Respondent's Exhibit W

University of Michigan
Autism and Communication
Disorders Center

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Department of Justice

Report of Catherine Lord, Ph.D., ABPP

Thimerosal Vaccine Litigation

I am a clinical psychologist and a professor of psychology, psychiatry and pediatrics at the University of Michigan. I am the Director of the University of Michigan Autism and Communication Disorders Center (UMACC). I am licensed as a psychologist in Michigan and Illinois and board certified in clinical psychology by the American Board of Professional Psychology (ABPP) and National Register of Health Service Providers in Psychology. I am one of four scientists who make up the Strategic Planning Committee for Autism Research for the National Institutes of Health and am on the planning committee for autism and related diagnoses for the American Psychiatric Association's Diagnostic and Statistical Manual V. I chaired a National Research Council committee on the Effectiveness of Early Intervention in Autism and am currently on the American Psychological Association Council for Division 53, which is the division that represents evidence-based practice with children and adolescents.

I received a B.A. summa cum laude from UCLA, where I worked with Dr. Ivar Lovaas doing behavioral treatment of children with autism. I then received a Ph.D. in psychology from Harvard University where I specialized in language and early social development. I did a postdoctoral internship in clinical psychology at University of North Carolina, Chapel Hill, working with the TEACCH (Treatment and Education of Children, Adolescents and Adults with Autism and Communication Handicaps) program, a statewide program for autism. I have had academic positions at the University of Minnesota, University of Alberta, University of North Carolina, and University of Chicago, before coming to Michigan in 2001. I also was a visiting scientist and then visiting professor at the Institute of Psychiatry in London and a visiting professor at Harvard Medical School/Boston Children's Hospital.

My primary research interests are the longitudinal follow-up of children with autism and quantifying the behavioral deficits associated with autism through the development of

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diagnostic instruments. This work has been published in major psychology and psychiatry journals including the Archives of General Psychiatry, the Journal of Consulting and Clinical Psychology, Biological Psychiatry, the Journal of Child Psychology and Psychiatry and Neuron. I am currently on the editorial board for Autism Research, Child Development, the Journal of Child Psychology and Psychiatry, the American Journal of Mental Retardation, and the Journal of Abnormal Child Psychology. I was an associate editor for the Journal of Autism and Developmental Disorders. I served as a member of an NIH study section and as an ad hoc reviewer for many NIH grants, as well as for the Wellcome Trust, the Canadian and British Medical Research Councils, Autism Speaks and many other public and private foundations.

My group's research work has shown that diagnoses of autism, using standardized parent interviews and observation schedules, are reliable across experienced experts for children down to age 2, and that these diagnoses are very stable up to age 9. Changes in behaviors associated with autism over time are predictable according to children's language level, social deficits and the frequency and severity of their repetitive behaviors, as well as their parents' involvement in behavioral treatments. Our work has also included studies of very early development and regression, which I will outline in more detail below.

I am most well-known as the author (with collaborators) of standardized instruments for diagnosis of autism, including the Autism Diagnostic Interview-Revised (ADI-R: with Sir Michael Rutter and Ann LeCouteur) and the Autism Diagnostic Observation Schedule (ADOS: with Michael Rutter and other researchers from North Carolina and Michigan), as well as the Social Communication Questionnaire (with Professor Rutter) and the Early Screening for Autism Scale (ESAC) with Dr. Amy Wetherby. The ADI-R and ADOS have become the gold standard for autism research and are required for use in NIH-funded projects, as well as in major autism consortia around the world. They have been translated into more than 35 languages and have allowed collaborations across research groups within and across different countries.

In my position at University of Michigan, I supervise research projects regarding diagnosis and assessment of young and school age children (funded by the Department of Education, the Simons Foundation and the National Institute of Deafness and Communication Disorders), longitudinal follow-up of children from age 2 to 22 (funded by NIMH, NICHD and Autism Speaks), genetics of autism (funded by the Simons Foundation) and early intervention (funded by NIMH and Autism Speaks). I spend about 25% of my time in direct clinical work with children and adults with autism and their families, doing assessments, consultation to schools and other programs and short-term treatment. I also supervise graduate students in clinical work and research, teach graduate courses and direct the autism clinic, as well as serve on various university and departmental committees.

