THE ENDOCRINE DISRUPTION EXCHANGE
Partners in Science

To: Eric Huber, Managing Attorney, Sierra Club Environmental Law Program
Bruce Baizel, Energy Program Director, Earthworks

From: Carol Kwiatkowski, Executive Director, TEDX

Date: June 29, 2018

Re: Scientific literature addressing the health effects of unconventional oil and gas development.

The following is an overview of the growing body of scientific evidence supporting the conclusion that significant health impacts can occur from exposure to chemicals used and released during unconventional oil and gas operations (UOG). It also includes a rebuttal to the criticisms of this research posed by the Colorado Department of Public Health and the Environment (CDPHE), and a recommendation for consideration of the full body of scientific evidence, including laboratory research, when assessing impacts from UOG. This information is presented at the request of the Sierra Club and Earthworks, for the purpose of a full consideration of health and the environment in Crestone's drilling permit application.

I am the Executive Director of The Endocrine Disruption Exchange (TEDX), a nonprofit scientific research institute. I am also adjunct faculty at the University of Colorado, Boulder, in the Department of Integrative Physiology, and North Carolina State University, in the Department of Biological Sciences. I have a PhD and a Masters degree in Cognitive Science from the University of Denver and I have published 38 peer-reviewed articles, 5 of which are relevant to UOG[1,2,3,4,5].

TEDX's Early Research

At TEDX we compile and disseminate scientific evidence on the health and environmental effects of exposure to chemicals that interfere with hormone (endocrine) action, otherwise known as endocrine disrupting chemicals. A major concern with endocrine disrupting chemicals is that they are associated with adverse health effects at very low concentrations, particularly

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[1] Colborn T, Kwiatkowski C, Schultz K, Bachran M. 2011. Natural gas operations from a public health perspective. Hum Ecol Risk Assess 17(5):1039-1056, doi: 10.1080/10807039.2011.605662.

[2] Colborn T, Schultz K, Herrick L, Kwiatkowski C. 2014. An exploratory study of air quality near natural gas operations. Hum Ecol Risk Assess 20(1):86-10, doi: 10.1080/10807039.2012.749447.

[3] Bolden AL, Kwiatkowski CF, Colborn T. 2015. New look at BTEX: Are ambient levels a problem? Environ Sci Technol 49(9):5261-5276, doi: 10.1021/es505316f.

[4] Bolden AL, Rochester JR, Schultz K, Kwiatkowski CF. 2017. Polycyclic aromatic hydrocarbons and female reproductive health: A scoping review. Repro Toxicol 73:61-74, doi: 10.1016/j.reprotox.2017.07.012.

[5] Bolden AL, Schultz K, Pelch KE, Kwiatkowski CF. 2018. Exploring the endocrine activity of air pollutants associated with unconventional oil and gas extraction. Environ Health 17(1):26, doi: 10.1186/s12940-018-0368-z.

when exposure occurs prenatally or in early childhood. Our involvement in studying the health impacts of UOG originated with our own research that began over a decade ago, which has since been supported by findings from numerous other scientific studies.

In 2011 we published a study[6] in which we identified 353 chemicals used during UOG, and reported that over one-third could affect the endocrine system. Further, nearly 75% could have skin/eye/sensory organ, respiratory, and gastrointestinal effects, approximately 40–50% could affect the brain/nervous system, immune and cardiovascular systems, and the kidneys, and 25% could cause cancer and mutations.

Over one-third of the chemicals we reviewed were volatile. In nearly every health effect category, more volatile chemicals had health effects than soluble ones. Notably, the 353 chemicals we identified were specific to drilling and fracking activities. They did not include other volatile chemicals that come up from underground, chemicals used during development and maintenance of the well pad and equipment, or emissions from mobile and stationary combustion sources, all of which include air pollutants associated with UOG.

Our findings prompted us to conduct an air sampling study[7] in Garfield County, on the western slope of Colorado, which is heavily impacted by UOG. Air samples were collected at a neighborhood location 0.7 miles from where a well pad with 16 wells was being built. There were also 130 producing wells within a mile radius of the sampling site.

