6.4 μg/L (US EPA, 2004). Higher perchlorate concentrations have been reported in monitoring wells associated with Superfund sites, or other groundwater and surface water not directly associated with drinking water (US EPA, 2002).
4.3 Epidemiological Studies of Human Exposure to Perchlorate (Drinking Water)

There have been several epidemiological studies that have assessed whether there are adverse effects on thyroid function in populations living in communities where perchlorate has been detected in drinking water. These studies have included assessments of neonates, children, and adults. The majority of these epidemiological studies have not found evidence of an association between perchlorate in drinking water and adverse effects on thyroid function.

One study was conducted in Clark County, Nevada, where the water supply was found to contain perchlorate concentrations ranging from 5-24 μg/L. The prevalence of thyroid diseases in this region was compared to other counties where perchlorate was not detected. The results of this investigation found no significant increase in the incidence of thyroid disease in association with perchlorate in drinking water in Clark County (Li, et al., 2001).

Another study was subsequently conducted in Las Vegas, Nevada, where perchlorate had been detected in drinking water at concentrations up to 15 μg/L. In that study, investigators assessed whether there was a significant increase in adverse effects on thyroid function (based upon TSH) in neonates, in comparison to neonates born in communities without perchlorate in drinking water. The results of this investigation found no evidence of adverse effects on neonatal TSH levels in association with environmental perchlorate exposures in drinking water (Li, et al., 2000a).

Another publication investigated whether neonates in Las Vegas had significant differences in thyroid hormone levels in comparison with newborns in regions without perchlorate in drinking water. Based upon an analysis of over 23,000 newborns there was no evidence of a significant effect (Li, et al., 2000b). A study conducted in regions of California and Nevada where perchlorate was detected in drinking water found no evidence of an increased
rate of congenital hypothyroidism, in comparison to areas of these states where perchlorate was not detectable (Lamm and Doemland, 1999). A lack of association between the detection of perchlorate in drinking water and congenital hypothyroidism was also reported in another study of newborns in Southern California (Kelsh, et al., 2003).

One epidemiological study conducted in Arizona reported that low-levels of perchlorate in drinking water may be associated with adverse health effects in neonates (Brechner, et al., 2000). The investigators reported that perchlorate was detectable in drinking water in Yuma, Arizona in 1999 at a concentration of 6 μg/L, and assumed that this reflected concentrations present during the study period (1994-1997). The drinking water for the city of Yuma, Arizona is derived from the Colorado River, which is known to have detectable concentrations of perchlorate. A comparison was made between newborn TSH levels in Yuma, Arizona and Flagstaff, Arizona (where drinking water originates from sources other than the Colorado River). The investigators reported that neonates in Yuma had TSH values significantly higher than in Flagstaff, which implied an adverse effect on thyroid function from exposure to perchlorate.

While this observation was not consistently demonstrated in another epidemiological investigation which used an analogous study design (Li, et al., 2000a), other questions have been raised with respect to the methods utilized in the Arizona study. Some scientists have suggested that the reason for the disagreement between studies may be explained by the fact that TSH levels in newborns are highly dependent upon gender, and that in the Arizona study the sex distribution was not reported or adjusted for in the statistical analysis (Goodman, 2001). Other investigators have suggested that the reason for differences in TSH levels is that the analyses were confounded by the age of the newborn, because TSH levels tend to be higher on days 0 and 1, and more TSH values were measured on days 0 and 1 in Yuma (57%) than in Flagstaff (30%)
(Crump and Weiss, 2001). In addition to uncertainties with respect to the origin of statistically significant differences between TSH levels in Yuma and Flagstaff, questions have been raised with respect to whether the findings have biological significance with respect to thyroid hormone function (Crump and Weiss, 2001).

Subsequent comments in the medical literature have reported that the exposure scenario initially described for Yuma, Arizona during the period of 1994-1997 is not accurately characterized as being continuous at 6 μg/L (Lamm, 2003). Levels that were measured in Yuma in August 1997 were reported as non-detectable (<4 μg/L), and levels in August 1999 were reported as ranging from 4-6 μg/L. Additional analyses have subsequently been conducted to assess the TSH values in neonates living just south of Yuma, Arizona (in Somerton and San Luis), where the population demographics are very similar but the drinking water originates from sources other than the Colorado River. The results of these analyses showed no difference in TSH values between neonates in Yuma, Arizona and the neighboring communities of San Luis/Summerton (Lamm, 2003). These analyses suggest that factors other than perchlorate in drinking water, including the timing of TSH measurement and the physiological distinctions between neonates born in Flagstaff, Arizona (at high altitude) and Yuma county (at sea level), may be explanatory in the differences that have been previously described (Lamm, 2003).