My career in the field of autism began in 1969 when I was an undergraduate at UCLA and thus has spanned nearly 40 years. In the more than 30 years in which I have been a licensed clinical psychologist, I would estimate that I have seen more than 4000 children and adults suspected of having an autism spectrum disorder (ASD), through either clinics or research, with more than two-thirds of these individuals meeting criteria for an ASD.

Regression in Autism Spectrum Disorders

I have been asked to comment about the scientific evidence concerning regression in autism spectrum disorders. Because most, but not all, of the research available is about children with narrow diagnoses of autism, but some involves children with the more broadly defined autism spectrum disorders, the terms autism, autism spectrum disorders and ASD will be used interchangeably below.

Regression in autism is the phenomenon in which children show losses of communication and/or social skills or behaviors, usually during the second year of life. This phenomenon was initially described in terms of a child with probable normal development who stopped talking for an extended period of time. It was referred to in Michael Rutter's papers in the 1960's, the first research to provide evidence that autism was a neurologically-based, rather than psychodynamically-based disorder (see Rutter & Lockyer, 1967). These accounts of regression were initially based on retrospective recall by parents, usually many years later, and though they referred to the phenomenon as a change from normal development to autism, there was no documentation of the normality of the child's early development.

A major advance in the last 10 years has been the recognition that the occurrence of a loss in skills or behavior does not necessarily imply that a child had completely normal development prior to that change. Thus, researchers have become aware, as described in more detail below, of the need to separate the documentation of a loss of skills or change in behavior from whether the child's progress preceding that change was truly normal (Luyster et al., 2005; Ozonoff et al., 2005). That is, because a child has lost skills, does not mean that the child had "normal development" prior to that time. In fact, in one study (Richler, et al., 2006), children who most clearly corresponded to definitions of a "regressive phenotype" had more early abnormalities than other children with ASD. Nevertheless, in much of the literature and parental reports, these two phenomena (loss and normality preceding loss) have often been confused.

There are several other developmental disorders that are characterized by the loss of skills (e.g., Rett syndrome, Landau-Kleffner Syndrome) or onset of psychiatric symptoms after a period of more normal development (e.g., adolescent onset of schizophrenia). However, what has been shown to be unique in autism is the particular pattern of loss of communication and social skills, without accompanying loss in motor or other skills, followed in many, but not all cases, by the return of language and communication with continued deficits in social skills. Numerous studies have now shown that this pattern, which has been reported in 20 – 40 percent of children with ASD is virtually unique to autism (Shinnar et al., 2001; Kurita, 1985; Hansen et al., 2008).

For years, although parents reported regressions, many scientists asked whether the parental reports were simply misstatements reflecting their own growing awareness of the discrepancy between their child's development and that of other children, rather than accurate reports of significant changes in developmental trajectory. There is now a wealth of evidence that regressions in autism do occur and that they follow a predictable pattern. This evidence comes from a number of sources which I describe below. Regressions are not concordant within families (e.g., siblings with autism do not typically both show regressions; Parr et al., 2002) and have not been found to be related to any etiological factor (as discussed in more detail below), including vaccinations. Causal accounts of autism spectrum disorders must be able to account for the phenomenon of regression.

In most early studies, regressions were defined by word loss. Our research and research by others showed that parents were most reliable over time and with each other when a regression was defined as a child spontaneously producing 3 or more meaningful words on a daily basis for at least a month followed by a period of at least a month when the child produced no meaningful words at all (Lord et al., 2004; Shinnar et al., 2001). Most children who lost words had acquired their first words at about 12 months, the same time as typical children, and significantly earlier than children with autism who did not show word losses. When parents of preschool children with autism were interviewed, the most common age at which regressions were noted to occur were 14 – 20 months (Lord et al., 2004; Luyster et al, 2005). Children who lost words were also noted to lose social skills at about the same time. Most parents reported that they realized their child had experienced a regression several months after the changes in behavior began to occur. Often they first sought help at an age associated with a milestone (e.g., 18 months, 2 years). These are often the numbers reported in medical records (Siperstein & Volkmar, 2004). About 75% of the children who had regressions began to speak again within the next year, but 25% of children with regressions did not produce meaningful words within several years (Richler et al., 2006). Analyses of the same parent interview in which parents had reported regressions, when it was administered again in later years, showed that parents "telescoped" dates, such that, the older the child was when the parent was interviewed, the later the date the parent reported the regression to occur.

