REPORT OF PLAINTIFFS' EXPERT
David O. Carpenter, MD

America Unites For Kids, et al.
v. Sandra Lyon, et al.
Case No. 2:15-cv-02124-PA (AJWx)

REPORT
David O. Carpenter, MD

My name is David O. Carpenter, and I am a public health physician, educated at Harvard College where I graduated *magna cum laude* in 1959 and at Harvard Medical School where I graduated *cum laude* in 1964. I have pursued a career in biomedical research and public health rather than patient care. I served as Director of the Wadsworth Center for Laboratories and Research of the New York State Department of Health from 1980-1985, then became the founding Dean of the School of Public Health of the University at Albany, a position I held until 1998. My present position is Director of the Institute for Health and the Environment at the University at Albany. The Institute has been designated as a Collaborating Centre of the World Health Organization. I am also Professor in the Department of Environmental Health Sciences in the School of Public Health. I have over 400 peer-reviewed publications in the general fields of neuroscience and environmental health and am active in research and training. I teach graduate courses in environmental health, radiation biology and neurobiology/neurotoxicology. My *Curriculum vitae* is attached.

QUALIFICATIONS:

Beginning in 1986 I directed a large, interdisciplinary research study on polychlorinated biphenyls (PCBs), funded by the Superfund Basic Research Program of the National Institute of Environmental Health Sciences, one of the National Institutes of Health. Our particular study, supported at over $2 million a year until 2000, was designed around the PCB contamination coming from the General Motors Foundry Site in Massena, NY, which is directly adjacent to the Mohawk Nation of Akwesasne, a Native American community of individuals who traditionally eat fish from waters now heavily contaminated with PCBs. Our investigations included health studies of the Mohawks, animal toxicology studies of effects of PCBs on the nervous, immune and endocrine systems and metabolism, determination of levels of PCBs in human body fluids, animals from the region, soils, sediments, air and water and investigation of several methods for destruction and removal of PCBs from contaminated soils, sediments and water. A laboratory for chemical measurement of PCBs is a central part of our research team and operated under my direction. This study involved over 1,600 members of the Mohawk Nation, where I have reviewed analyses of their PCB blood levels and clinical chemistry results, as well as results taken from questionnaires. The early investigations at Akwesasne were focused entirely on demonstrating that the Mohawks were exposed to PCBs from consumption of contaminated fish. In the grant that was funded in the period 1995-2000 we began to collect health information, the analysis of which and results of which are still being analyzed and published. We have smaller grant-funded studies of the same population ongoing in which we are collecting new data, and continue to submit research grant applications to expand study in this community.

I have also conducted health effects studies of other PCB-exposed populations, including an Alaskan Native population living on St. Lawrence Island, Alaska (funded by the National Institute of Environmental Health Sciences and the US Environmental Protection Agency), residents of Anniston, Alabama who live near to the Monsanto plant that manufactured PCBs

(funded by the Agency for Toxic Substances and Disease Registry) and people living along the PCB-contaminated portions of the Hudson River in New York and the Housatonic River in Massachusetts. I have published numerous articles based on both human exposure to PCBs and experimental studies with animals experimentally exposed to PCBs.

In addition, I have and continue to investigate the distribution of various human diseases in relation to residence near hazardous waste sites. These studies utilize the New York State dataset which records information on every inpatient in state-regulated hospitals, giving age, sex, race, method of payment and zip code of residence, as well as all (up to 15) diseases diagnosed in that patient. We have matched these data to a characterization of every zip code in so far as it has or abuts an identified hazardous waste site that either contains or does not contain persistent organic pollutants (primarily PCBs). While we do not have detailed individual information using these data, we have large numbers that allow us to observe patterns of disease in relation to residence near to waste sites. We have studied diseases such as diabetes, heart disease, stroke, hypertension, thyroid disease, endocrine disease, asthma and infections, and for each find elevations in incidence correlated with residence near to waste sites that contain PCBs. Because simply living in the same zip codes as one containing a hazardous waste site containing PCBs is unlikely to result in exposure coming from dermal contact or ingestion, we conclude that the route of exposure to the PCBs that result in the diseases listed above is inhalation. Because PCBs are semi-volatile chemicals, they are present in the air at low concentrations, varying with temperature. These results provide strong evidence that chronic exposure to PCBs in air is associated with elevations in a variety of human diseases.

