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Perchlorate exposure from food crops produced in the lower Colorado River region

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The Colorado River shows low levels of perchlorate derived from aerospace- and defense-related fuel industries once located near the Las Vegas Wash. At sufficiently high dosages perchlorate can disrupt thyroid function by inhibiting uptake of iodide. The Colorado River is the primary source of irrigation water for most food crops grown in Southern California and Southwestern Arizona. The objective of this study was to evaluate potential perchlorate exposure from food crops produced in the lower Colorado River region (LCRR). The major food commodities produced in the region were sampled and perchlorate levels were determined by ion chromatography followed by detection using either conductivity or tandem mass spectrometry, depending on analyte levels. The Monte Carlo module of the Dietary Exposure Evaluation Model (DEEM™) was used to derive an estimate of the 2-day average perchlorate intakes. Data were derived assuming that individuals residing in the LCRR get their fruits and vegetables from within the LCRR as well as from other areas in the United States, or assuming individuals living in the LCRR get their fruits and vegetables from the LCRR only. Perchlorate exposure estimates derived in this study are comparable to exploratory estimates by the US Food and Drug Administration. For infants and children, over 50% of the estimated perchlorate exposure was from milk. The relative impact of vegetables and fruit toward perchlorate exposure increased by age through adulthood. Cumulative perchlorate exposure estimates based on this hypothetical analysis could approach or exceed the NAS reference dose (RfD) for some population groups as drinking water levels exceeded 6 μg/l. However, few individuals are exposed to perchlorate in drinking water at levels above 4 μg/l in the United States and very few would be exposed to perchlorate levels exceeding the RfD, whether consuming food crops from within or outside the LCRR.
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Introduction

Perchlorate has been discovered in surface and ground water supplies throughout the United States. There is concern that these perchlorate-contaminated waters may represent a health risk both as sources of drinking water and irrigation water for food crops. Perchlorate has the potential to cause thyroid dysfunction by inhibiting iodide uptake by the sodium iodide symporter (Clark, 2000). A reference dose (RfD) of 0.7 μg/kg per day has been established by the US Environmental Protection Agency (USEPA, 2005). This action followed review of a human dose–response study (Greer et al., 2002) and a recommendation by the National Academy of Science (NAS, 2005) that inhibition of iodine uptake by the thyroid in humans was a key biochemical event that preceded any health effects caused by perchlorate. One epidemiological study examined perchlorate exposure in Chilean women and found no changes in thyroid hormone levels despite exposure doses estimated to be higher than the RfD (Tellez et al., 2005). However, another recent study found that estimated perchlorate doses below the reference dose were associated with altered thyroid hormone levels in women with low iodine intake (Blount et al., 2006a). One explanation of these different findings is that Tellez et al. (2005) examined only three women with average urinary iodine <100 μg/l, while Blount et al. (2006a) examined 348 women with urinary iodine <100 μg/l. Increased iodine intake could decrease the ability of a given dose of perchlorate to inhibit iodide transport.

Several plant species have been shown to absorb perchlorate from soil and irrigation water (Tan et al., 2004; Yu et al., 2004) and there is evidence that perchlorate accumulates in certain food crops (Jackson et al., 2005; Sanchez et al., 2005a, 2006a). Studies also show perchlorate detection in vegetables and milk samples collected nationally

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(FDA, 2004, 2007; Kirk et al., 2005; Sanchez et al., 2005a; Murray et al., 2008) and internationally (El Aribi et al., 2006; Dyke et al., 2007), and crops such as leafy vegetables and dairy products have been implicated in human exposure through biomonitoring (Blount et al., 2006b). A recent study showed detectable perchlorate in all urine samples collected across the United States indicating widespread human exposure, albeit at exposure doses estimated to be less than the RfD (Blount et al., 2007). The US Food and Drug Administration (FDA, 2007; Murray et al., 2008) also estimated dietary perchlorate exposures to be similar to those projected by the aforementioned urine analysis. The various sources of national perchlorate exposure are generally not well defined, but both anthropogenic and natural sources are known to exist (Mendiaratta et al., 1996; Dasgupta et al., 2005).

Perchlorate contamination in the Colorado River is well documented and is introduced into Lake Mead due to previous perchlorate salt manufacturing activities near the Las Vegas Wash. It has been reported that the Colorado River below Lake Mead has had perchlorate concentrations ranging from 2 to 9 μg/l (Sanchez et al., 2005b). The lower Colorado River is a crucial source of irrigation water for most food crops grown in Southern California and Southwestern Arizona. We have found trace levels of perchlorate in a number of food crops grown in the lower Colorado River region (LCRR) (Sanchez et al., 2005b, 2006a, b). Potential perchlorate exposures from the consumption of individual food crops produced with Colorado River water are low relative to the RfD. However, because we observed some level of exposure with each food crop evaluated, additional work was needed to evaluate hypothetical cumulative exposure from all major food crops produced in the region. In this paper, we provide cumulative estimates of perchlorate exposure from the major food crops produced in the LCRR.

Methods

Agricultural Commodities Sampled

To estimate the distribution of perchlorate concentrations in foods, agricultural commodities were drawn from fields in the LCRR. All fields selected for sampling were irrigated with water from the lower Colorado River. Areas sampled included the Coachella Valley and Imperial Valley of California and the Lower Colorado River Valley of California and Arizona. With few exceptions, the number of samples collected was generally proportional to the area of crop production in the region (Table 1). One exception was asparagus (*Asparagus officinalis*) for which we could only locate two sites to sample despite a reported production of 80 ha. Another was table grapes (*Vitis vinifera*), for which many producers declined to participate in the survey.

Samples were collected during production seasons from 2003 through 2006. Edible portions were diced, mixed thoroughly, and a subsample was placed in a freezer. The frozen samples were freeze-dried as space became available on a freeze drier and weights before and after freeze-drying were recorded. The samples were ground and stored in vials for extraction.

Very few dairies are physically located in the lower Colorado River region. However, a number of dairies in the region utilize feed and forage produced in the lower Colorado River region. For example, over 85,000 ha of alfalfa hay are produced in the lower Colorado River region making this area a major supplier of forage to animal husbandry industries in the western United States. In addition, many of these dairies are more directly impacted by Colorado River water transported outside the Colorado River region in the Central Arizona Project and California Aqueduct systems. Milk samples were collected directly from dairies in Arizona and southern California in 2004 and 2006 and it is assumed that most are likely impacted by perchlorate in Colorado River water. All milk samples were stored frozen until analysis.