An epidemiological study conducted in Chile provides important data assessing whether perchlorate in drinking water is associated with adverse effects on thyroid function in newborns and school-age children (Crump, et al., 2000). A study was conducted in three different cities of Chile, having different concentrations of perchlorate in drinking water: Taltal (100-120 μg/L), Chanaral (5-7 μg/L), and Antofagasta (<4 μg/L). Neonatal thyroid screening records were analyzed for all neonates born in these cities, for the period of February 1996 through January
1999. Thyroid function in school-age children was assessed by endocrinologists based upon blood testing and clinical assessment. The results did not show evidence of an adverse effect on thyroid function in newborns or school-age children, where perchlorate levels in drinking water were as high as 120 $\mu$g/L (Crump, et al., 2000).

Epidemiological studies of perchlorate in drinking water have been criticized as being ecological in nature. In other words, these studies have generally made assumptions relating to exposure in individuals, based upon drinking water measurements that relate to populations. The results of the epidemiological study in Chile have also been criticized because of concerns that maternal iodine nutrition in that geographic region may be different than other areas of the world. To strengthen the validity of exposure assumptions in these epidemiological studies, it would be helpful to confirm exposure at the individual level by utilizing biomarkers of exposure (which reflect internal dose). These types of measurements were conducted in the epidemiological study in Chile, and the results confirmed that higher levels of perchlorate were found in urine samples obtained from school-age children living in Taltal, where drinking water had the highest levels of perchlorate (Gibbs, et al., 2004). Perchlorate was not detectable in urine samples from children in the cities of Chanaral and Antofagasta. The results of these analyses provide data supporting the validity of the exposure assessments in this epidemiological study of populations with differing levels of perchlorate in their drinking water.

A more recent epidemiological study has been conducted in the same three cities in Chile. The results provide important information relating to perchlorate in drinking water and the relationship to thyroid function during pregnancy and in the neonate (Tellez, et al., 2005). This longitudinal study monitored 184 women throughout pregnancy. Data was collected on perchlorate in tap water samples for these individuals, and biological monitoring was also
conducted for perchlorate in urine, serum, and breast milk samples. Maternal intake of iodine was also assessed using biomarkers. Analyses were conducted to assess whether there was a relationship between perchlorate in drinking water and thyroid function in pregnancy and in the neonate.

The results of this study found that individual tap water measurements closely correlated with public drinking water measurements reported for the three different Chilean cities (Taltal, Chanaral, and Antofagasta). No significant adverse effect on thyroid hormone levels was observed in association with exposure to perchlorate in drinking water during early and late pregnancy, or among neonates born in these three cities (Tellez, et al., 2005). Levels of maternal intake of iodine in this study were similar to measurements reported among the general population in the United States (including pregnant females). Based upon the measurements of perchlorate in biological samples obtained in this study, the investigators concluded that the diet was an important source of exposure to perchlorate in addition to drinking water.

4.4 Epidemiological Studies of Human Exposure to Perchlorate (Occupational Studies)

Occupational exposure to perchlorate has been studied to assess the possibility of adverse effects on thyroid function among workers with high levels of inhalation exposure. One study assessed a cohort of workers with long-term exposure to airborne ammonium perchlorate dust (at an average single-shift dose of 36 μg/kg), and no significant changes or adverse effects on thyroid hormone or functions were observed (Gibbs, et al., 1998). Another study assessed perchlorate exposure and effects on thyroid function in workers at a perchlorate manufacturing plant (Lamm, et al., 1999). Estimated doses from airborne perchlorate in exposed workers ranged from 0.2 - 436 μg/kg/day. No significant changes in thyroid hormone or TSH levels among exposed workers were observed.
A more recent publication studied workers with long-term, intermittent occupational exposure to perchlorate at a manufacturing facility (Braverman, et al., 2005). Transient inhibitory effects on the uptake of iodide by the thyroid gland were observed among these workers, but there was no evidence of adverse effects on TSH or other thyroid function parameters in comparison to control subjects without a history of occupational exposure. The doses described in these occupational studies are generally much higher than doses that might be encountered from dietary or drinking water exposure, and several orders of magnitude lower than doses that have been used in the pharmacological treatment of hyperthyroidism.

