In the United States Court of Federal Claims

No. 03-654V
Filed: July 24, 2009

ROLF and ANGELA HAZLEHURST, parents of WILLIAM YATES HAZLEHURST,	)	Vaccine Act—Omnibus Autism Proceeding: In a proceeding to determine the relationship, if any, between the measles, mumps, and rubella vaccine and the development of regressive autism, the special master did not err in relying on evidence generated in another litigation and offered on the eve of hearing, failing to consider evidence that would not have altered her conclusion, or declining to rule whether regressive autism is a distinct phenotype from classic autism.
Petitioners,	)	
v.	)	
SECRETARY, DEPARTMENT OF HEALTH & HUMAN SERVICES,	)	
Respondent.	)	

Curtis R. Webb, Twin Falls, ID, attorney of record for petitioners.

Linda S. Renzi and Lynn E. Ricciardella, with whom were Assistant Attorney General Tony West, Director Timothy P. Garren, Acting Deputy Director Catharine E. Reeves, and Assistant Director Gabrielle M. Fielding, Torts Branch, Civil Division, U.S. Department of Justice, Washington, DC, for respondent.

OPINION

WIESE, Judge.

Petitioners, Rolf and Angela Hazlehurst, seek review of a decision entered by the special master on February 12, 2009, denying their son, William Yates Hazlehurst, compensation under the National Childhood Vaccine Injury Act of 1986 ("the Vaccine Act"), 42 U.S.C. §§ 300aa-1 to -34 (2006), for a neurological injury, identified as regressive autism, allegedly caused by the administration of the measles, mumps, and rubella ("MMR") vaccine. Petitioners contend that the special master improperly based her decision on evidence that should have been excluded, disregarded other evidence that should have been considered, and declined to decide an issue of fact necessary for a reasonable resolution of their claim. The matter has

been briefed by the parties and the court heard oral argument on June 11, 2009. For the reasons set forth below, petitioners' motion for review is denied.

BACKGROUND

This case is the second of three test cases heard by the Office of Special Masters as part of the Omnibus Autism Proceeding ("the omnibus proceeding"), a global effort to determine the relationship, if any, between the MMR vaccine, vaccines containing thimerosal, and autism (or autism spectrum disorders).[1] In order to address the approximately 5,000 autism claims pending before the court, a panel of attorneys representing the various petitioners, referred to as the Petitioners' Steering Committee ("the steering committee"), identified three general theories of causation: (1) that vaccines containing thimerosal, when combined with the MMR vaccine, can cause autism; (2) that vaccines containing thimerosal alone can cause autism; and (3) that the MMR vaccine alone can cause autism. The steering committee then selected three test cases that fell within the same general causation theory, namely that vaccines containing thimerosal acting in combination with the MMR vaccine can cause or contribute to the development of autism. These test cases—Cedillo v. Secretary, Dep't of Health & Human Servs., No. 98-916V, Hazlehurst v. Secretary, Dep't of Health & Human Servs., No. 03-654V (the instant case), and Snyder v. Secretary, Dep't of Health & Human Servs., No. 01-162V—were in turn assigned to three different special masters for resolution.

A hearing was held in the first case, Cedillo, in June 2007. At the hearing, petitioners presented testimony from six expert witnesses, including experts in toxicology, immunology, molecular biology, virology, neurology, and gastroenterology. Respondent countered with evidence from nine expert witnesses, in the subject areas addressed by petitioners as well as pediatric psychiatry and epidemiology. By agreement of the parties, the record in the present case includes all of the general causation evidence admitted in the Cedillo and Snyder hearings.[2]

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[1] A description of the procedural history of the omnibus proceeding, including the creation of the Petitioners' Steering Committee, can be found in Hazlehurst v. Secretary, Dep't of Health & Human Servs., No. 03-654V, 2009 WL 332306, at *1–3 (Fed. Cl. Feb. 12, 2009). Although petitioners in the instant suit agreed to have their claim serve as a test case, petitioners' counsel was not a member of the Petitioners' Steering Committee.

[2] Hearings were conducted in Hazlehurst and Snyder on October 15–18, 2007, and November 5–9, 2007, respectively. As the special master explained in her decision, the parties in each of the test cases presented general causation evidence (continued...)

The petition in the instant case was filed on March 26, 2003. According to the record, William Yates Hazlehurst was born on February 11, 2000. During the first year of his life, Yates received the standard childhood vaccinations, including up to 11 vaccines possibly containing thimerosal. On February 8, 2001, three days before his first birthday, Yates additionally received the MMR vaccine.

While the record indicates that Yates developed normally prior to receiving the MMR vaccine, in the month following the vaccination, Yates became, in the words of his family, "wild," "very hyperactive," and "out of control." By the summer of 2001, Yates had lost all meaningful speech and had developed an obsession with letters and numbers. Also during this period, Yates began to experience chronic diarrhea and abdominal pain.