Composite water samples were collected at the Imperial Diversion Dam where approximately 5 billion cubic meters of Colorado River water is diverted to irrigate crops in the LCRR.

Analytical Methods

For plant material, we used an extraction procedure in which 600 mg of freeze-dried product was weighed into centrifuge tubes, 15 ml of deionized (DI) water was added, the tubes were boiled for 30 min, and the contents were placed in a refrigerator overnight with occasional gentle shaking (Ellington and Evans, 2000). The tubes were then centrifuged for 30 min and the supernatants filtered through 0.2-μm Gel-man ion membrane syringe filters. Two ml of the above extract (extract one) was reacted with 1000 mg DD-alumina. Vials were gently agitated two or three times over a 24-h period. Eighteen ml of DI water were then added to this mixture. After stirring and settling, this solution was filtered through another 0.2-μm Gel-man ion membrane syringe filter and the resulting solution was labeled ''extract 2''. This sample was stored in the freezer until analysis.

For lettuce, perchlorate analyses could be performed by ion chromatography conductivity detection (IC–CD) using a Dionex 2500 described previously (Sanchez et al., 2005a, b). Briefly, this unit consists of an IP 25 isocratic pump, an EG50 eluent generator, a continuous regenerating trap column, a CD 25 conductivity detector, the 2-mm AG16/AS16 guard and separation column pair, and an AMMS III suppressor. The columns, suppressor, and detector are housed in a LC 30 chromatography oven. We used 50 mM KOH eluent and 50 mM sulfuric acid suppression. A minimum of 10% of the samples were extracted with a

Table 1. Crops included in the assessment, area of production in lower Colorado River region (LCRR), percentage of total US crop, number of samples collected, and observed perchlorate concentrations.

Crop	Area of production in LCRR hectares (ha)	LCRR as a percentage of total US crop (%)		Perchlorate (μg/kg fw)	
			n	Range	Mean
Artichokes (*Cynara scolymus*)	307	14.5	7	13.0–29.3	17.2
Asparagus (*Asparagus officinalis*)	81	3.8	2	11.0–11.3	11.2
Broccoli (*Brassica oleracea italica*)	9516	18.0	55	3.5–106.9	23.8
Cabbage (*Brassica oleracea capitata*)	1042	4.6	19	4.6–63.2	18.5
Carrots (*Daucus carota sativus*)	7227	28.0	30	10.4–53.9	28.8
Cauliflower (*Brassica oleracea botrytis*)	3519	25.6	38	0.2–40.7	12.5
Celery (*Apium graveolens*)	553	4.3	9	7.1–41.6	17.8
Dates (*Phoenix sylvestris*)	2925	100	29	68.8–274.0	138.4
Durum wheat (*Triticum turgidum durum*)	30,131	7.5	48	6.3–160.0	16.7
Eggplant (*Solanum melongena*)	141	13.8	3	8.6–18.1	12.3
Grapefruit (*Citrus Paradise*)	1010	3.1	15	0.6–16.2	3.3
Grape (*Vitis vinifera*)	3485	7.4	15	21.1–87.3	30.8
Green beans (*Phaseolus vulgaris*)	303	1.3	8	18.8–776	134.3
Lemon (*Citrus limon*)	7085	32.1	33	0.6–14.8	2.3
Lettuce Head (*Lactuca sativa*)	25,669	32.9	144	5–47	13.1
Lettuce Leaf (*Lactuca sativa*)	21,252	45.8	104	5–245	38.3
Melon (*Cucumis melo*)	5887	15.2	51	6.4–34.4	14.3
Dairy milk			41	0.9–11.0	5.8
Onion (*Allium cepa*)	4033	5.4	21	6.0–28.0	12.4
Orange (*Citrus sinensis*)	2905	0.5	21	0.2–19.2	5.5
Pepper (*Capsicum annuum*)	1804	10.6	26	3.8–72.6	18
Spinach (*Spinacia oleracea*)	2951	15.2	16	14.2–608.5	211.3
Squash (*Cucurbita* sp)	79	0.3	14	7.9–23.9	16.1
Sweet corn (*Zea mays*)	3376	5.4	18	13.4–39.3	24.2
Tomato (*Lycopersicon esculentum*)	137	0.03	13	6.2–24.7	11.2
Watermelon (*Citrullus lanatus*)	1564	4.7	21	1.1–71.4	12

Non-detect concentrations were assigned a value equal to method detection limit/2. *n* = number of samples. These percentages were calculated by expressing the total production in the LCRR relative to total US production and were used to adjust the residue distributions in Scenario A, which assumed that crops grown in the LCRR are distributed nationally and that residents of the region get their crops from the LCRR as well as other regions. Sources of data included Imperial County, 2005; Riverside County-Coachella District, 2005; Riverside County-Palo Verde Valley, 2005; USDA-NASS, 2005; Yuma County, 2005. We also made adjustments on area of production based on personal interviews with Agricultural Commissioners and Cooperative Extension Agents.

100 μg/l perchlorate standard to yield an addition of 10 μg/l perchlorate standard after the dilution. The method detection limit (MDL) was determined using the procedure outlined in US Environmental Protection Agency (EPA) method 314.0 (USEPA, 1999) using seven replicates of a standard in reagent water. As a standard practice we ran 10% duplicate extractions in addition to the 10% spiked additions. Duplicate aliquots of a given extraction were always analyzed. We generally repeated the analysis if the recovery of standards and standard additions was less than 85% and the variation among the duplicates exceeded 25%. The calculated MDL was 0.2 μg/l using a 0.5 μg/l standard. We set the minimum reporting level (MRL) for lettuce extracts at 1.5 μg/l. Therefore, an MRL of 1.5 μg/l by IC–CD corresponded to an approximate perchlorate level of 20–25 μg/kg for leafy vegetables at typical dry matter concentrations and with the extraction ratio utilized. We set values at 5 and 10 μg/kg below the MDL and below the MRL, respectively. In addition, approximately 10% of the lettuce samples were also analyzed by IC-tandem mass spectrometry (MS/MS) as described below and the agreement between these results verified that the original determinations were accurate.