4.5 Studies of Low-Dose Perchlorate Exposure in Healthy Human Subjects

A small number of studies have been published investigating the effects of low doses of perchlorate in thyroid function in healthy adults (without thyroid disease). One study was conducted in healthy male volunteers, involving the administration of 10 milligrams of perchlorate in drinking water for 14 days. A significant decrease in the uptake of iodine by the thyroid was observed at this dose, but there was no evidence of adverse effects on thyroid hormones or TSH concentrations (Lawrence, et al., 2000). The same investigators conducted a similar investigation using lower doses (3 mg) for a period of 14 days, and found no evidence of an effect of perchlorate on thyroid hormones or TSH concentrations (Lawrence, et al., 2001). At a dose of 3 mg for 14 days, no significant effect was observed in this investigation on the uptake of iodine by the thyroid gland.

Another recent study was conducted in healthy adults to determine the highest dose of perchlorate at which there is no effect on the uptake of iodine by the thyroid gland (Greer, et al., 2002). Given that inhibition of iodine uptake by the thyroid gland has to occur before adverse effects can take place in thyroid function, the dose of perchlorate where no inhibition of iodine
was observed was considered the no observed effect level (NOEL). This study involved the controlled administration of perchlorate in drinking water to 37 male and female volunteers for 14 days. Perchlorate was ingested at 0.007 mg/kg/day, 0.02 mg/kg/day, 0.1 mg/kg/day, or 0.5 mg/kg/day. The study found that a perchlorate dose of 0.007 mg/kg/day did not result in a statistically significant inhibition of iodine uptake by the thyroid gland (Greer, et al., 2002). No difference in the NOEL was observed between males and females in this study.

### 4.6 Human Health Risk Assessments on Perchlorate

In 2005, the National Academy of Sciences (NAS) issued a report that summarized the human health risks of perchlorate ingestion (NAS, 2005). The report was prepared based upon a request from the United States Environmental Protection Agency, Department of Defense, Department of Energy, and the National Aeronautics and Space Administration, for an independent panel of experts to assess the adverse health effects of perchlorate ingestion from a clinical, toxicological, and public health perspective. Members of the committee were chosen for their expertise in relevant fields including pediatrics, endocrinology, physiology, animal toxicology; neurotoxicology, developmental toxicology; physiologically based pharmacokinetic modeling, epidemiology, biostatistics, and risk assessment.

The charge to the NAS committee included the following:

- To evaluate the current state of the science regarding potential adverse effects of disruption of thyroid function in humans and laboratory animals at various stages of life. Specifically, evaluate whether science supports the model that predicts potential adverse neurodevelopmental and neoplastic effects from changes in thyroid hormone regulation that result from disruption of iodide uptake by the thyroid gland, and indicate the level of confidence in the model.
• To assess the levels at which chronic inhibition of iodide uptake may lead to adverse (not just adaptive) health effects in humans, especially sensitive populations.

• To assess the levels at which changes in thyroid hormones may lead to adverse (not just adaptive) health effects in humans, especially sensitive populations, and indicate the level of confidence in those values.

• To determine whether EPA's findings in its 2002 draft risk assessment, *Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization*, are consistent with current scientific evidence. Specifically, determine whether EPA considered all relevant literature (both supporting and nonsupporting), consistently critiqued that literature, and then used appropriate scientific studies to develop its health risk assessment.

The NAS committee reviewed the data relating to the use of perchlorate to treat hyperthyroidism, and concluded that the perchlorate dose required to cause hypothyroidism in adults would probably be more than 0.40 mg/kg/day (assuming a 70 kg body weight), but that the dose may be lower in pregnant women, infants, children, and people with low iodide intake. The committee reviewed the epidemiological data on perchlorate in drinking water, and concluded that the available evidence did not support a causal association between perchlorate exposure in drinking water and congenital hypothyroidism, or changes in thyroid function in newborns (at drinking water levels up to 120 μg/L). The committee also reviewed epidemiological data on perchlorate in adults in association with occupational exposure and drinking water, and concluded that at the doses described in these studies (as high as 0.5
mg/kg/day) the evidence did not support a causal association between perchlorate and hypothyroidism or other thyroid disorders in adults.

The committee reviewed animal toxicology studies of perchlorate and its effect on thyroid function, noting that there were some similarities to human physiology, but there were some significant quantitative differences that limited their utility and applicability to human health risk assessment. The committee reviewed animal studies on neurobehavioral effects from developmental exposure to perchlorate, and found the available data inadequate to determine whether gestational or lactational exposure to perchlorate has an adverse effect on behavioral function in rats.