Analyses of a larger and more detailed data set consisting of focused interviews about regression of all families from 10 NIH-funded research groups who had reported regression earlier found very similar results regarding age of regression (Luyster et al, 2005) and links between word loss and social changes. A group of children who showed the same social losses, but without word loss, were identified, suggesting that the core of autism regression is a decrease in social communication, with word loss as the most obvious but not necessarily the most important change. Other studies (Goldberg et al, 2007; Werner & Dawson, 2005; Hansen et al., 2008) had identified similar phenomena.

Our work found no associations between regression and social class or maternal education, gender or birth order, nor were there associations with seizures, prenatal or postnatal difficulties or early history of infections or frequent antibiotics (Richler et al., 2006). Children who had regressions had slightly lower verbal IQs in school age (Hansen et al., 2008). Additional work by Rogers and colleagues (2008) also found no differences in imitation skills between children with and without regressions. However, when considered altogether, there was no evidence of a distinct regressive phenotype. Most interesting was that, when parents were asked about the acquisition of different infant social and communication skills, a very high proportion of children showed evidence of deficits that preceded the regression (Luyster et al., 2005), suggesting that these children were not meeting normal social and/or communication milestones before the regression occurred.

Medical records were obtained for children in the study. There was no relation between timing of vaccinations and timing or occurrence of regression (Richler et al, 2006). This lack of relationship has also been reported in numerous epidemiological studies. No systematic research has found evidence of an association between autism spectrum disorders and thimerosal or specific vaccinations.

Studies looking at parent-collected videotapes of their children during infancy and parent retrospective reports showed a similar pattern of regression as described above (Werner & Dawson 2005). Most children whose parents reported regressions showed a clear loss of skills when videotapes before and after the time of regression were compared, but many of these children also failed to show normal social and communication milestones before this time. Almost all parents reported a gradual worsening. These authors reported a small late onset group of children for whom losses were only evident later in the second year or early in the third year of life.

New information about regressions is emerging as we speak from ongoing studies of very young (from birth or 6 – 12 months) children suspected of having autism or at high risk for autism because of sibling status. These studies are able to use observational methods as well as parent reports and videotapes to document changes in the first few years of life in children with autism. Preliminary results suggest that most children who later receive autism diagnoses are not distinguishable from typical children at 6 months, but have clear evidence of social and communication abnormality (recognizable in formal testing) by 12 months (Zwaigenbaum et al, 2005; Bryson et al., 2007). A significant number of these children show worsening in cognitive skills between 14 and 24 months (Landa, Garett-Mayer, 2006). A smaller subset of children show systematic worsening of social and communication skills over the same period (Lord et al., 2007). These changes were not associated with gender, maternal education, treatment or birth order.

Thus, gradual worsening of social and nonverbal communication skills is a general phenomenon in autism, which is particularly apparent in some children who acquire meaningful words relatively early and then stop talking for months and sometimes a year or longer. Explanations of the pathophysiology of ASD will need to take these phenomena into account. At this point, there is no clear evidence that the phenomenon of regression is linked to environmental factors or that children who experience this trajectory differ in etiology or in any other aspect of development from children with ASD who do not, except perhaps in the occurrence of this apparently autism-specific phenomenon.

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References

1. Bryson SE, Zwaigenbaum L, Brian J, Roberts W, Szatmari P, Rombough V, McDermott C. *A prospective case series of high-risk infants who developed autism*. J Autism Dev Disord. 2007 Jan; 37(1): 12-24. Epub 2007 Jan 9.

2. Fombonne E, Chakrabarti S. *No evidence for a new variant of measles-mumps-rubella-induced autism*. Pediatrics. 2001 Oct; 108(4): E58.

3. Goldberg WA, Osann K, Filipek PA, Laulhere T, Jarvis K, Modahl C, Flodman P, Spence MA. *Language and other regression: assessment and timing*. J Autism Dev Disord. 2003 Dec; 33(6): 607-16.

