Respondent's Exhibit OO

HEALTH SYSTEM *Department of Neurology*

ROBERT S. RUST, M.A., M.D.
THOMAS E. WORRELL, JR. PROFESSOR OF EPILEPTOLOGY AND NEUROLOGY
PROFESSOR OF PEDIATRICS
CLINICAL AND TRAINING DIRECTOR, CHILD NEUROLOGY
CO-DIRECTOR, F.E.DREIFUSS COMPREHENSIVE EPILEPSY AND CHILD NEUROLOGY CLINICS
PO Box 800394
CHARLOTTESVILLE VA 22908

U.S. Department of Justice
P.O. Box 146
Benjamin Franklin Station
Washington, DC 20044

William Mead (hereafter "WM")

The petitioners allege that WM developed autism as a result of receiving thimerosal-containing immunizations. I have already discussed this theory in the context of JK and [redacted] (see my report of March 14, 2008). Similar to my discussion of the other two children presented under this theory, I will organize my comments about WM with reference to the report prepared in this case by Dr. Elizabeth Mumper (WM Exh. 16).

WM's medical history prior to his diagnosis of autistic disorder can be summarized as follows: WM was born on May 5, 1998. During his first four months of life, the records document an enlarged head circumference (from the 50th to the 95th percentile). WM Exh. 3 at 34. This pattern of increased head growth rates during infancy is unusual in children. It is important to consider underlying diagnoses that entail the intracranial accumulation of blood or cerebrospinal fluid, such as hydrocephalus or intracranial hemorrhage. WM did not have these disorders, however. Thus, it is most likely that the accelerated rate of increase in his head circumference was the result of accelerated brain growth. Among the various serious conditions that are associated with such a pattern of brain growth are Alexander's disease, Tay-Sachs disease, Canavan disease, and Rett syndrome. WM has none of these none of these conditions. He does, however, have autistic disorder (DSM-IV 299.0), which may also exhibit this pattern of head growth. Indeed, the original publications by Kanner (1943)[1] that first defined the condition, noted particularly an association between large heads and autism. Recent

[1]Kanner L. Autistic disturbances of affective contact. Nervous Child, 1943;2:217-250

University of Virginia Health System, School of Medicine
PO Box 800394, Charlottesville Virginia 22908-0394
TEL: (434) 924-5538 FAX: (434) 982-1726 E-MAIL: rsr6f@virginia.edu

publications have re-emphasized this feature, which may be the earliest indicator of the development of autistic disorder, preceding not only the behavioral manifestations (including regressive ones) that permit autism to be diagnosed, but also the post-natal environmental influences alleged in this and other cases to be "causes" of autism[2]. It is likely that this pattern of head growth represented a manifestation of WM's inevitable ensuing development of autistic disorder, a manifestation preceding all of the other influences alleged by the petitioners to have "caused" his autism.

WM had 6 courses of antibiotics in 1998-1999, primarily for reactive airway disease, bronchitic wheezing, and ear infections. WM Exhs. 1 at 11, 12, 15, 27, 30; 2 at 1-3. This is not an abnormally large number of such processes, particularly in a child with reactive airway disease. In most instances, these events are considered likely to have been provoked by community acquired viral infection, and are certainly not indicative of immunodeficiency. WM experienced the usual number of illnesses during those early years of life, including the slightly enhanced vulnerability experienced by children with evidence for atopy, such as wheezing.[3] WM's pattern of illness, including improvement in the third year of life, is quite typical in normal children with or without atopy. There is no evidence to support Dr. Mumper's statement that this improvement was the result of "biomedical interventions undertaken as a result of his autism diagnosis." WM Exh. 16 at 2. It is important not only that WM's course was typical of normal children; it is also important to stress that Dr. Mumper's comment, without support in reliable medical literature, not only implies that these illnesses represent a form of vulnerability to the development of autism, but that the "treatments" provided for autism improved the health of WM's respiratory system. The entire ungainly apparatus of theories assembled to support the views in Dr. Mumper's report have no better example of unsupported circular reasoning than this.