A total of 61 chemicals were detected, with methane, ethane, propane, toluene, formaldehyde, acetaldehyde, and naphthalene found in every sample. More than half the chemicals we detected have been shown in the primary literature to affect the brain and central nervous system, causing headache, dizziness, confusion, memory loss, tingling in the extremities, peripheral neuropathy, all similar to complaints from residents and workers in the gas fields. They can also damage the liver and the metabolic system, and the endocrine system, affecting reproductive health, development in the womb, and other endocrine related endpoints. They affect the immune system and the heart, causing hypertension, they irritate the skin, eyes and other sensory organs, the respiratory system, and more. Many of these are health problems that are not expressed until much later in life, long after exposure occurs.

At the time we published our early research, few other studies were available on the health impacts of UOG. That has changed dramatically, as now our online database of UOG related health research lists 137 peer-reviewed studies[8]. In 2017 alone, 24 original research articles and 10 reviews/scientific commentaries were published. Twenty-one articles have already been published in 2018. The next sections of this letter will focus on air pollution and health effects specific to Colorado residents.

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[6] Colborn T et al. 2011.

[7] Colborn T et al. 2014.

[8] FrackHealth Database. The Endocrine Disruption Exchange. Available at: https://endocrinedisruption.org/audio-and-video/fracking-related-health-research-database/search-the-database.

Air pollution

Numerous studies attest to the fact that UOG creates air pollution. We recently published a review of 48 peer-reviewed studies that analyzed air samples near UOG. They measured a total of 221 chemicals in the air, 106 of which were found in at least two different studies. They include alkanes, alkenes, alkynes, aromatics, aldehydes, and polycyclic aromatic hydrocarbons (PAHs). Benzene, ethylbenzene, toluene and xylenes (BTEX) were among the top 10 most frequently found chemicals[9]. They are recognized hazardous air pollutants (HAPs), with well known respiratory, cardiovascular, neurological and carcinogenic effects, as well as having endocrine disrupting effects.

Ten of the studies in our review sampled the air in Colorado, with eight being in the Denver-Julesburg Basin (detecting approximately 76 chemicals). Atmospheric research conducted on the Front Range provides some of the most compelling evidence for UOG related air pollution[10,11,12,13]. For example, multiple studies from NOAA researchers collecting top-down emission concentrations found high levels of non-methane volatile organic compounds and traced it to UOG extraction.

It is my understanding that it will take at minimum three years of continuous drilling by Crestone to complete well build-out on all pads. In addition to the numerous air pollutants associated with drilling and fracking, well pad development requires heavy equipment similar to that used to build roads. Associated air pollution during well pad development includes diesel exhaust and increased particulate matter. Thousands of diesel truck trips will be required to deliver the chemicals and water used during drilling and completion. Diesel exhaust emits toxic chemicals like BTEX and is a major contributor to particulate pollution, associated with cardiovascular disease and respiratory conditions such as shortness of breath, pulmonary inflammation, and aggravation of asthma symptoms[14]. As setback distances are measured from the center of the well pad rather than the pad perimeter, homes and businesses nearest to the perimeters where equipment may be located, or along the truck route, will be exposed to higher concentrations of these pollutants.

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[9] Bolden AL et al. 2018.

[10] Gilman JB, Lerner BM, Kuster WC, de Gouw JA. 2013. Source signature of volatile organic compounds from oil and natural gas operations in Northeastern Colorado. Environ Sci Technol 47(3):1297-1305, doi: 10.1021/es304119a.

[11] Pétron G, Frost G, Miller BR, Hirsch AI, Montzka SA, Karion A, Trainer M, Sweeney C, Andrews AE, Miller L, et al. 2012. Hydrocarbon emissions characterization in the Colorado Front Range: A pilot study. J Geophys Res Atmos 117:D04304, doi: 10.1029/2011JD016360.

[12] Pétron G, Karion A, Sweeney C, Miller BR, Montzka SA, Frost GJ, Trainer M, Tans P, Andrews A, Kofler J, et al. 2014. A new look at methane and nonmethane hydrocarbon emissions from oil and natural gas operations in the Colorado Denver-Julesburg Basin. J Geophys Res Atmos 119(11):6836-6852, doi: 10.1002/2013JD021272.

[13] Swarthout RF, Russo RS, Zhou Y, Hart AH, Sive BC. 2013. Volatile organic compound distributions during the NACHTT campaign at the Boulder Atmospheric Observatory: Influence of urban and natural gas sources. J Geophys Res Atmos 118(18):10,614-610,637, doi: 10.1002/jgrd.50722.