For all samples other than lettuce, perchlorate was frequently below the MDL by IC–CD and we employed ion chromatography/tandem mass spectroscopy (IC/MS/MS) using stable isotope-labeled internal standard methodology reported previously (Valentin-Blasini et al., 2005). Briefly, 0.5 ml of the aqueous sample extract was spiked with isotopically labeled internal standards ($Cl^{18}O_4^-$) and diluted 1:1 with DI water. This solution was subsequently analyzed using ion chromatography–electrospray ionization–tandem mass spectrometry. Perchlorate was quantified based on the peak area ratio of analyte to stable isotope-labeled internal standard. A subset of samples (10%) were analyzed further using standard addition, and produced acceptable percent differences of $<10\%$. Absolute assay accuracy was verified by the blind analysis of four different reference solutions

containing perchlorate (AccuStandard, New Haven, CT, USA); analysis of these proficiency testing solutions across the study time period yielded an average percent difference of −5.2%. The perchlorate MDL was estimated to be 0.02 μg/l and the MRL was 0.1 μg/l. The percentage dry matter of the edible portions of crops ranged from 4% for some leafy vegetables to over 90% for Durum wheat. Therefore, an MRL of 0.1 μg/l by IC/MS/MS would correspond to an approximate perchlorate level ranging from 2.5 μg/kg for leafy vegetables to 25 μg/kg for wheat. Most crops had perchlorate levels above the MRL by IC/MS/MS. Two notable exceptions were citrus and wheat. For citrus we assumed that the perchlorate levels were 0.625 μg/kg when not detected and 1.25 μg/kg when perchlorate was detected but below the reporting level. These estimates are based on typical dry matter contents and the extraction ratio that was utilized. For wheat grain we assumed perchlorate levels of 6.25 μg/kg below the MDL and 12.5 g/kg below the MRL based on the extraction ratio utilized.

For milk, perchlorate was also analyzed by IC/MS/MS using the stable isotope-labeled internal standard methodology reported previously (Valentin-Blasini et al., 2005). Milk samples (0.5 ml) were spiked with stable isotope-labeled perchlorate ($Cl^{18}O_4^-$). Milk proteins were subsequently precipitated by addition of 3 ml of cold ethanol (−20°C). Samples were centrifuged (3016 g, −5°C) for 35 min. Supernatant was transferred to a clean centrifuge tube and evaporated to dryness under a stream of nitrogen at 60°C. The sample was resuspended in 1.0 ml of DI water and added to a preconditioned C18 SPE cartridge. The breakthrough fraction and a subsequent 1-ml wash of DI water were collected, mixed, and 1 ml was transferred to an autosampler vial for IC-MS/MS analysis. Water samples were run by either IC–CD or IC/MS/MS using methods described previously.

Consumption Data

Data from the US Department of Agriculture's (USDA) Continuing Survey of Food Intakes by Individuals (CSFII) from 1994 through 1996 and the 1998 Supplemental Children's Survey data (USDA, 2000) were used to estimate consumption. The USDA survey samples were drawn from all private households and designed to provide multistage stratified area probability samples representative of the 48 contiguous states. The stratification plan took into account geographic location, degree of urbanization, and socioeconomic status. The 48 states were grouped into nine census geographic divisions; then all land areas within the divisions were divided into three urbanization classifications: central city, suburban, and non-metropolitan. Each successive sampling stage selected increasingly smaller, more specific locations. Participants in the 1994–96 & 1998 CSFII were interviewed two times, on two non-consecutive days, to collect information on food consumption in the previous 24 hours. The Day 1 and the majority (95%) (5% of the interviews were conducted by telephone.) of the Day 2 interviews were conducted in person. The 2 interview days were typically separated by 3–10 days, and were scheduled to be on different days of the week. A multi-pass interview approach was used to help survey participants remember all the foods they had consumed the previous day. The consumption data collected by the survey included what foods were consumed as well as the amounts consumed, the times and places of consumption, the sources of the foods (e.g., restaurant, school cafeteria, vending machine, home prepared, and so on.), and several other variables, pertaining to the food, method of preparation, meal name, and so forth. The survey also collected information on water directly consumed and not added to food or used to prepare foods (e.g., soups or juices). For each household included in the survey, information was also collected about the source(s) of the water (e.g., bottled, tap, and so on) typically used for drinking and preparing foods. That information was subsequently used to allocate the amount of water (both direct and indirect) that was reported to have been consumed by each survey participant to the various sources. CSFII did not estimate breast milk consumption by infants but did collect information regarding the breastfeeding status of infants and children less than 3 years of age. Based on the CSFII, 28% of the infants less than 1 year of age were breastfed. Perchlorate is typically detected in breast milk (Kirk et al., 2005) and thus the data presented here underestimate perchlorate exposure for breast fed infants. Specifically, using the range of mean perchlorate levels in breastmilk extracted from Kirk et al., 2005; Pearce et al., 2007; Kirk et al., 2007, and breastmilk intake estimates compiled by the US EPA (USEPA, 2002. Child-specific Exposure Factors Handbook [interim final]. EPA/600/P-00/002B. Washington, DC Office), estimated mean perchlorate intakes from breastmilk range from 4.3 to 24.5 μg/day for infants 1–6 months old, while upper percentile estimates range from 6.0 to 34.1 μg/day.

The consumption data collected by the CSFII survey referred to foods as consumed, for example, pizza, mixed salad, fruit salad, and so on. These intakes were converted to raw agricultural commodities (RACs) using data provided in EPA's Food Commodity Intake Database (FCID) (USEPA, 2000). The FCID contains a "translation (or recipe) file" that breaks the food codes used in the CSFII into agricultural commodities.

Although consumption data from more recent surveys are currently available, for example, NCHS's 2003–2004 National Health and Nutrition Examination Survey (NHANES) (NCHS, 2006), the data from the CSFII survey were deemed more appropriate for our analysis, because they included consumption data for two non-consecutive days for more than 20,000 individuals, about two times the number of individuals included in the NHANES survey. Other

NHANES surveys, for example, the 1999–2000 (NCHS, 2004a) or the 2001–2002 NHANES (NCHS, 2004b) collected consumption data for 1 day only.

Exposure Model

An indirect estimate of the dietary intake of a contaminant can be derived as the product of two parameters: (1) the concentration of the contaminant in the food at the time of consumption and (2) the amount of the food consumed. Under this general framework, dietary exposure can be estimated as either the product of point estimates of the consumption and contaminant (i.e., residue) concentration (e.g., averages or upper percentile estimates) or by combining the probability distributions of food intakes and residue concentrations, for example, using Monte Carlo methods (NRC, 1993).