Dr. Mumper's statement that biomedical interventions for WM's autism improved his airway illnesses violates the following aspects of generally accepted medicine and science:

1) The statement appears to imply that there is something unusual about the number and types of airway illnesses WM experienced during his early childhood. This is incorrect. The number and type of illnesses were, in fact, within the normal range;

2) The statement appears to imply that the bouts of illness recurred until the "biomedical interventions" were introduced and began to take effect. Once again, this is simply incorrect because similar improvements occur in the natural history of such illnesses in normal children;

---

[2]Courchesne E. et al., JAMA 2003; 290:337-344

[3]Celedon et al., Pediatrics 1999; 104:495-500

3) The statement appears to allege that WM's illnesses represent a form of immunodeficiency that perhaps has something to do with his vulnerability to thimerosal, or is the result of thimerosal. If this is, in fact, petitioners' argument, it is made without reference to any information found in credible medical literature, and it is so loosely constructed that it is difficult to follow;

4) There is no supportive information from credible, peer-reviewed medical literature to provide any understanding of the basis upon which thimerosal might be implicated in infectious conditions of the airway;

5) There is no supportive information to provide any understanding as to how the "biomedical interventions" provided to WM may have in any understandable way influenced the course of his airway disease, which was quite normal in its evolution.

Given the known prevalence in early childhood of the illnesses experienced by WM, the antibiotics administered to him were not exceptional when compared to children of the same age who did not develop autism.

Dr. Mumper's statement that "chronic diarrhea" was present for "over a year" (WM Exh. 16 at 2) is not supported by the medical records. The record of 5/15/00 mentions diarrhea (WM Exh. 1 at 22), and the note of 7/11/00, when WM was 26 months old, says that diarrhea had been present on and off for 6 months (WM Exh. 1 at 21). According to the medical records, then, these intermittent (not continuous) bouts of diarrhea started at about 20 months of age. WM's diarrhea did not begin in temporal proximity to WM's receipt of MMR and varivax vaccinations, as implied by Dr. Mumper (WM Exh. 16 at 2). The office note of 5/15/00 states that WM had no words and, as is so characteristic of autism, he was not pointing to things. WM Exh. 1 at 22. If one then considers that WM was manifesting symptoms of autism at 24 months of age, the diarrhea had only been manifested as a few intermittent bouts over four months prior to demonstrating those autistic features. And if one accepts Dr. Mumper's statement that "social withdrawal, toe walking, twirling. . ." emerged at "15-18 months" (WM Exh. 16 at 2), then WM's autism preceded the interval during which bouts of intermittent diarrhea occurred.

Bouts of diarrhea are common in children during the second year of life, and sometimes occur in the wake of treatment with antibiotics. In my experience, however, there is the additional and important consideration with regard to the bowel habits of children with autism: the frequency with which stool retention is found to be the cause of recurrent diarrhea as the result of acquired megacolon and overflow diarrhea (see my report of March 14, 2008 at 3, 6-7, 10-11).

Bouts of noninvasive candidal infection manifested by WM are not uncommon in children. In fact, such infections become recurrent in at least 2-4% of children. They were increasingly common in the late 1990s in association, it is thought, with use of antibiotics for treatment of viral respiratory illnesses. They were and are more common in children treated with antibiotics and with corticosteroids for airway illnesses. This familiar condition is usually not indicative of immunodeficiency. The number of candidal infections WM experienced is not out of the ordinary for children, the overwhelming majority of whom do not develop autism.

Dr. Mumper's assertion that there are "clearly documented improvements after interventions designed to treat underlying medical problems, many of them associated with mercury toxicity" (WM Exh. 16 at 2) is a vague and sweeping generalization apparently intended to take the place of the usual sequence of medical and scientific explication. WM's medical records do not support the occurrence of any "clearly documented improvements" (whatever may be meant by that statement) after "interventions designed to treat underlying medical problems. . ." The last clause in that point fails to hold up against scrutiny with reference to credible, peer-reviewed medical literature. Dr. Mumper's allegation that WM experienced "medical problems compatible with mercury toxicity" is, within reasonable medical and scientific certainty, unproven and based upon complex hypotheses that fall well outside the bounds of accepted medical science. Please see the detailed discussion in my prior reports regarding JK and [redacted] cases as to why Dr. Mumper's opinion is medically incorrect (see my report of March 14, 2008 at 11, 16).

Dr. Mumper's statements regarding WM's laboratory findings (WM Exh. 16 at 2 at points #11-13) suffer from the same deficiencies with regard to scientific evidence, reliable laboratory data, or validation within the available medical records as have been reviewed in detail in the JK and [redacted] reports (see my report of March 14, 2008 at 7, 8, 15).

Dr. Mumper's statement that there is an "absence of documented chromosomal abnormalities or dysmorphic features to suggest a classic genetic cause for [WM's] autism" (WM Exh. 16 at 2) is uninformative. Such a statement could be made about the majority of boys who develop autistic disorder or, indeed, about more than 85% of children who manifest mental retardation or cerebral palsy. However, insofar as assigning comparative value to medical hypotheses, there is far more evidence and reason to believe that autistic disorder is the result of genetic determination rather than receipt of thimerosal.