4. Goldberg WA, Thorsen KL, Osann K, Spence MA. *Use of Home Videotapes to Confirm Parental Reports of Regression in Autism*. J Autism Dev Disord. 2007 Dec 5; [Epub ahead of print].

5. Hansen RL, Ozonoff S, Krakowiak P, Angkustsiri K, Jones C, Deprey LJ, Le DN, Croen LA, Hertz-Picciotto I. *Regression in autism: prevalence and associated factors in the CHARGE Study*. Ambul Pediatr. 2008 Jan-Feb; 8(1): 25-31.

6. Kurita H. *Infantile autism with speech loss before the age of thirty months*. J Am Acad Child Psychiatry. 1985 Mar; 24(2): 191-6.

7. Landa R, Garrett-Mayer E. *Development in infants with autism spectrum disorders: a prospective study*. J Child Psychol Psychiatry. 2006 Jun; 47(6): 629-38.

8. Lord C, Shulman C, DiLavore P. *Regression and word loss in autistic spectrum disorders*. J Child Psychol Psychiatry. 2004 Jul; 45(5): 936-55.

9. Lord C, Coffing M, Luyster R, Petrak R, Richler J. *Searching for the forest in the trees: individual trajectories in toddlers who may have autism*. Presented at the biennial meeting of the Society for Research on Child Development, Boston, MA. Mar 2007.

10. Luyster R, Richler J, Risi S, Hsu WL, Dawson G, Bernier R, Dunn M, Hepburn S, Hyman SL, McMahon WM, Goudie-Nice J, Minshew N, Rogers S, Sigman M, Spence MA, Goldberg WA, Tager-Flusberg H, Volkmar FR, Lord C. *Early regression in social communication in autism spectrum disorders: a CPEA Study*. Dev Neuropsychol. 2005; 27(3): 311-36.

11. Ozonoff S, Williams BJ, Landa R. *Parental report of the early development of children with regressive autism: the delays-plus-regression phenotype*. Autism. 2005 Dec; 9(5): 461-86.

12. Parr J, Baird G, Le Couteur A, Rutter M, Bailey A, & The International Molecular Genetic Study of Autism Consortium (IMGSAC). *Phenotypic characteristics of autistic regression in an international multiplex sample.* Poster Session at the World Congress on Psychiatric Genetics, Brussels, Belgium (2002)(Abstract).

13. Richler J, Luyster R, Risi S, Hsu WL, Dawson G, Bernier R, Dunn M, Hepburn S, Hyman SL, McMahon WM, Goudie-Nice J, Minshew N, Rogers S, Sigman M, Spence MA, Goldberg WA, Tager-Flusberg H, Volkmar FR, Lord C. *Is there a 'regressive phenotype' of Autism Spectrum Disorder associated with the measles-mumps-rubella vaccine? A CPEA Study*. J Autism Dev Disord. 2006 Apr; 36(3): 299-316.

14. Rogers S, Young GS, Cook I, Giolzetti A, Ozonoff S. *Deferred and immediate imitation in regressive and early onset autism*. J Child Psychol Psychiatry 2008 Jan 21 (e-published).

15. Rutter M, Lockyer L. *A five to fifteen year follow-up study of infantile psychosis. I. Description of sample*. Br J Psychiatry. 1967 Nov; 113(504): 1169-82.

16. Shinnar S, Rapin I, Arnold S, Tuchman RF, Shulman L, Ballaban-Gil K, Maw M, Deuel RK, Volkmar FR. *Language regression in childhood*. Pediatr Neurol. 2001 Mar; 24(3): 183-9.

17. Siperstein R, Volkmar F. *Brief report: parental reporting of regression in children with pervasive developmental disorders*. J Autism Dev Disord. 2004 Dec; 34(6): 731-4.

18. Werner E, Dawson G. *Validation of the phenomenon of autistic regression using home videotapes*. Arch Gen Psychiatry. 2005 Aug; 62(8): 889-95.

19. Zwaigenbaum L, Bryson S, Rogers T, Roberts W, Brian J, Szatmari P. *Behavioral manifestations of autism in the first year of life*. Int J Dev Neurosci. 2005 Apr-May; 23(2-3): 143-52.