I have reviewed medical records and/or serum PCB levels of over 3,000 residents of Anniston, Alabama, Crystal Springs, Mississippi, Chicago, Illinois and Bedford, Indiana who have been exposed to PCBs as a result of residential proximity to industrial contaminated sites, and have provided medical monitoring advice in these and other cases.

In recognition of my contributions in the general field of environmental health, I have and continue to serve on several national and international advisory committees. From January 1997 until February 2001 I was a member of the National Advisory Environmental Health Sciences Council of the National Institute of Environmental Health Sciences. This Committee was appointed by the United States Secretary of Health and Human Services to advise the Director and Staff of the Institute on all matters of policy, scientific direction and priorities. In 1997, I was also appointed to be a member of the Great Lakes Science Advisory Board of the International Joint Commission, which is a binational Commission between Canada and the United States that deals with issues related to the Great Lakes. I was reappointed and served on this board until 2012. In 1999, I was invited to be a member of the Expert Panel Review team for the Agency for Toxic Substances and Disease Registry, a panel assembled to review the newest edition of the publication, *Toxicological Profiles for Polychlorinated Biphenyls*. I have been a member of the Board of Directors of the Pacific Basin Consortium for Environmental and Health Sciences for several years. From 2004 to 2007, I assumed the position of Chair of the Board, and am the Treasurer at present. This is an international organization concerned with health effects of environmental contaminants, remediation of hazardous wastes and other environmental problems such as climate change, with membership open to individuals and organizations from all countries in the Pacific Basin. In 2001, I was appointed as a member of

the Committee on Implications of Dioxins in the Food Supply, a committee of the US National Academy of Sciences, and the report from this committee was released in July, 2003. I was a member of the Children's Health Protection Advisory Committee to the US Environmental Protection Agency between 2003 and 2008. I was a coauthor and the spokesperson for a study of contaminants in farmed and wild salmon first published in Science in January, 2004, and which has received international attention. The study was supported by the Pew Charitable Trust. In November 1999, I was awarded the Homer N. Carver Lecture Award by the Section on the Environment of the American Public Health Association for contributions to the field, and in 2001, I was selected to be the Academic Laureate of the University at Albany Foundation for distinguished service to the University. I serve as Chair of the Advisory Committee to the World Health Organization and National Institute of Environmental Health Sciences on their joint programs. In 2008 the Institute for Health and the Environment was designated a Collaborating Centre of the World Health Organization in recognition of our international efforts in the area of environmental health. In 2013 I served as an Invited Specialist to the International Agency for Research on Cancer in their review of the carcinogenicity of PCBs, which resulted in PCBs being declared a Group 1, known human carcinogen.

Because of my public health background in environmental health and my research experience in both human and animal studies involving PCBs, I believe that I am qualified to evaluate and review the scientific validity of the plaintiff's complaint of imminent and substantial endangerment to human health posed by the PCB content in the air, dust, soil and school buildings in Malibu, California.

I am a public health physician, not a practicing physician, and study of the health effects resulting from exposure to PCBs and other environmental contaminants is my public health specialty.

COMPENSATION:

My usual compensation for involvement in legal cases is $400.00 per hour, paid to the Research Foundation of SUNY to be used for support of my students and staff, plus personal reimbursement for any travel expenses incurred. Given the nature of this case I will waive all fees unless funds become available, with the exception of any travel costs.

PREVIOUS DEPOSITIONS AND TESTIMONY (past five years):

Ronald Cybart et al., Michael Campanelli, and Donald and Theresa Shea, et al.v. CL&P. Deposed for the plaintiffs. 15 July 2011.

Maria Snoops vs. Lyon Associates, Inc. and Insurance Co of the state of Pennsylvania. Deposed for the plaintiff, 1 November 2011.

John Edward Martinez and Gladys Yolanda Martinez v. Entergy Corporation, et al., Deposed for the plaintiff, 19 December 2011.

AHM and David Mark Morrison vs. Portland Public Schools. Deposed for the plaintiffs,

25 January 2012.

Judy Prescott Barnett v Robert E. Carberry et al. Deposed for the plaintiff, 6 April 2012.