[14] Webb E, Hays J, Dyrszka L, Rodriguez B, Cox C, Huffling K, Bushkin-Bedient S. 2016. Potential hazards of air pollutant emissions from unconventional oil and natural gas operations on the respiratory health of children and infants. Rev Environ Health 31(2):225-243, doi: 10.1515/reveh-2014-0070.

Many air pollutants associated with UOG are ozone precursors. Since 2004, the Northern Front Range has exceeded national ozone standards. Unfortunately, the 2008 regulations to control UOG emissions do not appear to be as effective as hoped[15]. In 2016, Evans et al reported significant contributions of UOG to ozone, specifically attributing transport of air pollutants from the Denver-Julesburg basin in the direction of the Boulder Atmospheric Observatory[16].

Even relatively low levels of ozone can cause health effects in humans. In the short term, ozone can cause difficulty breathing, coughing and sore throat. It can also make the lungs more susceptible to infection and can continue to damage the lungs even when the symptoms have disappeared. In the long term, ozone can inflame and damage the airways, aggravating lung diseases like asthma, emphysema, and chronic bronchitis. Children are particularly vulnerable because their lungs are still developing until about age 18, and they don't process chemicals as efficiently as adults because their immune and metabolic systems are not fully developed. As their lungs grow in the presence of ozone, children may suffer from decreased lung function and immune response making them more susceptible to lung infections[17]. Women exposed to higher ozone during pregnancy have been shown to deliver preterm, low birth weight babies with decreased lung function[18].

Colorado health impacts

Public health scientists from the University of Colorado School of Public Health have published numerous studies on possible health effects of living in close proximity to UOG. In 2018, McKenzie et al conducted a risk assessment demonstrating that both air pollutants and acute and chronic health risks, such as neurological and development effects and cancer, increased with increasing proximity to UOG[19]. Earlier work from this team concluded that residents living less than a half mile from wells are at greater risk of experiencing health effects than those living further away[20].

Witter et al's 2013 risk assessment identified cancer, birth defects, and exacerbation of chronic diseases like asthma, COPD and cardiac disease as possible long term health effects of UOG[21]. They also identified more immediate, probable health effects from air emissions, including headaches and other neurological symptoms, and airway and mucous membrane irritation. These immediate effects were supported by symptoms of residents living within a half mile of well development, as reported in the COGCC inspection/incident database.

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[15] Thompson C, Hueber J, Helmig D. 2014. Influence of oil and gas emissions on ambient atmospheric non-methane hydrocarbons in residential areas of Northeastern Colorado. Elem Sci Anth 3:35, doi: 10.12952/journal.elementa.000035.

[16] Evans JM, Helmig D. 2016. Investigation of the influence of transport from oil and natural gas regions on elevated ozone levels in the Northern Colorado Front Range. J Air Waste Manag Assoc 64(2):196-211, doi: 10.1080/10962247.2016.1226989.

[17] Webb E et al. 2016.

[18] American Lung Association. 2017. State of the Air. Available at http://www.lung.org/assets/documents/healthy-air/state-of-the-air/sota-2018-full.pdf

[19] McKenzie LM, Blair BD, Hughes J, Allshouse WB, Blake N, Helmig D, Milmoe P, Halliday H, Blake DR, Adgate JL. 2018. Ambient non-methane hydrocarbon levels along Colorado's northern Front Range: Acute and chronic health risks. Environ Sci Technol doi: 10.1021/acs.est.7b05983.

[20] McKenzie LM, Witter RZ, Newman LS, Adgate JL. 2012. Human health risk assessment of air emissions from development of unconventional natural gas resources. Sci Total Environ 424:79-87, doi: 10.1016/j.scitotenv.2012.02.018.

[21] Witter RZ, McKenzie L, Stinson KE, Scott K, Newman LS, Adgate J. 2013. The use of health impact assessment for a community undergoing natural gas development. Am J Public Health 103(6):1002-1010, doi: 10.2105/AJPH.2012.301017.

Other research has investigated the health impacts of prenatal exposure to UOG. In 2014 McKenzie et al published a study using a retrospective cohort of 125K birth records in 57 rural Colorado counties. Their results showed a linear relationship between well density/proximity and the likelihood of a baby having a congenital heart defect. Neural tube defects were also associated with a higher density/proximity score[22]. In a recent case-control study of childhood risk, McKenzie et al concluded that children with acute lymphocytic leukemia were more likely to live near oil and gas wells[23].