The committee reviewed the EPA’s 2002 Risk Assessment on Perchlorate, and disagreed with the reliance upon animal data and the toxicological endpoints relied upon in establishing the reference dose. The NAS committee concluded that the inhibition of iodide uptake by the thyroid gland is a more accurate measure of effect of perchlorate, as it is the key event that must occur for any effect on thyroid function. For this reason, the committee recommended using the inhibition of iodide uptake as an upstream, nonadverse effect which would represent a conservative and health protective approach towards deriving the reference dose. The committee felt that human data, specifically clinical data collected in a controlled environment, provided a more reliable basis for the risk assessment than animal data.

The committee recommended the study by Greer as the point of departure for the determination of an RfD for perchlorate (Greer, et al., 2002). The committee agreed the NOEL for iodide uptake inhibition from perchlorate in this study (0.007 mg/kg/day) was consistent with other clinical studies that had assessed the same endpoint, and that in the absence of inhibition of iodide uptake, there could be no progression to adverse effects. For the purpose of determining
an RfD for perchlorate, an uncertainty factor of 10 was recommended to account for sensitive populations (defined as pregnant women who may have hypothyroidism or iodide deficiency). This resulted in a recommendation for a perchlorate RfD of 0.7 μg/kg/day. The committee concluded that this dose should protect the health of the most sensitive populations.

4.7 State Standards and Recommendations for Perchlorate in Drinking Water

While the NAS recommendations for the perchlorate RfD (0.7 μg/kg/day) have been accepted by the US EPA, other states have chosen more protective public health recommendations. The state of Massachusetts has recently recommended a RfD for perchlorate of 0.07 μg/kg/day, based upon the study by Greer, et al., and an uncertainty factor of 100 (Massachusetts Department of Environmental Protection, 2006). The state of California has recommended a drinking water level of 6 μg/L as a public health goal for perchlorate (Ting, et al., 2006). This recommendation was also derived from the study by Greer, et al., but the State of California utilized a benchmark dose (BMD) software program to analyze the same data the NAS committee had relied upon in their determination of the RfD for perchlorate. The recommendations in Massachusetts and California reflect differences in the approach towards the risk assessment process. These recommendations have been based upon alternative interpretations and the application of different uncertainty factors to the same scientific study by Greer, et al., which was relied upon by the NAS Committee.

4.8 Perchlorate in Perspective with Risks from other Environmental Chemicals with the Same Mechanism of Toxicity

There are other environmental chemicals which share the same mechanism of effect as perchlorate, in terms of being capable of inhibiting the uptake of iodide by the thyroid gland. Nitrate is an example of such a chemical, which is a normal component of the human diet
originating from vegetables (including beets, celery, lettuce, and spinach) as well as drinking water. Nitrate is 240 times less potent than perchlorate in terms of inhibitory effects on iodide uptake by the thyroid gland, but can be detected in much higher concentrations than perchlorate in some agricultural commodities. One recent North American study of lettuce and other leafy vegetables reported that the relative potential for inhibition of iodide uptake from nitrate was 2 orders of magnitude greater than perchlorate, based upon the amounts of chemicals detected (Sanchez et al., 2005).

Thiocyanate is another important example of a chemical which has the same mechanism of effect as perchlorate. Thiocyanate is present in milk, cruciferous vegetables, other foods, and cigarette smoke. A number of scientific studies have been conducted in humans, examining thyroid effects and serum thiocyanate concentrations in populations with chronic dietary exposure as well as in sensitive subpopulations. Perchlorate has been reported to be 15 times more potent than thiocyanate, in terms of the ability to inhibit iodide uptake in the thyroid gland (Tonacchera, et al., 2004). Given a similar mechanism of effect, and an understanding of the relative potencies of perchlorate and thiocyanate, one recent study reviewed the thiocyanate literature to estimate a serum perchlorate concentration and thus the perchlorate dose that would be expected to induce similar effects (Gibbs, 2006). The results of this analysis predicted that no adverse effects on iodide uptake inhibition would occur from serum perchlorate measurements below 3.3 μmol/L. To achieve this serum concentration would require a perchlorate dose of 0.27 mg/kg/day. A dose of this magnitude would translate into a drinking water level of 9 mg/L (ppm), assuming a 70 kg adult drinking 2 liters of water on a daily basis.