Association Quebecoise de Lutte Contre La Pollution Atmospherique et al. vs. Hydro Quebec, et al. Testified for the plaintiffs, 17-18 May 2012.

FortisBC vs Citizens for Safe Technology. Testified for the plaintiff, 15 March 2013.

John Edward Martinez and Gladys Yolanda Martinez v. Entergy Corporation et al., Deposed for the plaintiff, 21 June 2013.

Village of Stillwater et al. and Saratoga County Water Authority v. General Electric Company. Deposed for the plaintiff, 10 April 2014. Ron Plain and Ada Lockridge v. Director, Ministry of the Environment et al., Deposed for the plaintiff, 13-14 May 2014.

Harry Naeole vs. Alaska Barge & Transport, Employers, continental Insurance Company/CAN, Carrier. Deposed for the plaintiff, 27 May 2014.

Case No U-17767. Before the Michigan Public Service Commission in the matter of the application and request of the Detroit Edison Company seeking approval and authority to implement its proposed Advanced Metering Infrastructure opt out program. Testified to the Commission. 6 July 2015

Edwin Spirer, et al. v. Monsanto Company, et al. Deposed for the plaintiffs, 17-18 December 2015.

POLYCHLORINATED BIPHENYLS (PCBs): HISTORY, ROUTES OF EXPOSURE AND MECHANISMS OF ACTION:

PCBs were manufactured in the US between1929 to 1976 and were useful compounds for a variety of purposes. They are heavy oils that were used in transformers and electrical capacitors on the basis of being relatively good electrical insulators, as hydraulic fluids, as an oil additive to paints, window caulking, ceiling and floor tiles and many other products. PCBs were made by addition of chlorines to biphenyl, and were sold in the US primarily as Aroclor mixtures manufactured by the Monsanto Corporation, with the number of different commercial Aroclor mixtures based on the average degree of chlorination.

There are ten possible positions around the biphenyl molecule where chlorines can be added, and as a consequence there are a theoretical 209 possible PCB congeners. The positions are usually expressed as from 2 to 6, with the 2 and 6 positions being those closest to the biphenyl ring described as "*ortho*", those opposite (4) called "*para*" and the remainder (3 and 5) called "*meta*". Positions around the second ring are usually identified by adding a prime to the number, such that 2, 2' biphenyl is a PCB with two chlorines, one on each ring at the 2 position. The numbers and positions of the chlorines determine both the physical and biological properties of each congener. Those with fewer chlorines are in general more water soluble, more volatile and more easily metabolized. Those with chlorines only in the *meta* and *para* positions tend to assume a planar configuration and have dioxin-like activity. Those with more than one *ortho* chlorine do not show significant dioxin-like activity. PCBs that exist in a planar configuration activate the aryl hydrocarbon receptor (AhR) and have actions similar to those of dioxins and furans. This is the basis of the toxic equivalent factor (TEF) as defined by the World Health Organization (WHO) and many other publications by scientists in this area of research (Safe, 1990; Ahlborg et al., 1992; Walker et al., 2005). While coplanar PCBs are not as potent in

activation of the AhR as 2, 3, 7, 8-tetrachloro-dibenzo-*p*-dioxin, the most toxic dioxin congener, in many circumstances the concentration of the coplanar PCBs is much greater than that of dioxins and furans such that the majority of AhR receptor activity comes from PCBs. This large body of evidence provides proof that the health effects reported for dioxin-exposed populations are directly relevant to individuals exposed to PCBs, although PCBs may exert many other actions via different pathways.

No person exposed to PCBs is exposed only to either the dioxin-like or to the non-dioxin-like PCB congeners, however. Because the non-dioxin-like PCB congeners have different mechanisms of action and result in other diseases, a PCB-exposed person is at risk for all of the diseases caused by dioxin and other diseases caused by the non-dioxin-like congeners.