The impact of noise has also been studied by researchers in Colorado. Noise from UOG operations does not occur solely on the well pad, but also comes from truck traffic to and from the pad. In 2018, Blair et al found noise levels with the potential to impact health during both the day and at night at a UOG site where noise mitigation measures were in place[24]. According to a review by Hays et al, UOG activities produce noise at levels that can increase the risk of adverse health outcomes, including annoyance, sleep disturbance, and cardiovascular disease[25].

Evidence from other states.

Evidence from other states supports the findings in Colorado. Using well density and level of intensity metrics to better define exposure, studies from Johns Hopkins have found associations between asthma, sensory irritation, neurological effects, and preterm birth[26,27,28]. Adverse birth outcomes reported in retrospective cohort studies include low birth weight[29] and infant mortality[30,31]. Currie et al (2017) used a unique approach of comparing siblings born before and after UOG in their study of over 1 million births in Pennsylvania. They found lower birth weight,

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[22] McKenzie LM, Guo R, Witter RZ, Savitz DA, Newman LS, Adgate JL. 2014. Birth outcomes and maternal residential proximity to natural gas development in rural Colorado. Environ Health Perspect 122(4):412-417, doi: 10.1289/ehp.1306722.

[23] McKenzie LM, Allshouse WB, Byers TE, Bedrick EJ, Serdar B, Adgate JL. 2017. Childhood hematologic cancer and residential proximity to oil and gas development. PloS ONE 12(2):e0170423, doi: 10.1371/journal.pone.0170423.

[24] Blair BD, Brindley S, Dinkeloo E, McKenzie LM, Adgate JL. 2018. Residential noise from nearby oil and gas well construction and drilling. J Expo Sci Environ Epidemiol doi: 10.1038/s41370-018-0039-8.

[25] Hays J, McCawley M, Shonkoff SBC. 2017. Public health implications of environmental noise associated with unconventional oil and gas development. Sci Total Environ 580:448-156, doi: 10.1016/j.scitotenv.2016.11.118.

[26] Rasmussen SG, Ogburn EL, McCormack M, Casey JA, Bandeen-Roche K, Mercer DG, Schwartz BS. 2016. Association between unconventional natural gas development in the marcellus shale and asthma exacerbations. JAMA Intern Med 176(9):1334-1343, doi: 10.1001/jamainternmed.2016.2436.

[27] Tustin AW, Hirsch A, Rasmussen S, Casey J, Bandeen-Roche K, Schwartz B. 2016. Associations between unconventional natural gas development and nasal and sinus, migraine headache, and fatigue symptoms in Pennsylvania. Environ Health Perspect 125:189-197, doi: 10.1289/EHP281.

[28] Casey JA, Savitz DA, Rasmussen SG, Ogburn EL, Pollak J, Mercer DG, Schwartz BS. 2016. Unconventional natural gas development and birth outcomes in Pennsylvania, USA. Epidemiology 27(2):163-172, doi: 10.1097/ede.0000000000000387.

[29] Stacy SL, Brink LL, Larkin JC, Sadovsky Y, Goldstein BD, Pitt BR, Talbott EO. 2015. Perinatal outcomes and unconventional natural gas operations in Southwest Pennsylvania. PloS ONE 10(6):e0126425. Doi: 10.1371/journal.pone.0126425.

[30] Whitworth KW, Marshall AK, Symanski E. 2017. Maternal residential proximity to unconventional gas development and perinatal outcomes among a diverse urban population in Texas. PloS one 12(7):e0180966, doi: 10.1371/journal.pone.0180966.

[31] Busby C, Mangano JJ. 2017. There's a world going on underground —infant mortality and fracking in Pennsylvania. J Environ Prot 8(4):381-393, doi: 10.4236/jep.2017.84028.

and worse infant health scores among those living within 3 km of UOG. The largest effects were seen among those living within 1 km[32].

Others have studied symptoms of Pennsylvania residents living in close proximity to UOG activity, reporting impacts to the respiratory system (wheezing, shortness of breath) and neurological system (headache, dizziness) as well as skin and sensory organ irritation, and other effects[33,34,35]. Further, hospitalization rates are higher among residents living near UOG[36,37]. It should be clear from this summary that there is a large and growing body of evidence from human health studies both within and outside of Colorado.