While the results of the analysis by Gibbs suggest that a very high level of perchlorate in drinking water would be needed to result in iodide uptake inhibition, the fact that there are other
important chemicals in the diet and drinking water that share a similar mechanism of effect is important in the context of cumulative risk. Cumulative risk refers to the assessment of effects associated with concurrent exposure to chemicals that share a common mechanism of toxicity. There is relatively little information in the scientific literature assessing concurrent exposure to chemicals that can affect the thyroid gland, but the results of recent reviews and scientific studies suggest that exposure to nitrate and thiocyanate from drinking water or food accounts for a more significant proportion of iodine uptake inhibition in comparison to perchlorate (De Groef, et al., 2006, Sanchez et al., 2005). As information accumulates to assess human exposure to perchlorate and other chemicals with similar mechanisms of toxicity, these types of data will be useful to scientists in assessing cumulative risks associated with environmental chemicals that can have adverse effects on human thyroid function.

5 Conclusions

Perchlorate is one of several important environmental chemicals capable of affecting human thyroid function. The developing fetus, neonate, and pregnant women are considered to be sensitive populations at higher risk of adverse outcomes from exposure to perchlorate. A risk assessment on perchlorate, conducted by the National Academy of Sciences, resulted in the recommendation of a reference dose of 0.7 μg/kg/day, a value which has been accepted by the US EPA. The NAS risk assessment concluded that the available evidence did not support a causal association between perchlorate exposure in drinking water and congenital hypothyroidism or changes in thyroid function in newborns (at drinking water levels up to 120 μg/L).

Data are accumulating which confirm the frequent detection of perchlorate at low levels in certain agricultural commodities and dairy products. Studies of human exposure to
perchlorate from the diet or drinking water have generally reported estimated doses that are well below the RfD as recommended by the NAS. There is general agreement that additional data is needed to more accurately assess human exposure to perchlorate from all possible sources.

Cumulative risks from perchlorate should be assessed in the context of human exposure to other common environmental chemicals that share the same mechanism of effect (including nitrates and thiocyanate).

With respect to the incidence of perchlorate in the northern parts of Morrow and Umatilla Counties, while there is no consistent spatial or temporal pattern of perchlorate in well water, there is little variability in results for wells sampled multiple times. The data does not suggest a few point sources only, such as the FUDS, but a diffuse mixture of small point sources and/or non-point sources. As described in Oregon DEQ’s report on the 2003 Lower Umatilla Basin Groundwater Management Area Synoptic Sampling Event (DEQ 2006b), these sources may include:

- Naturally occurring geologic deposits (e.g. caliche, evaporite)
- Historical use of Chilean caliche as nitrate fertilizer
- Demolition of ordinance in Umatilla Chemical Depot
- Activities conducted at the Boardman Bombing Range
- Activities conducted at the Cold Springs Bombing Range
- Activities conducted at the Boeing Jet Engine Test Facility
- The use of sodium hypochlorite as industrial sanitizing solution
- The use of household bleach to “shock treat” domestic wells for bacteria

We agree with this list, as well as their analysis of the monitoring data in which they report a slight correlation of perchlorate with nitrate, no correlation with well type (alluvial or
basalt), a negative correlation of perchlorate with well depth for basalt wells only, and a trend for wells with high levels of other ions to be more likely to also harbor perchlorate.

6 Recommendations

Based on the findings in this report we make the following recommendations:

- The State of Oregon conducts public health surveillance for congenital hypothyroidism. This may serve as a useful source of epidemiological data to assess the incidence and prevalence of this condition, temporal trends, and possibly spatial correlations with the detection of perchlorate as well as other environmental chemicals sharing a similar mechanism of effect on the thyroid gland.

- Continue sampling ground and surface water, with emphasis on sources used for irrigation, livestock, and food processing. Information can be used to aid producers and processors in choosing water sources with no or minimal perchlorate contamination.

- There is a need to better understand what crops grown in the region are most at risk to perchlorate in irrigation water. Studies similar to those conducted by Charles Sanchez and others at the University of Arizona should be considered.

- The success of management and remediation strategies for perchlorate depends heavily on a thorough understanding of the sources. The use of stable isotope analysis (Bao and Gu 2004; Erickson 2004) coupled with sampling strategies directed by robust analysis of regional geochemistry and hydrology, should better define distribution and provide the ability to distinguish natural and man-made sources of perchlorate.
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Figure 2. Lower Umatilla Basin Perchlorate Study Area