Each individual PCB congener has its own profile of actions in biological systems. Therefore, it is very important to have measurements of PCBs in any individual's body include measurement of individual congeners. However, we still have inadequate information on the actions of many individual congeners, such that in many cases one is not able to use all of the information that is obtained from measurement of all of the individual congeners (DeCaprio et al., 2005). Various investigators have proposed different patterns of response dependent upon classes of activity of PCB congeners. As mentioned above, those that activate the AhR act like dioxin to induce activity of cytochromes P450 (CYP) 1A1, 1A2 and 1B1. These actions result in proliferation of endoplasmic reticulum in liver, an actual increase in liver size, and alteration in liver function. The size of the thymus gland is reduced, resulting in a reduction in immune function. Since the AhR is one of the greater steroid hormone family of receptors, its activation results in gene induction, with increased or decreased levels of a very large number of gene products. There are four coplanar PCB congeners with at least four chlorines.

The majority of PCB congeners are not AhR activators, but act at several other sites. One important class of congeners is those that cause induction of a different class of cytochrome P450s, that being CYP 2B1 and 2B2. These congeners induce a wasting syndrome and as well as thymic atrophy in experimental animals and presumably also in humans. A third major group of congeners have activities at both of these sites, and are called "mixed" congeners. These are mono-ortho congeners, and activate both the 1A and B and 2B P450s. There are nine major congeners in this group, and they contribute significantly to total TEF because some are present in relatively high concentrations (Erikson, 1997). Fitzgerald et al. (2004) have demonstrated that adults exposed to PCBs are able to more rapidly metabolize caffeine using a caffeine breath test if they have high levels of PCBs. These observations demonstrate that exposure alters liver function in ways that affect metabolism of many substances in addition to PCBs through prolonged induction of the P450s, in this case CYP 1A2.

Some congeners with *ortho* chlorines have a different profile of actions and health effects that appear not to be dependent upon any CYP activity. These PCBs show short-latency effects on the nervous (Kodavanti et al. 1993; Carpenter et al., 1997; Tan et al., 2003) and immune systems (Jeon et al., 2002; Tan et al., 2004a), causing a relatively rapid cell death that is a result of disruption of the membrane structure (Tan et al. 2004b), an effect not seen by coplanar PCBs. These congeners have also been found to stimulate insulin release from a human beta receptor cell line, to reduce synthesis of the neurotransmitter dopamine in neurons, and to

activate neurophils to produce reactive oxygen species (ROS) (Fischer et al., 1998).

Not only do different PCB congeners have unique sites and mechanisms of action, but also their metabolites may have biological activity and may be persistent in living organisms for a period of time (Connor et al., 1997; Sandau et al., 2000). Many of the endocrine disruptive actions of PCBs may be primarily a result of the actions of metabolites, especially hydroxylated metabolites (Garner et al., 1999).

We have demonstrated that we can detect various patterns of PCBs in human blood (DeCaprio et al., 2005). As indicated above, lower chlorinated PCBs are more volatile, and in analysis of a subset of Mohawks we can identify a pattern in their blood that is similar to that in the air. This provides direct evidence that inhalation is an important route of exposure. Others show patterns that correlate with rates of fish consumption. The congener patterns that correlate with fish consumption are not identical to those in the fish, which reflects the differing rates of metabolism of various congeners in the human body. We found two patterns that do not reflect any seen in either exposure pathway, and which we believe to reflect genetic differences in metabolism of PCBs.

Others (Wolff et al., 1997) have classified PCB congeners in groups on the basis of commonality of action, or on the basis of degree of chlorination (Moysich et al., 1998). The coplanar and AhR activating PCBs, for example, are antiestrogenic by virtue of the fact that they induce P450 1A1, which is the P450 which degrades estrogen (Spink et al., 1990). In contrast most other PCBs are estrogenic. A recent report demonstrated estrogenic activity of thirteen congeners, PCBs 17, 18, 30, 44, 49, 66, 74, 82, 99, 103, 110, 128, and 179 (DeCastro et al., 2006), and found that inhalation was the major source of exposure to estrogenic PCB activity. This makes sense since the lower chlorinated congeners are also more volatile, and many of the congeners listed above are lower chlorinated. In the body the hydroxylated metabolites of the PCBs have even greater estrogenic activity than most of the parent PCBs. Since the great majority of PCBs are not AhR activators, the net activity of most PCB mixtures is estrogenic. This variation in action of different PCB congeners is particularly important in developing an understanding of the relationship between exposure to PCBs and risk of breast cancer. Estrogen is by far the best-documented risk factor for breast cancer (Colditz et al., 1995). Thus exposure to AhR-activating PCBs might be expected to be protective from breast cancer on the basis of induction of P450s that degrade estrogen, whereas exposure to the estrogenic congeners might be expected to promote risk. Other categories of PCBs include those with particular persistence, which is characteristic of those congeners with higher degrees of chlorination, especially of the meta and para positions.