It is difficult to accurately estimate chronic dietary exposure because of the general lack of long-term food consumption data. Owing to respondent burdens and costs, most surveys using food records or recall methodology can capture only a few days of consumption for the same individual, particularly when extensive details (e.g., food quantity, source, ingredients, and preparation method) are collected. Following the approach used by FDA (Yost et al., 2004; FDA, 2006; Tsuji et al., 2007), we estimated long-term intakes of perchlorate using the distribution of 2-day average intakes. Specifically, we used the Monte Carlo module of the Dietary Exposure Evaluation Model (DEEM^{TM}) to derive an estimate of the 2-day average perchlorate intakes. The Monte Carlo module in DEEM™ uses the following general algorithm:

(1) For each population of interest (e.g., total United States, women of child-bearing ages, and so on), identify the foods consumed by individual 1 on day 1 of the survey
(2) Randomly select a concentration value for the first food of interest, and estimate the exposure for individual 1 on day 1 from food 1 as the product of the amount consumed and the randomly selected concentration value
(3) Repeat Step (2) above for all foods consumed on day 1 by individual 1
(4) Sum all exposures derived in steps 2 and 3, to estimate individual 1's total exposure for day 1
(5) Repeat Steps (1) to (4) to estimate individual 1's total exposure for day 2
(6) Derive a 2-day average exposure as the average of the total exposures derived in Steps (4) and (5) above
(7) Repeat the process in steps (1) to (6) above a large number of times (typically 1000 times)
(8) Repeat the process in steps (1) to (7) for every individual in the population of interest
(9) Compile all 2-day exposure estimates derived for all individuals in the population of interest in a single distribution, and derive summary statistics (e.g., mean and various percentiles) for that distribution.

We matched the consumption data, expressed as RACs, to the sampled crops listed in Table 1. RACs reported in EPA's FCID database as "fresh" (e.g., "Carrot, Uncooked, Fresh"; or "Carrot, Cooked, Fresh") were assigned the corresponding entire distribution of perchlorate residues, while RACs corresponding to processed commodities ("Canned", "Frozen" or "Dried") were assigned the average of the corresponding distribution of perchlorate residues. We derived perchlorate intake estimates for two scenarios. The first scenario (Scenario A) assumed that crops grown in the LCRR are distributed nationally, and that individuals living in the LCRR get their fruits and vegetables from the LCRR region as well as from other areas in the United States. The second scenario (Scenario B) assumed that crops grown in the LCRR remain in the LCRR and individuals living in that region get their fruits and vegetables from the LCRR only. Thus, for scenario A, it was assumed that crops grown outside the LCRR do not have perchlorate contamination, and the distributions of residues (for the "fresh" RACs) or average residues (for the "processed" RACs) were adjusted accordingly. For scenario B, the perchlorate residues generated by the survey were used without further adjustment.

Samples with non-detected perchlorate concentrations were assigned a level equal to 1/2 the MDL.

Results and discussion

The proportions of various food crops consumed in the United States that are produced in the LCRR vary by crop (Table 1). For dates (*Phoenix sylvestris*) there are almost 3000 ha in the LCRR, which is essentially 100% of the US production. For many cool season crops such as lettuce (*Lactuca sativa*), broccoli ((*Brassica oleracea italica*), and carrots (*Daucus carota sativus*), over 90% of what is consumed in the US during the winter period is produced in the LCCR and total US production on an annual basis ranged from 18 to 46%. Of the citrus crops, the LCRR provides less than 1% of the orange (*Citrus sinensis*), approximately 3% of grapefruit (*Citrus paradise*), but over 30% of the lemon (*Citrus limon*) crops consumed in the United States. For other crops, such as fresh tomatoes (*Lycopersicon esculentum*), negligible production (0.03%) occurs within the LCRR.

Perchlorate concentration data for lettuce, citrus, cole crops, and durum wheat (*Triticum turgidum durum*) have been presented in previous publications (Sanchez et al., 2005b, 2006a, b, 2007) but other data have not been previously reported. The perchlorate concentrations varied by crop with the higher concentrations generally associated with leafy vegetables; spinach (*Spinacia oleracea*) was the highest of these. Dates were the exception to this trend since they had the highest perchlorate levels of the fruit crops tested

due to the fact that they are generally consumed as a lower moisture-content food. Generally, the lowest concentrations were with the citrus crops such as lemons. The range for green beans (*Phaseolus vulgaris*) includes one very high value that was re-analyzed and verified. This very high value was collected from an organic farm in the Imperial Valley of California, and we suspect the grower used Chilean nitrate, a known source of perchlorate (Urbansky et al., 2001). Previous work has shown generally higher perchlorate concentrations in organic compared to conventionally produced leafy vegetables (Sanchez et al., 2005a). Although the mean value for green beans is high because of one high value and our relatively small sample size due to limited acreage in the LCRR, the median value for green beans was 34.1 μg/kg, a value close to many of the other vegetables sampled. Fortunately, the algorithms in the DEEM™ are such that this one value would not unduly bias the exposure estimates.

We derived intake estimates for the following population groups: (i) all ages, (ii) infants less than one year, (iii) children ages 1–6 years, (iv) children 7–12 years, and (v) women of childbearing ages (13–49 years). We also estimated perchlorate intake estimates for Scenarios A (assuming that individuals residing in the LCRR get their fruits and vegetables from the LCRR as well as from other areas and that crops grown outside the LCRR do not have perchlorate contamination) and B (assuming individuals living in the LCRR get their fruits and vegetables from the LCRR region only), respectively (Figures 1 and 2). Scenario B is extremely conservative since it is not possible for individuals to derive all their produce from the LCRR. For example, cool season vegetables such as lettuce, spinach, broccoli and cauliflower (*Brassica oleracea botrytis*) are harvested in this region from the middle of November through early April. Warm season vegetables such as melons (*Cucumis melo*), sweet corn, and peppers (*Capsicum annuum*) are generally harvested over a 60-day period in the late fall and over an 80-day period in the late spring. Thus, products from the LCRR are generally available less than 6 months out of the year. The exception would be milk, which is produced all year round, but the concentrations of perchlorate we found in milk are similar to those found nationally (FDA, 2004). In addition, the production of some crops within the LCRR, such as oranges and tomatoes, are insufficient to meet the consumption demand within the region.