The genetic determination of autism is supported by the developmental nature of the disorder. The pathology seen in post-natal mercury toxicity is not developmental, it is destructive. The appearance of that injury pathologically is not only ***different*** from that of autistic disorder (or Rett syndrome for that matter), it is ***remarkably different*** with virtually no significant pathological overlap (see my report of March 14, 2008 at 3, 4, 13). The same is true of the comparison of clinical manifestations of autistic disorder as

compared to post-natal mercury-related injury to the nervous system. The differences are diametrically and overwhelmingly different.

In her report on WM, Dr. Mumper voiced her disagreement with the American Academy of Pediatrics's practice parameter that emphasizes the importance of not withholding vaccinations during minor illnesses that occur during a child's first few years of life. WM Exh. 16 at 3. Practice parameters are the result of careful consideration by widely-accepted experts of information that is found in peer-reviewed medical literature. This information is carefully weighed by leading experts who assign greater or lesser merit to that information based upon study design, perceived flaws in studies, size of studies, and other factors. Great care is taken for the very sound reason that opinion is often a far more precarious perch from which to decide practice issues than is the application of close scrutiny to the available science. My own opinion would strongly endorse the practice parameter and would not be swayed by the unreported experience of a single clinician.

The statements that comprise the bulk of the consideration of WM's medical records reiterate those made in two prior summaries by Dr. Mumper for JK and [redacted], for which I have provided my opinions (see my report of March 14, 2008). These include the points made in the section prefaced by the statement "In my best medical judgment. . ." (WM Exh. 16 at 3). Additional points made in this section of Dr. Mumper's report include unproven assertions for which the paucity of supportive data in peer-reviewed medical and scientific literature is equally striking. I have considered most of these points in my earlier reports. These statements are not only unproven, but are also scientifically ungainly, and many of these conclusions are without any substantial support when considered in reference to WM's medical records.

There is no reliable information upon which Dr. Mumper can base the assertion that thimerosal, or for that matter, mercury in general, provokes or worsens "allergy symptoms or asthma flares." WM Exh. 16 at 4. It is much more likely that WM's vulnerability to asthma and allergies is genetic and entirely uninfluenced by thimerosal exposure.

Dr. Mumper's statement that a "threshold effect" was reached where WM "was not able to compensate for the toxic load and developed health consequences which affected his growth" (WM Exh. 16 at 4) is an almost incomprehensible point for which no support from scientific or medical literature is provided.

In the JK and [redacted] cases, I have already reviewed Dr. Mumper's "analysis. . . in relation to the literature" (see my report of March 14, 2008 at 5). The validation of these extraordinary assertions would require carefully supporting such arguments with data derived from credible, peer-reviewed medical literature and then examined for their relevance to the present case. Citations that are made to mainstream medical studies are distorted, as I have discussed in prior report (see my report of March 14, 2008 at 5, 18).

Thus it is particularly important to define what is meant by toxicity, for known mercury toxicity is not the same as the toxicity asserted in Dr. Mumper's reports, either clinically or pathologically. Nor do recommendations concerning levels of mercury thought to represent a possible threat of toxicity amount to proof of toxicity. Such levels are established with exceeding care not to represent levels at which all individuals become intoxicated, but to make sure that no individual develops toxicity.

The section beginning "Laboratory evidence of impairments" (WM Exh. 16 at 5) contains the following misleading assertions:

1) The question as to the amount of zinc required to achieve clearance of metals is the subject of abundant, and often difficult to interpret, literature concerning copper excretion in Wilson disease, as well as in lead poisoning. The most credible information suggests that zinc may be beneficial in enhancing EDTA chelation of these toxic metals. However, there is little reliable information concerning the role that zinc may have in alleged microtoxicity, or in alleged long term persistence of ethyl mercury in tissues after early childhood immunization. Low zinc levels can be caused by inadequate supply, or by utilization, among other explanations. Dr. Mumper's assertion that low zinc levels are evidence of the body's attempt to excrete mercury (WM Exh. 16 at 5) is one that would require careful support drawn from the available peer-reviewed medical literature, and with specific pertinence to the alleged microintoxicatory effects of tiny quantities of ethyl mercury. I am not aware of such supportive information.