Responding to the 2017 CDPHE Assessment

In 2017, the CDPHE released an Assessment of Potential Public Health Effects from Oil and Gas Operations in Colorado[38]. In it, they found multiple volatile organic compounds are released into the air in Colorado from UOG. However, the CDPHE report focused only on chemicals that were reported at least 50 percent of the time. Because of this, the report may underestimate the health risk by ignoring potentially harmful chemicals that were detected less frequently in this particular data set.

CDPHE also concluded that because the subset of substances they did review did not exceed government safety levels, there is no risk to health from increased exposure to these chemicals. While government safety levels are an important source of information for risk estimates, they have many flaws that could lead to underestimation of actual risk. First, the underlying assumption in developing 'safe' levels of exposure is that lower levels are safe. Thus, high doses of chemical exposure are tested for health effects, and then lower 'safe' levels are extrapolated from the high dose findings, without the lower concentrations actually being tested. It is now well established that significant health effects can occur from exposure to extremely low concentrations of environmental pollutants[39], well within the range of human exposure. This is especially true for chemicals that affect the endocrine system. The endocrine system is responsible for regulating vital functions such as growth, metabolism, and behavior. There is a

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[32] Currie J, Greenstone M, Meckel K. 2017. Hydraulic fracturing and infant health: New evidence from Pennsylvania. Sci Adv 3(12):e1603021, doi: 10.1126/sciadv.1603021.

[33] Weinberger B, Greiner LH, Walleigh L, Brown D. 2017. Health symptoms in residents living near shale gas activity: A retrospective record review from the Environmental Health Project. Prev Med Rep 8:112-115, doi: 10.1016/j.pmedr.2017.09.002.

[34] Steinzor N, Subra W, Sumi L. 2013. Investigating links between shale gas development and health impacts through a community survey project in Pennsylvania. New Solut 23(1):55-83, doi: 10.2190/NS.23.1.e.

[35] Rabinowitz PM, Slizovskiy IB, Lamers V, Trufan SJ, Holford TR, Dziura JD, Peduzzi PN, Kane MJ, Reif JS, Weiss TR, et al. 2015. Proximity to natural gas wells and reported health status: Results of a household survey in Washington County, Pennsylvania. Environ Health Perspect 123(1):21-26, doi: 10.1289/ehp.1307732.

[36] Peng L, Meyerhoefer C, Chou SY. 2018. The health implications of unconventional natural gas development in Pennsylvania. Health Econ doi: 10.1002/hec.3649.

[37] Jemielita T, Gerton GL, Neidell M, Chillrud S, Yan B, Stute M, Howarth M, Saberi P, Fausti N, Penning TM, et al. 2015. Unconventional gas and oil drilling is associated with increased hospital utilization rates. PloS one 10(7):e0131093, doi: 10.1371/journal.pone.0131093.

[38] Colorado Department of Public Health & Environment. 2017. Assessment of Potential Public Health Effects from Oil and Gas Operations in Colorado. Available at: https://www.colorado.gov/pacific/cdphe/oil-and-gas-health-assessment

[39] Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR, Jr., Lee DH, Shioda T, Soto AM, vom Saal FS, Welshons WV, et al. 2012. Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev 33(3):378-455, doi: 10.1210/er.2011-1050.

large body of independent peer-reviewed science addressing health impacts from low level exposure to chemicals released during UOG (see for example our review of BTEX[40]).

Second, government standards do not take into account 24 hour exposure during prenatal and childhood development, our primary time period of concern. Third, they are based on exposures to single chemicals, not the many cumulative and potentially synergistic combinations of air pollutants that occur during UOG[41]. Fourth, standards are based on averages, which fail to address the spikes in air pollution that occur during different stages or events in UOG, which may be where the most harm occurs. Finally, standards only exist for a small subset of chemicals associated with UOG, which leads to a false estimate of overall safety. In my professional opinion, determining acceptable risk by comparing chemical concentrations found near UOG to government safety standards vastly underestimates the true risk of exposure to UOG.

The CDPHE report also provided a critique of the human health studies. Many of the studies are subject to common weaknesses of epidemiological research: indirect exposure measurements (e.g. that do not account for phases of well development), inability to control for all possible covariates, and confidence intervals close to the null (small effect sizes). Colorado researchers have recently developed an improved exposure model to address some of these concerns. They can now account for fluctuations in the intensity of chemical exposures during different phases of UOG development and for different production volumes across well pads[42]. This is particularly important for assessing effects during fetal development, where specific windows of vulnerability exist. It is also important to recognize that some of the limitations of previous studies actually make it *harder* to detect hazards. For example, the failure to differentiate active from inactive wells would make the true effect more difficult to detect, leading to an *under*estimation of risk.