On the other hand, scenario A has the potential to underestimate exposure because it assumes that products produced outside the LCRR have no perchlorate. In reality perchlorate has been found in agricultural products nationally and internationally outside the LCRR (FDA, 2004; Jackson et al., 2005; Sanchez et al., 2005a; El Aribi et al., 2006; Murray et al., 2008), including areas where there is no known contamination of water. Nevertheless, for instances in which we assume that individuals consume products from

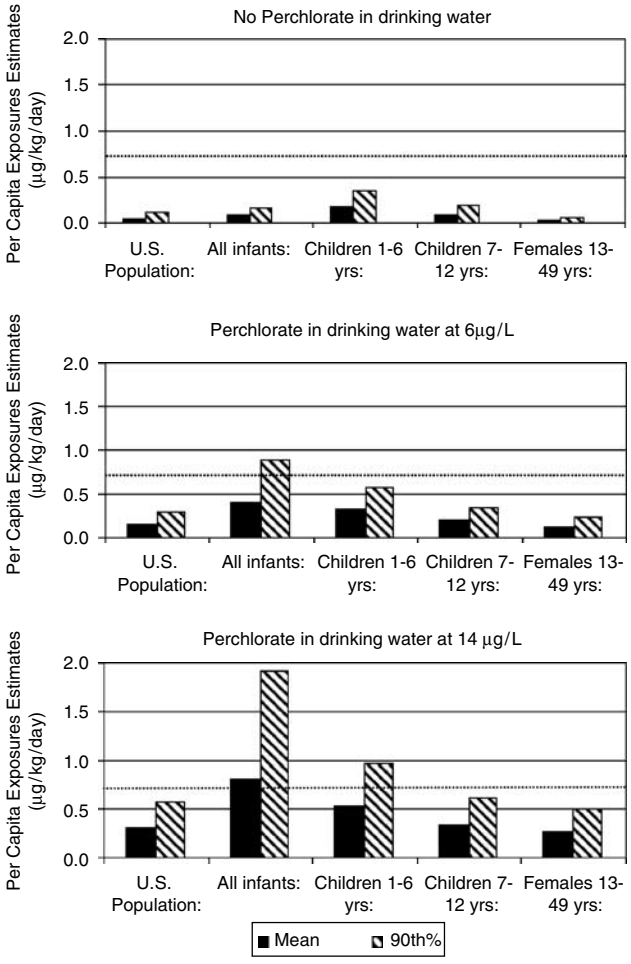

Figure 1. Estimated perchlorate exposures by population group at three levels of drinking water exposure assuming that individuals residing in the Lower Colorado River Region (LCRR) get their fruits and vegetables from the LCRR region as well as from other areas in the US. Dashed line shows reference dose.

within and outside the LCRR, our estimates of exposure (Table 2) agree closely with those exploratory data reported by the FDA (FDA, 2007; Murray et al., 2008) for similar population groupings. In fact, in almost all cases, the estimates derived by the FDA are between the corresponding estimates derived in this study, further attesting to the ubiquity of perchlorate in the food supply. It is noteworthy that the FDA considered their estimates of exposure "highly conservative" because they focused on crops grown in regions where water sources are known to be contaminated with perchlorate. Further, as indicated by the FDA (FDA, 2006), the 1994–96 & 1998 CSFII survey provided only a snapshot of food consumption for a short period of time, hence the intake estimates based on that survey, including those reported in this study, are generally conservative estimates of average daily chronic intakes.

The relative contribution of various food sources to exposure is a function of both the amounts of individual

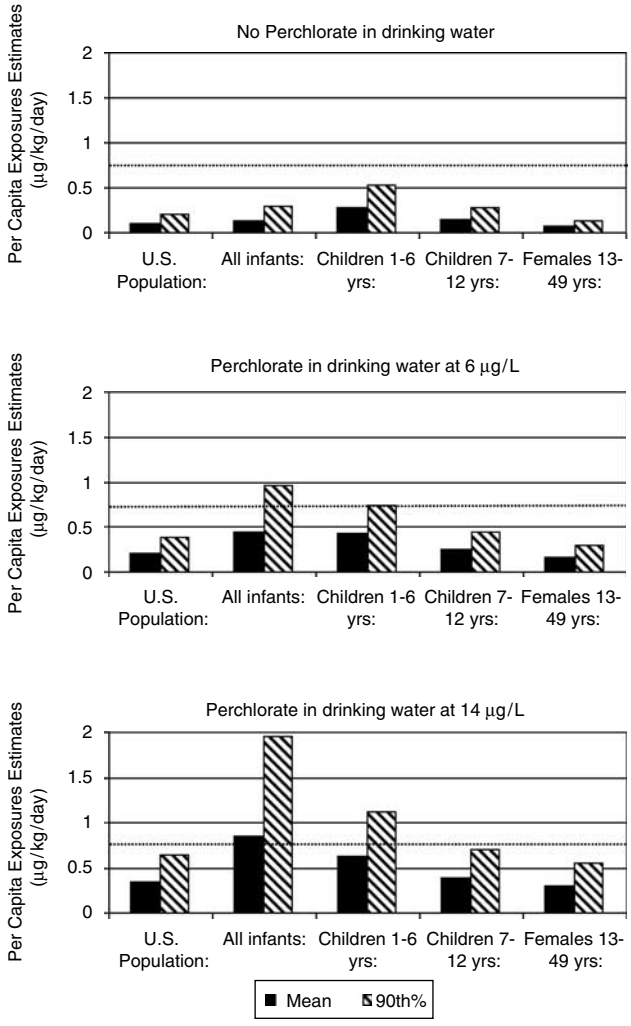

Figure 2. Estimated perchlorate exposure by population group assuming individuals living in the Lower Colorado River Region (LCRR) get their fruits and vegetables from the LCRR region only. Dashed line shows reference dose.

food products consumed and the perchlorate concentrations in these food crops (Table 3). Some crops with high perchlorate concentrations are consumed in small amounts and contribute negligibly to the total perchlorate exposure. For example, dates always contributed well below 1% of the estimated exposure and spinach contributed 5% or less, depending on the population group. Conversely, other commodities with more modest perchlorate concentrations, such as carrots and oranges, could be significant sources of exposure in certain population groups due to their higher consumption.

The relative contribution of various food sources to total estimated perchlorate exposure varies with age due to differing food consumption habits (Table 3). For infants (ages 0–1 year) and children (ages 1–12 years), over 50% of the perchlorate exposure is estimated to be from milk. The relative impact of vegetables and fruits toward perchlorate exposure increases by age through adulthood. For the total US population, the combined exposure from vegetables and fruits is estimated to exceed that of milk. For adult women, the total perchlorate exposure due to vegetables alone is estimated to exceed that of milk. Generally, less than 5% of perchlorate exposure was estimated to be from pasta derived from durum wheat, regardless of the population group. Overall, the trends generally agree with national estimates reported by Murray et al., 2008.