2) Dr. Mumper's assertion that WM's low levels of amino acids, as noted in a Massachusetts General Hospital laboratory report (WM Exh. 13 at 29-30), is evidence of mercury toxicity (WM Exh. 16 at 5) is not in keeping with the manner in which such laboratory results are normally interpreted.

3) The problems with Dr. Mumper's hypothesis of mercury metabolism in humans has been addressed in reference to JK and [redacted]. See my report of March 14, 2008 at 3-5, 9, 10, 13-14.

4) Indirect measurements of amino acids in body fluids, of the sort obtained by Metametrix laboratory, are not at all reliable methods of determining the cause or indeed the presence of intracellular abnormalities of energy metabolism. (WM Exh. 16 at 5; WM Exh. 15 at 79-80.) Metametrix, in particular, must be considered with reference to its history of lawsuits for nonstandard test methods, alleged fraudulent assertion of theories of medicine and treatment, as well as negligence and racketeering. Even without this extraordinary information, the method of inferring intracellular chemical activities by the fluids sampled is rejected on its own lack of merits.

5) As I noted in the JK and [redacted] cases, "intestinal dysbiosis" is a discredited theory that is not accepted in mainstream medicine (see my report of March 14, 2008 at 7, 10-11). The concept, and its application in this case, are meaningless.

6) William's levels of Vitamin A, which were reported as slightly below the lab's normal reference range (WM Exh. 15 at 56), are not known to be associated with any neurologic disease or immunological dysfunction, despite Dr. Mumper's implication (WM Exh. 16 at 5).

7) It is unknown whether WM's low levels of "essential elements," as alleged by Dr. Mumper (WM Exh. 16 at 5), are at all meaningful in this context, or with regard to the alleged hypothesis of mercury toxicity. As the results referenced are from Metametrix Laboratory (WM Exh. 5 at 34), I am doubtful that the proffered results represent reliable data.

8) All of the remaining points in this section are either questionable upon a theoretical basis or questionable on a clinical basis with regard to WM. For example, there is no evidence in the medical records that WM has impaired "ability to fight infections" (WM Exh. 16 at 5). The record shows the normal array of childhood viral illnesses, and nothing more.

Reference to the complex issues involving T helper cell regulation (WM Exh. 16 at 6) represents a particularly egregious and obvious lack of understanding of this aspect of immune function. The citation of teeth grinding and other clinical behaviors as evidence of mercury intoxication (WM Exh. 16 at 6) is without any support whatsoever in credible medical literature. Such behaviors are not manifestations of known cases of mercury intoxication, with the exception of loss of developmental milestones. The loss of developmental milestones is a very important manifestation of methyl mercury intoxication, but the pattern of loss is extraordinarily different from that seen in autistic disorder (see my report of March 14, 2008). The most striking losses in development in mercury intoxication involve motor function, something that is strikingly preserved in autistic disorder.

The records of Dr. Green (WM Exhs. 5; 15) do not provide any convincing evidence of a beneficial effect of chelation therapy as a treatment of WM's autism. Many patients have been subjected to this form of treatment upon unsubstantiated grounds. No carefully controlled trials have established any benefit of chelation therapy in the treatment of autism, and such therapy carries possible risk, both from neglect of treatments that have established benefits, and toxicities related to the chelation itself. While practitioners of chelation, with their own and often poorly regulated laboratories, have secured testimonials concerning benefit from patients and their families, subjective attestations are not the kind of proof required by science. Even in mainstream medicine, we are well-aware that some of the treatments we provide have as much or more placebo effect as a biochemical effect. Despite the expense and risks of such treatments, those of

us who practice in the bounds of accepted scientific medicine note little, if any, benefit to children in whom we know are undergoing chelation therapies. This set of observations excludes instances where chelation has a proven benefit, such as Wilson disease. The alleged microtoxicity of thimerosal is not among the conditions in which this approach has been shown to have a proven benefit.

All of the remaining points in Dr. Mumper's report have been addressed in my prior report, and partake of oversimplification; lack of substantial support in the credible medical literature; utilization of a limited number of non-mainstream laboratories; and other flaws that render the clumsy apparatus of hypotheses borrowed and piled one on top of another to attempt to prove an association between autistic disorder and thimerosal. This entire apparatus fails to be proven; fails to be validated by experience; and fails to make sense.

Conclusion

In my education, training, review of the literature, and nearly thirty years of experience, I strongly disagree with Dr. Mumper's opinion that thimerosal in WM's vaccines contributed in any way to his development of autism.

March 19, 2008
Date

Robert S. Rust, M.D.