Finally, the CDPHE report only assessed 12 epidemiologic studies, and did not evaluate the contributions of the growing body of supporting evidence from the more than 40 additional peer-reviewed studies evaluating experimental animal, observational animal, in vitro, and modeling data.

Laboratory research

Laboratory research is a critical component of the total body of evidence available to answer the question of whether UOG affects human health. It is used precisely because it helps scientists predict human outcomes in the natural environment and can lend support to findings from epidemiological studies. In particular, it can address the limitations of such research with regard to exposure timing (e.g. during prenatal development), dose, and control of covariates.

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[40] Bolden AL et al. 2015.

[41] Brown D, Weinberger B, Lewis C, Bonaparte H. 2014. Understanding exposure from natural gas drilling puts current air standards to the test. Rev Environ Health 29(4):277-292, doi: 10.1515/reveh-2014-0002.

[42] Allshouse WB, Adgate JL, Blair BD, McKenzie LM. 2017. Spatiotemporal industrial activity model for estimating the intensity of oil and gas operations in Colorado. Environ Sci Tech 51(17):10243-10250, doi: 10.1021/acs.est.7b02084.

In laboratory experiments using animal models relevant to humans, exposure to UOG chemicals resulted in numerous adverse impacts. Specifically, male rodents exposed prenatally to a mixture of chemicals used during hydraulic fracturing were shown to have increased testosterone, decreased sperm counts, and heavier testes and thymus[43]. Effects in female rodents included hormone suppression, changes in uterine, ovary, heart, and body weights, and disrupted folliculogenesis[44]. In addition, new research found altered mammary gland development[45] as well as impaired immune system development and function[46] in prenatally exposed female mice.

Other species provide supporting evidence as well. Zebrafish embryos exposed to flowback/produced water had increased embryo deformations and mortality, reduced metabolic rates, and altered cardio-respiratory gene expression[47,48], and embryonically exposed juveniles had decreased metabolic rates and fitness[49]. Exposure in juvenile rainbow trout showed adverse impacts to multiple pathways, including biotransformation and oxidative stress pathways, and potential endocrine disruptive effects[50]. Finally, exposure of Daphnia to flowback/produced water resulted in decreased reproduction and altered gene expression[51] and physical immobility[52].

Research using *in vitro* assays also supports the laboratory and epidemiological findings. For example, studies of chemicals detected in water collected near UOG operations, such as spill sites and surface water near wastewater injection sites, were shown to have hormone activity in estrogen, androgen, progesterone, glucocorticoid, and thyroid hormone receptor assays[53,54].

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[43] Kassotis CD, Klemp KC, Vu DC, Lin C-H, Meng C-X, Besch-Williford CL, Pinatti L, Zoeller RT, Drobnis EZ, Balise VD, et al. 2015. Endocrine-disrupting activity of hydraulic fracturing chemicals and adverse health outcomes after prenatal exposure in male mice. Endocrinology 156(12):4458-4473, doi:10.1210/en.2015-1375.

[44] Kassotis CD, Bromfield JJ, Klemp KC, Meng CX, Wolfe A, Zoeller RT, Balise VD, Isiguzo CJ, Tillitt DE, Nagel SC. 2016. Adverse reproductive and developmental health outcomes following prenatal exposure to a hydraulic fracturing chemical mixture in female C57Bl/6 mice. Endocrinology 157(9):3469-3481, doi: 10.1210/en.2016-1242.

[45] Sapouckey SA, Kassotis CD, Nagel SC, Vandenberg LN. 2018. Prenatal exposure to unconventional oil and gas operation chemical mixtures altered mammary gland development in adult female mice. Endocrinology 159(3):1277-1289,doi: 10.1210/en.2017-00866.

[46] Boulé LA, Chapman TJ, Hillman SE, Kassotis CD, O'Dell C, Robert J, Georas SN, Nagel SC, Lawrence BP. 2018. Developmental exposure to a mixture of 23 chemicals associated With unconventional oil and gas operations alters the immune system of mice. Toxicol Sci:kfy066-kfy066, doi: 10.1093/toxsci/kfy066.