Although milk is estimated to be the single largest source of perchlorate to total exposure, it is also a significant source of protein, vitamins and nutrients (Wattiaux, 1999), including iodide (Pearce et al., 2005). Similarly, vegetable and fruit crops are a significant source of nutrients and vitamins for Americans accounting for 35, 25 and 16% of average consumption of vitamin A, vitamin C, and dietary fiber, respectively (Barraj et al., 2007). Consumption of milk, vegetables, and fruit is encouraged by the (USDA, 2005) as part of a healthy and nutritionally balanced diet and avoiding

Table 2. Comparison of perchlorate exposure estimates calculated in this study with similar population groups in US Food and Drug Administration (FDA) study.

Estimate perchlorate exposure (μg/kg-bw/d)							
FDA estimates			Our estimates (excluding water)				
Population	Monte Carlo estimate		Scenario A[a]		Scenario B[b]		Population
	Mean	90th Percentile	Mean	90th Percentile	Mean	90th Percentile	
All ages (2+ years)	0.05	0.12	0.05	0.113	0.096	0.202	All ages (0+ years)
Children (2–5 years)	0.17	0.34	0.182	0.349	0.284	0.530	Children (1–6 years)
Females (15–45 years)	0.04	0.07	0.029	0.063	0.067	0.130	Females (13–49 years)

[a]The first scenario (Scenario A) assumed that crops grown in the LCRR region are distributed nationally, and that individuals living in the LCRR region get their fruits and vegetables from the LCRR region as well as from other areas in the United States.
[b]The second scenario (Scenario B) assumed that crops grown in the LCRR region remain in the LCRR region and individuals living in that region get their fruits and vegetables from the LCRR region only.

Table 3. Percentage of estimated perchlorate dose by food source.

Crop	US population	Infants	Children (1–6 years)	Children (7–12 years)	Females (13–49 years)
	Percent of total estimated perchlorate dose by food source				
Artichokes	<0.01	<0.01	<0.01	<0.01	<0.01
Asparagus	0.10	0.08	0.04	0.07	0.14
Broccoli	2.94	1.21	1.65	2.36	3.18
Cabbage	1.26	0.08	0.35	0.64	1.24
Carrots	5.97	23.77	4.43	4.22	6.77
Cauliflower	0.21	0.08	0.11	0.07	0.14
Celery	1.05	0.15	0.53	0.79	<0.01
Dates	0.10	<0.01	0.04	<0.01	<0.01
Durum wheat	4.51	1.51	3.69	5.08	4.83
Eggplant	<0.01	<0.01	<0.01	<0.01	0.14
Grapefruit	0.21	<0.01	0.07	0.07	0.28
Grape	7.34	4.91	12.73	8.93	5.52
Green beans	7.34	3.62	4.19	3.43	7.04
Lemon	0.10	<0.01	0.04	0.07	0.14
Lettuce head	3.14	<0.01	0.84	2.07	4.77
Lettuce leaf	0.52	<0.01	0.07	0.21	0.97
Melon	1.47	0.30	1.06	1.07	1.66
dairy milk	41.93	57.36	57.16	53.90	35.64
Onion	2.52	0.68	1.16	1.72	3.45
Orange	5.56	1.13	5.28	5.86	6.22
Pepper	0.94	<0.01	0.25	0.43	1.38
Spinach	3.88	2.79	1.55	1.93	5.25
Squash	0.73	0.68	0.21	0.14	1.10
Sweet corn	1.89	0.38	1.23	2.00	2.21
Tomato	4.51	0.91	1.86	2.86	5.84
Watermelon	1.78	0.38	1.48	2.07	2.07

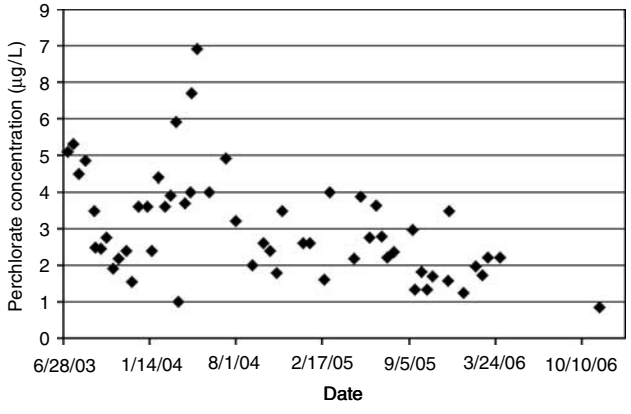

Figure 3. Perchlorate concentrations of Colorado River water at the Imperial Diversion Dam over study period.

milk, fresh fruits and vegetables due to trace levels of perchlorate is not advised.

Over the sampling period, the perchlorate content of the Colorado River varied from 1 to 8 μg/l (Figure 3). More recently, concentrations in the river have been approximately 2 μg/l, which likely reflects the impact of successful remediation efforts directed toward the Las Vegas Wash (NDEP, 2006). Many residents of the LCRR use bottled water for drinking, but Colorado River water delivered through municipal water sources for cooking. Furthermore, many municipalities in the region augment water from the Colorado River with other surface and well water as a supply to the city water systems. Thus, it is difficult to estimate perchlorate exposure from drinking water because of uncertainty regarding the amounts of water that people consume and the concentrations of perchlorate in that water. In accordance with the approach used by FDA (FDA, 2007), we initially ran our baseline exposure assessment assuming drinking water concentrations of perchlorate were 0 μg/l. In addition, we ran two additional sensitivity analyses in which we set the perchlorate concentrations in drinking water at 6 and 14 μg/l, respectively. The 6-μg/l concentration corresponds to the Public Health Goal set for perchlorate in drinking water by the California Office of Environmental Health Hazard Assessment. This level has recently been established as an MCL in California. The 14 μg/l concentration is the advisory health-based guidance level set by the Arizona Department of Health Sciences. These two sensitivity analyses should be viewed with caution because very few individuals drink water that contains perchlorate at these concentrations. Thus, exposure estimates derived in these

Table 4. Water perchlorate concentrations at which populations will obtain reference dose of perchlorate when added to hypothetical food exposures in the LCRR.