It is important to recognize that each individual PCB congener may have multiple sites of action in biological systems, mediated by binding to very different receptor sites or targets. Furthermore, different individual PCB congeners may have the same action, but do so via completely independent mechanisms.

It has usually been assumed that ingestion was the primary route of exposure to PCBs (ATSDR, 2000; IOM, 2003). PCBs are fat soluble, and bioaccumulative. Fish are an especially important route, especially fish from contaminated fresh waters (ATSDR, 2000). However,

inhalation and dermal absorption are also important routes. Animal studies have shown that inhalation of vapor phase PCBs is actually a more efficient route of exposure than ingestion, and that inhaled vapor phase PCBs can bioaccumulate and cause pathological changes (Casey et al., 1999). Vapor phase PCBs are significantly elevated near to PCB-contaminated hazardous waste sites (Chiarenzelli et al., 2000; Hermanson et al., 2003), and our previous investigations have provided strong evidence that inhalation is an important route of exposure (DeCaprio et al, 2005; Fitzgerald et al., 2006) and a cause of health effects among individuals who live near to such contaminated sites (Baibergenova et al., 2003; Kudyakov et al., 2004; Seergev and Carpenter, 2005; Shcherbatykh et al., 2005; Huang et al., 2006). Liebl et al. (2004) have also demonstrated accumulation of lower chlorinated PCB congeners in humans as a result of breathing contaminated indoor air. Because PCBs are lipophilic substances, they are easily absorbed through the skin, a route of exposure that is of particular importance in occupational settings where direct dermal contact occurs with PCBs. In occupational situations exposure is usually a combination of inhalation and dermal absorption (Mallin et al., 2004). I have recently reported that a husband and wife team, related only by marriage, were employed at a plant that was removing waste oils from old transformers and capacitors (Carpenter, 2015). Both were instructed to smell the oils to determine whether or not they contained significant concentrations of PCBs. Both developed thyroid cancer and malignant melanoma, the cancer most strongly associated with PCB exposure. The husband, a non-smoker, also developed primary lung cancer which metastasized to his brain and killed him. These observation indicate strongly that inhalation of PCBs can cause cancer.

PCBs are usually reported as wet weight concentrations, although it may be preferable to report the results as lipid-adjusted values, since all of the PCBs are found in the lipid fraction. In general lipid-adjusted PCB values are 200-250 times larger than wet weight values. Reporting PCB levels after lipid adjustment is especially important if the subject is not fasting, although some (Schisterman et al., 2005) have cautioned that lipid-adjustment may introduce bias. Studies from CDC have shown that there is no difference between fasting and non-fasting results provided that lipid adjustment is made (Phillips et al., 1989). The half-life of PCBs in the human body is long, but varies with the congener in that many of the lower chlorinated congeners are more rapidly metabolized, whereas many of the highly chlorinated congeners persist even for decades. The rates of removal are also a function of body burden. Wolff et al. (1992) reported a half-life of serum PCBs of 3-5 years for individuals with high serum PCBs but of 13-17 years for those with lower values. I usually consider an average half life to be 10 years, but at the same time recognize that the half-life varies greatly among different congeners.

DETERMINATION OF DISEASE CAUSATION FROM EXPOSURE TO PCBs:

The evidence for causality for human disease resulting from exposure to an environmental contaminant is usually evaluated by consideration of the factors identified by Hill (Hill, 1965). These are a) strength of association, b) consistency of association. c) specificity, d) temporality, e) dose-response relationship, f) plausibility, g) coherence, h) experimental evidence and i) analogy. These are appropriate standards for evaluating whether or not there is a relationship between exposure and disease, and together consideration of these factors leads to a general "weight of evidence". Hill did not imply that each of these factors must be met in every