[47] He Y, Flynn SL, Folkerts EJ, Zhang Y, Ruan D, Alessi DS, Martin JW, Goss GG. 2017. Chemical and toxicological characterizations of hydraulic fracturing flowback and produced water. Water Res 114:78-87, doi: 10.1016/j.watres.2017.02.027.

[48] Folkerts EJ, Blewett TA, He Y, Goss GG. 2017. Cardio-respirometry disruption in zebrafish (Danio rerio) embryos exposed to hydraulic fracturing flowback and produced water. Environ Pollut 231:1477-1487, doi: 10.1016/j.envpol.2017.09.011.

[49] Folkerts EJ, Blewett TA, He Y, Goss GG. 2017. Alterations to Juvenile Zebrafish (Danio rerio) Swim Performance after Acute Embryonic Exposure to Sub-lethal exposures of hydraulic fracturing flowback and produced water. Aquat Toxicol 193:50-59, doi: 10.1016/j.aquatox.2017.10.003.

[50] He Y, Folkerts EJ, Zhang Y, Martin JW, Alessi DS, Goss GG. 2017. Effects on biotransformation, oxidative stress, and endocrine disruption in rainbow trout (Oncorhynchus mykiss) exposed to hydraulic fracturing flowback and produced water. Environ Sci Technol 51(2):940-947, doi: 10.1021/acs.est.6b04695.

[51] Blewett TA, Delompre PL, He Y, Folkerts EJ, Flynn SL, Alessi DS, Goss GG. 2017. The sub-lethal and reproductive effects of acute and chronic exposure to flowback and produced water from hydraulic fracturing on the water flea Daphnia magna. Environ Sci Technol 51(5):3032-3039, doi: 10.1021/acs.est.6b05179.

[52] Blewett TA, Delompré PLM, Glover CN, Goss GG. 2018. Physical immobility as a sensitive indicator of hydraulic fracturing fluid toxicity towards Daphnia magna. Sci Total Environ 635:639-643, doi: 10.1016/j.scitotenv.2018.04.165.

[53] Kassotis CD, Tillitt DE, Davis JW, Hormann AM, Nagel SC. 2014. Estrogen and androgen receptor activities of hydraulic fracturing chemicals and surface and ground water in a drilling-dense region. Endocrinology 155(3):897-907, doi: 10.1210/en.2013-1697.

Altered hormone activity was also found in extracted groundwater samples near UOG sites in Wyoming[55]. One study of wastewater samples demonstrated dose-dependent toxicity in human and rat cells, altered gene expression, and impaired cell behavior, with some effects at very low concentrations[56]. A study using Marcellus Shale flowback water induced malignant cell transformation *in vitro*[57]. Most recently, fracking chemicals, wastewater, and surface water collected near UOG activity spurred fat cell development and proliferation in mouse cells[58].

Notably, many of the effects described above were found in developing organisms (i.e. via prenatal exposure), are related to the endocrine system, and occurred at low exposure concentrations. This highlights the importance of assessing impacts on the endocrine system with regard to UOG exposure. Such effects can have widespread and long lasting implications for overall health.

Evidence to the contrary

The evidence I have presented thus far is overwhelmingly in support of significant health hazards and risks from UOG. In fact, a recent review found only two studies since 2000 failed to find significant health effects associated with UOG[59]. Nonetheless, other sources of data are occasionally offered to refute this scientific research. For example, CDPHE surveillance data on health impacts in different Colorado counties have been used to deny the existence of adverse health effects in communities living near UOG. There are many reasons why this is not an appropriate response to the wealth of data I have so far presented. First, the outcomes in these data tables are limited to health impacts surveyed, which may be more or less relevant for UOG. Second, in some counties the major population center is not near the UOG activity, so there will be fewer cases per capita in those counties, which underestimates the risk of people living near UOG. Finally, the CDPHE reports are simply data tables. They have not been analyzed and interpreted by CDPHE scientists, nor have they been peer-reviewed by outside experts (a fact that CDPHE uses to caution people against over-interpretation). Without such expert analysis and review, high level conclusions about what the data indicate are easily biased. Until the surveillance data is peer-reviewed and published it should not be cited to refute legitimate scientific studies.