Population	Drinking water amount (l)	Body weights (kg)	Perchlorate concentrations (μg/l)	
			Mean	90th percentile
US population	2	60	18.1	15.0
All infants	1	8	4.8	3.5
Children 1–6 years	1	15	6.3	2.6
Children 6–12 years	1	31	17.0	12.9
Females 13–49	2	60	19.0	17.1

sensitivity analyses are expected to result in unrepresentative (conservative) exposure estimates. Cumulative perchlorate exposure estimates based on the hypothetical analysis performed here could approach or exceed the NAS RfD for infants and children as drinking water levels exceed 6 μg/l (Figures 1 and 2). Another approach for evaluating potential cumulative exposure to food and water is estimating the drinking water perchlorate concentrations that would put selected population groups at the reference dose when added to our hypothetical food exposure estimates (Table 4). Using this approach we estimate that an infant weighing 8 kg and drinking 1 l of water, would receive the RfD of perchlorate when drinking water perchlorate levels are 4.8 and 3.5 μg/l, for the mean and 90th percentile food exposure estimates, respectively. Similarly, young children weighing 15 kg would receive the RfD of perchlorate when drinking water perchlorate levels are 6.3 and 2.6 μg/l, for the mean and 90th percentile food exposure estimates, respectively. These data collectively show that infants and children are more at risk in exceeding the reference dose due to generally greater food and water consumption relative to body weight.

It has been reported by EPA that of 3858 public water supplies tested, only 160 (4.1%) detected perchlorate $\geq$4 μg/l (USEPA, 2007), the original MRL using EPA method 314.0 (USEPA, 1999). Further, perchlorate levels in all but two of 51 bottled water samples tested by FDA were below the MDL of 0.02 μg/l. The bottled water samples were collected at retail locations and included artesian water, well water, distilled water, drinking water, purified water, and spring water. Current data indicate that perchlorate in drinking water seldom exceeds 4 μg/l in the United States, and thus few individuals would likely be exposed to perchlorate doses exceeding the RfD, whether consuming produce within or outside the LCRR.

To conclude, low levels of perchlorate were found in all food crops produced in the LCRR. Perchlorate exposure estimates derived in this study are comparable to nationwide estimates by the US FDA. For infants and children, over 50% of the estimated perchlorate exposure was from milk. The relative impact of vegetables and fruits toward perchlorate exposure increased by age through adulthood. These data show a potential for cumulative perchlorate exposure estimates for some population groups to approach and exceed the NAS RfD in rare instances when drinking water perchlorate levels exceed 4 μg/l.

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Disclaimer

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References

Barraj L., Blount B., Sanchez C., Scrafford C., and Krieger R. *Avoiding Perchlorate Exposures from Fresh Fruits and Vegetables: At What Costs?* Presented at the 2007 Annual Society of Toxicology meeting, Charlotte, NC, 2007.

Blount B.C., Pirkle J.L., Osterloh J.D., Valentin-Blasini L., and Caldwell K.L. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. *Environ Health Persp* 2006a: 114: 1865–1871.

Blount B.C., Valentin-Blasini L., Osterloh J.D., Mauldin J.P., and Pirkle J.L. Perchlorate exposure of the US population, 2001–2002. *J Exposure Sci and Environ Epid* 2007: 17: 400–407.

Blount B.C., Valentini-Blasini L., and Ashley D.L. Assessing human exposure to perchlorate using biomonitoring. *J ASTM Int* 2006b: 3(7): 1–6; doi:10.1520/JAI100398.

Clark J.J. Perchlorate toxicology (Chapter 3). In: Urbansky ET (ed.) *Perchlorate in the Environment*. Kluwer/Plenum, New York, NY, 2000, pp 15 –30.

Dasgupta P.K., Martinelango P.K., Jackson W.A., Anderson T.A., Tian K., and Tock R.W. The origin of naturally occurring perchlorate: the role of atmospheric processes. *Environ Sci Tech* 2005: 39: 1569–1575.

Dyke J.V., Kazuaki I., Obitsu T., Yoshiharu H., Dagupta P.K., and Blount B.C. Perchlorate in dairy milk. Comparisons of Japan *versus* the United States. *Environ Sci Techol* 2007: 41: 88–92.

El Aribi H.Y., Le Blanc J.C., Antonsen S., and Sakuma T. Analysis of perchlorate in food and beverages by ion chromatography coupled with tandem mass spectroscopy (IC-ESI-MS/MS). *Analytica Chimica Acta* 2006: 567: 39–47.

Ellington J.J., and Evans J.J. Determination of perchlorate at parts-per-billion levels in plants by ion chromatography. *J Chromatr* 2000: 898: 193–199.

FDA. *Exploratory data on perchlorate in food*. Food and Drug Administration: Washington, DC, 2004: www.cfsan.fda.gov/~dms/clo4data.html.

FDA. Office of food additive safety, center for food safety and applied nutrition. Guidance for industry. *Estimating Dietary Intake of Substances in Food* 2006. Available at: http://www.cfsan.fda.gov/~dms/opa2cg8.html.

FDA. *Preliminary Estimation of Perchlorate Dietary Exposure Based on FDA 2004/2005 Exploratory Data* 2007: http://www.cfsan.fda.gov/~dms/clo4ee.html.

Greer M.A., Goodman G., Pleus R.C., and Greer S.E. Health effects for environmental perchlorate contamination: the dose response for inhibition of radioiodide uptake in humans. *Environ Health Perspect* 2002: 110: 927–937.

Imperial County. *Agricultural Crop and Livestock Report* 2005: http://www.imperialcounty.net/ag/clereports.htm.

Jackson W.A., Joseph P., Laxman P., Tan K., Smith P.N., Yu L., and Anderson T.A. Perchlorate accumulation in forage and edible vegetation. *J Agric Food Chem* 2005: 53: 369–373.

Kirk A.B., Dyke J.V., Martin C.F., and Dasgupta P.K. Temporal patterns of perchlorate, thiocyanate, and iodide excretion in human milk. *Environ Health Perspect* 2007: 115: 182–186.

Kirk A.B., Martinelngo P.K., Tian K., Dutta A., Smith E.E., and Dasgupta P.K. Perchlorate and iodine in dairy and breast milk. *Environ Sci Techol* 2005: 39: 2011–2017.

Mendiaratta S.K., Dotson R.L., and Brooker R.T. Perchloric acid and perchlorates. In: Kirk Othmer (ed.) *Encyclopedia of Chemical Technology*. John Wiley and Sons Inc, New York, NY, 1996, pp 157–170.

Murray C.W., Egan S.K., Kim H., Nega B., and Bolher P.M. US Food and Drug Administration's total diet study: dietary intake of perchlorate and iodide. *J Exposure Sci and Environ Epid* 2008: 17: 1–10.

National Academy of Science. *Health Implications of Perchlorate Ingestion*. National Research Council of the National Academies Press, Washington, DC, 2005.

National Agricultural Statistics Service. 2005: http://www.nass.usda.gov/Primarily data on 2005 cropping season.

National Centers for Health Statistics (NCHS). *The National Health and Nutrition Examination Survey (NHANES) 1999–2000* 2004a Public Data Release (http://www.cdc.gov/nchs/about/major/nhanes/NHANES99_00.htm).

