Respondent's
Exhibit N

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Vincent J. Matanoski
Assistant Director
Torts Branch, Civil Division
U.S. Department of Justice
P.O. Box 146
Benjamin Franklin Station
Washington, D.C. 20044-0146

Re: Cedillo v. HHS, Fed. Cl. No. 98-916V

Dear Mr. Matanoski:

As a description of my background and qualifications, I received a BA from Southern Methodist University in Biology (1972) and an MD from The University of Texas Medical Branch at Galveston (1977). I completed a residency in Psychiatry and a fellowship in Child and Adolescent Psychiatry at the University of Chicago from 1981-1986. I was chief resident and chief fellow. I completed a post-doctoral research fellowship from 1986-1987 in which I continued research in the neurochemistry of autism that was begun during my fellowship. I was appointed an Assistant Professor in 1987 and rose to the rank of Professor at the University of Chicago by 2000. Since, 2005, I have been Visiting Professor of Psychiatry and now Professor of Psychiatry at the University of Illinois at Chicago, where I am the Visiting Director of Autism and Genetics. Since 1993, my laboratory has been involved in the genetic study of autism, as well as continuing to be engaged in studies of neurochemistry and clinical pharmacology of autism. I have been engaged in the clinical assessment and treatment of children, adolescents and adults with autism for over 20 years. I am currently serving as co-chair of the Autism and Intellectual Disability Committee of the American Academy of Child and Adolescent Psychiatry. The above information and additional information as well as my publications are provided in my CV.

Autism is a "strongly genetic disorder" (Bailey et al., 1995). The evidence in support of this statement comes from the relative recurrence risk to different family members. A disorder with almost complete genetic and almost no environmental influence has the following pattern in terms of risk to relatives. Identical twins share 100% of their DNA, fraternal (non-identical) twins share 50% of their DNA, and siblings (brothers and sisters) share 50% of their DNA. If a child has disorder X, the risk of the identical twin having disorder X is much higher than the risk

of the fraternal (non-identical) twin having disorder X. Moreover, the risk to the fraternal twin would be no more than the risk to siblings.

In autistic disorder (as defined narrowly by research criteria), the risk to identical twins of a child with autistic disorder is 60% or higher (the risk is over 90% for autism spectrum disorder in the identical twin). The recurrence risk for fraternal twins (Bailey et al., 1995, Tab D) is no more than the 4.5% recurrence risk for siblings (Jorde et al., 1991) (Veenstra-VanderWeele and Cook, 2004). This is the distinctive pattern of a disorder with strong genetic influence and relatively little environmental influence.

Fraternal twin pairs share environment more strongly than sibling pairs. Therefore, if there was significant environmental influence or significant environmental interaction with genetic factors, the risk of a fraternal twin would be higher than that for a sibling. This is not the case in autism where the risk to fraternal twins is no more than the risk to siblings.

Citation was made in support of a gene-environment interaction given these data by Kinsbourne with reference to a paper by Purcell (2002). Review of the cited paper shows that it is a simulation paper that does not address the genetic or environmental influence of autism. The authors did not mention autism in the paper. The paper addresses a situation, different from autism, in which a disorder is assumed to be 50% genetic and 50% environmental. The simulation was designed as a tool and not to address any aspect of the genetics or genetic-environmental interaction in autism or a similar disorder. To restate, this paper is not relevant to autism, which has over 90% heritability (genetic influence).

For purposes of explanation, the simplest description of gene expression is that in any cell in the body at any time, each gene is either turned off or turned on (expressed). One analogy might be looking down a long city street and seeing that the lights are either red or green (the yellow lights indicate genes that are only partially turned on). Therefore, some genes are being given stop signals and others are being given green signals to go (= turn on = be expressed). In the case of some diseases, a "faulty" gene only causes a problem at the time it is turned on.

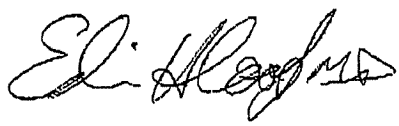
Given this background, it is important to note that one of the autism spectrum disorders, Rett disorder, is due to mutation in the MECP2 gene. Although the mutations are present at birth, the onset occurs between 6 and 24 months after an initial period of normal development. The regression is related to the expression of this gene at that time in development without an environmental trigger.

In other words, a mutation of the MECP2 gene in Rett disorder is present from conception. However, the effect of this mutation does not manifest itself in clinical presentation until the time that neurons are maturing when the expression of normal MECP2 is critical. This time corresponds to the time of regression in Rett disorder (and corresponds in time to most cases of regressive autism – between 6 and 24 months). The regression in Rett disorder at this time includes regression in communication and social skills, similar to regressive autism (Kim and Cook, 2000). Although it often includes a regression in purposeful use of the hands, this is not

always the case, which is the main reason that Rett disorder must be considered before diagnosis of autistic disorder in young girls with autism spectrum disorder.

In conclusion, it is important to note that genetic research does not provide support for a specific environmental factor in autism.

Sincerely,



Edwin H. Cook, Jr., M.D.
Professor of Psychiatry

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