Distance matters

The question of what is a safe distance for UOG in relation to human activity is being asked in states and localities across the country. The answer can be based in science but is ultimately a

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[54] Kassotis CD, Iwanowicz LR, Akob DM, Cozzarelli IM, Mumford AC, Orem WH, Nagel SC. 2016. Endocrine disrupting activities of surface water associated with a West Virginia oil and gas industry wastewater disposal site. Sci Total Environ 557-558:901-910, doi: http://dx.doi.org/10.1016/j.scitotenv.2016.03.113.

[55] Kassotis CD, Vu DC, Vo PH, Lin C-H, Cornelius-Green JN, Patton S, Nagel SC. 2018. Endocrine-disrupting activities and organic contaminants associated with oil and gas operations in Wyoming groundwater. Arch Environ Contam Toxicol doi: 10.1007/s00244-018-0521-2.

[56] Crosby LM, Tatu CA, Varonka M, Charles KM, Orem WH. 2018. Toxicological and chemical studies of wastewater from hydraulic fracture and conventional shale gas wells. Environ Toxicol Chem doi: 10.1002/etc.4146.

[57] Yao Y, Chen T, Shen SS, Niu Y, DesMarais TL, Linn R, Saunders E, Fan Z, Lioy P, Kluz T, et al. 2015. Malignant human cell transformation of Marcellus Shale gas drilling flow back water. Toxicol Appl Pharmacol 288(1):121-130, doi: 10.1016/j.taap.2015.07.011.

[58] Kassotis CD, Nagel SC, Stapleton HM. 2018. Unconventional oil and gas chemicals and wastewater-impacted water samples promote adipogenesis via PPARγ-dependent and independent mechanisms in 3T3-L1 cells. Sci Total Environ doi: 10.1016/j.scitotenv.2018.05.030.

[59] Wright R, Muma RD. 2018. High-volume hydraulic fracturing and human health outcomes: A scoping review. J Occup Environ Med 60(5):424-429, doi: 10.1097/jom.0000000000001278.

question of how much risk one is willing to impose on people living near UOG. As of yet, there is no scientific basis for a gradient of safe distances. Significant health effects have been demonstrated at distances of 500 feet[60], 2,640 feet[61,62], and 3,280 feet[63,64,65]. The following table shows the health effects that have been found within these distances. It does not include studies that used more elaborate metrics by combining distance with variables such as density and stage of well development. Exhibit A maps these distances in relation to the proposed Crestone well pad locations.

Distance below which health effects were seen	**Types of health effects found within distance**	**Study***
500 feet	cancer, developmental, hematological, neurological	McKenzie 2018[19]
2640 feet	developmental	Whitworth 2017[30]
2640 feet	cancer, hematological, neurological, respiratory	McKenzie 2012[20]
3280 feet	developmental	Currie 2017[32]
3280 feet	cardiovascular, gastrointestinal, musculoskeletal/motor function, neurological, ocular and sensory, respiratory, skin and connective tissues	Weinberger 2017[33]
3280 feet	respiratory, skin and connective tissues	Rabinowitz 2015[35]

*Numbers refer to footnotes above.

In a review published in 2016, Haley et al concluded that even the most protective setbacks, up to 1500 feet among the three states evaluated (PA, TX and CO), are not sufficient[66]. Unfortunately, it could be decades before we have conclusive evidence of how close is too close.

[60] McKenzie LM et al. 2018.

[61] McKenzie LM et al. 2012.

[62] Whitworth KW et al. 2017.

[63] Currie J et al. 2017.

[64] Weinberger B et al. 2017.

[65] Rabinowitz PM et al. 2015.

[66] Haley M, McCawley M, Epstein AC, Arrington B, Bjerke EF. 2016. Adequacy of current state setbacks for directional high-volume hydraulic fracturing in the Marcellus, Barnett, and Niobrara Shale plays. Environ Health Perspect 124(9):1323-1333, doi: 10.1289/ehp.1510547.

In sum

I believe the current body of scientific evidence supports the conclusion that people are at significant risk for health effects from UOG. Keep in mind that these studies do not account for all possible chemical interactions, vulnerabilities of sensitive populations (e.g. infants), or outcomes that may arise long after initial exposures. As researchers continue to improve their scientific methods, and the strength of the evidence increases, the health and well being of entire communities continues to be threatened. In the interest of the people of the state of Colorado, and as a model for the nation, I urge you to make the most health protective decisions possible.

Sincerely,

Carol Kwiatkowski, Ph D
Executive Director