National Centers for Health Statistics (NCHS). *The National Health and Nutrition Examination Survey (NHANES) 2001–2002* 2004b, Public Data Release (http://www.cdc.gov/nchs/about/major/nhanes/nhanes01-02.htm).

National Centers for Health Statistics (NCHS). *The National Health and Nutrition Examination Survey (NHANES) 2003–2004* 2006. Public Data Release (http://www.cdc.gov/nchs/about/major/nhanes/nhanes2003-2004/nhanes03_04.htm).

National Research Council (NRC). Committee on pesticides in the Diets of Infants and Children. *Pesticides in the Diets of Infants and Children*. National Academy Press, Washington, DC, 1993.

Nevada Department of Environmental Quality. *Lake Mead Water Quality Forum* 2006, summary. 2006 http://ndep.nv.gov/forum/minutes_021506.pdf.

Pearce E.N., Pino S., He X., Bazrafshan H.R., Lee S.L., and Braverman L.E. Sources of dietary iodine: bread, cows' milk, and infant formula in the Boston area. *J Clin Endrocrinol* 2005: 89: 3421–3424.

Pearce E.N., Leung A.M., Blount B.C., Bazrafshan H.R., He X., Pino S., Valentin-Blasini L., and Braverman L.E. Breast milk iodine and perchlorate concentrations in lactating boston-area women. *J Clin Endrocrinol Metab* 2007: 92: 1673–1677. doi:10/1210/jc.2006-2738

Riverside County -Palo Verde Valley. *Acreage and Agricultural Crop Report*. Agricultural Commissioner's Office, Indio, CA, 2005.

Riverside County-Coachella Valley. *Acreage and Agricultural Crop Report*. Agricultural Commissioner's Office, Indio, CA, 2005.

Sanchez C.A., Blount B.C., Valentin-Blasini L., and Krieger R.I. Perchlorate, thiocyanate, and nitrate in edible cole crops (*Brassica sp.*) produced in the lower Colorado River region. *Bull Environ Contam Toxicol* 2007: 79: 655–659.

Sanchez C.A., Crump K.S., Krieger R.I., Khandaker N.R., and Gibbs J.P. Perchlorate and nitrate in leafy vegetables of North America. *Environ Sci Techol* 2005a: 39: 9391–9397.

Sanchez C.A., Krieger R.I., Khandaker N.R., Valentin-Blasini L., and Blount B.C. Potential perchlorate exposure from Citrus sp. irrigated with contaminated water. *Analytica Chimica Acta* 2006a: 567: 33–38.

Sanchez C.A., Krieger R.I., Khandaker R.N., Moore R.C., Holts K.C., and Neidel L.L. Accumulation and perchlorate exposure potential of lettuce produced in the lower Colorado River region. *J Agric Food Chem* 2005b: 53: 5479–5486.

Sanchez C.A., Krieger R.I., Valentin-Blasini L., Blount B.C., and Khandaker N.R. Perchlorate accumulation and potential exposure from durum wheat irrigated with Colorado River water. *J ASTM Int* 2006b: 3(7): 1–6; doi:10.1520/JAI100398.

Tan K., Anderson T.A., Jones M.W., Smith P.N., and Jackson W.A. Accumulation of perchlorate in aquatic and terrestrial plants on a field scale. *J Environ Qual* 2004: 33: 1638–1646.

Tellez R.T., Chacon P.M., Abarca C.R., Blount B.C., Landingham C.B., Crump K.S., and Gibbs J.P. Long-term environmental exposure to perchlorate in drinking water and thyroid function during pregnancy and the neonatal period. *Thyroid* 2005: 15: 963–975.

Tsuji J., Yost L., Barraj L., Scrafford C., and Mink P. Use of background inorganic arsenic exposures to provide perspective on risk assessment results. *Regul Toxicol Pharmacol* 2007: 48(1): 59–68.

US Department of Agriculture (USDA). CSFII Data Set and Documentation: The 1994-96, 1998 Continuing Surveys of Food Intakes by Individuals. *Food Surveys Research Group. Beltsville Human Nutrition Research Center. Agricultural Research Service* 2000.

US EPA. *Child-specific Exposure Factors Handbook [interim final]*. EPA/600/P-00/002B. Washington, DC: Office, 2002.

US EPA (Environmental Protection Agency). *Food Commodity Intake Database [FCID Raw Data File]*. Office of Pesticide Programs, Washington, DC. Available from the National Technical Information Service, Springfield, VA; PB2000-5000101 2000.

US EPA. *"Reference Dose for Chronic Oral Exposure"* 2005: http://www.epa.gov/iris/subst/1007.htm.

US EPA. *Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant List-Preliminary Determinations* 2007: http://www.epa.gov/EPAFR-Contents/2007/May/Day-01/w7539.htm.

US EPA. US EPA Method 314.0. Determination of perchlorate in drinking water using ion chromatography. *US Environmental Protection Agency*. National Exposure Research Laboratory and Office of Research and Development, Cincinnati, OH 45268, 1999.

Urbansky E.T., Brown S.K., Magnuson M.L., and Kelly C.A. Perchlorate levels in samples of nitrate fertilizer derived from Chilean caliche. *Environ Pollut* 2001: 112: 299–302.

USDA. *Dietary guidelines for Americans* 2005: http://www.health.gov/dietaryguidelines/dga2005/document/html/chapter5.htm.

Valentin-Blasini L., Mauldlin J.P., Maple D., and Blount B.C. Analysis of perchlorate in human urine using ion chromatography and electrospray tandem mass spectroscopy. *Anal Chem* 2005: 77: 2475–2481.

Wattiaux M.A. *Dairy Essentials: Nutrition and Feeding, Reproduction and Genetic Selection, Lactation and Milking, and Raising Dairy Heifers*. Babcock Institute for Int'l Dairy R&D, University of Wisconsin, Madison, 1999, p140.

Yost L.J., Tao S.H., Egan S.K., Barraj L.M., Smith K.M., Tsuji J.S., Lowney Y.W., Schoof R.A., and Rachman N.J. Estimation of dietary intake of inorganic arsenic in US children. *Hum Ecol Risk Assess* 2004: 10: 473–483.

Yu L.u., Canas J.E., Cobb G.P., Jackson W.A., and Anderson T.A. Uptake of Perchlorate in terrestrial plants. *Ecotox Env Safety* 2004: 58: 44–49.

Yuma County. *Agric Stat* 2005: http://ag.arizona.edu/yuma/.