Yates's developmental and gastrointestinal issues led petitioners to seek out a number of treatments over the next several years. In July 2002, after a series of evaluations for developmental and speech delays, Yates was diagnosed as demonstrating a significant number of behaviors consistent with autism. Two months later, in September 2002, Yates began treatment with Dr. Jean-Ronel Corbier, a pediatric neurologist, for that condition. Over the next several months, Yates additionally underwent an immunological evaluation and a colonoscopy. The results of both tests were normal.

In June 2007, petitioners filed an amended petition with this court alleging that Yates's MMR vaccination, or a combination of the MMR vaccination and the vaccines containing thimerosal that Yates had received during his first 12 months, caused him to develop regressive autism.[3] The special master summarized petitioners' theory as follows:

> [P]etitioners assert that the measles component of the MMR vaccine causes an immune dysfunction that impairs the vaccinee's ability to clear the measles virus. Unable to properly clear the measles virus

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[2](...continued)
(related to whether vaccines containing thimerosal in combination with the MMR vaccine could cause autism) and specific causation evidence (regarding whether the administered vaccines had caused the autistic condition of the child whose particular case was being heard). Hazlehurst, 2009 WL 332306, at *3.

[3] Petitioners define regressive autism as a condition characterized by the loss of previously acquired skills rather than by the failure to develop certain skills in the first instance. Whether regressive autism is a distinct category from classic autism is the subject of debate, however, and is the focus of Section III of the discussion below.

> from the body, the vaccinee experiences measles virus persistence which leads to chronic inflammation in the gastrointestinal system and, in turn, chronic inflammation in the brain. Petitioners argue that the inflammation in the brain causes neurological damage that manifests as autism.

Hazlehurst v. Secretary, Dep't of Health & Human Servs., No. 03-654V, 2009 WL 332306, at *86 (Fed. Cl. Feb. 12, 2009).

The special master convened a hearing in this case in October 2007. As noted above, both parties relied in part on the general causation evidence presented in the Cedillo hearing. In addition, petitioners offered the case-specific testimony of Dr. Corbier, Yates's pediatric neurologist, and respondent offered the testimony of Dr. Thomas T. MacDonald (a gastrointestinal immunologist), Dr. Christine McCusker (a pediatric immunologist), and Dr. Robert S. Rust (a pediatric neurologist).

During the hearing, Dr. Corbier testified that differences in the timing of the first appearance of the symptoms associated with autism suggest that there are differences in the underlying causes of autism. The earlier the onset of the symptoms, Dr. Corbier opined, the more likely that the cause of the autism is genetic, prenatal, or metabolic. In the case of regressive autism, however, Dr. Corbier testified that the causal factors are "very likely [to be] genetic influences and external environmental factors." Hazlehurst Tr. at 270A.

Dr. Corbier went on to note that studies have implicated the MMR vaccine as an environmental factor that can contribute to the development of regressive autism in children who fit within a particular clinical profile. That profile, according to Dr. Corbier, consists of children who developed normally before receiving the MMR vaccination, displayed symptoms of regressive autism within one to nine months following the receipt of the MMR vaccine, and experienced gastrointestinal problems.[4] Consistent with this profile, Dr. Corbier observed that Yates had developed normally before his MMR vaccination, regressed within several months after the receipt of the MMR vaccine, and suffered from lymphonodular hyperplasia colitis (inflamation of the gut). Hazlehurst Tr. at 302A. Dr. Corbier therefore concluded that Yates's receipt of the MMR vaccine played a significant role in the development of Yates's regressive autism. Hazlehurst Tr. at 302A–303.[5]

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[4] Dr. Corbier additionally noted that the presence of immunologic problems in such children strengthens the case for MMR-vaccine causation but is not an essential part of the clinical profile. Hazlehurst Tr. at 314A.

[5] In their post-hearing brief, petitioners explained that although their claim (continued...)

Central to Dr. Corbier's theory were several studies purporting to find the presence of the measles virus in the biological material of autistic children who had received the MMR vaccine. These studies came from primarily two sources: the work of Dr. Andrew Wakefield of the Royal Free Hospital in London, England, and his colleagues Drs. John O'Leary and Orla Sheils at the Unigenetics laboratory in Dublin, Ireland; and the research of Dr. Stephen Walker and his colleagues at Wake Forest University School of Medicine in Winston-Salem, North Carolina ("the Walker group").[6] According to the special master, Dr. Wakefield was the principle proponent of the hypothesis that the receipt of the MMR vaccine results in the development of autism spectrum disorders and gastrointestinal problems in certain children. Dr. Wakefield's work, the special master explained, helped to precipitate litigation in the United Kingdom examining the causal connection, if any, between the MMR vaccine and autism ("the UK litigation"). In order to support the UK

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[5](...continued)
had originally been designated by the steering committee as a test case for Theory I—identifying the combination of the MMR vaccine and vaccines containing thimerosal as a cause of autism—it became clear at the hearing that a much stronger case could be made linking Yates's condition solely to the MMR vaccine. Petitioners thus focused exclusively on MMR causation in making their case. As a result, the special master limited her specific causation discussion to the causal connection, if any, between the MMR vaccine and the development of Yates's regressive autism. In order fully to address the steering committee's general causation theory, however, the special master nevertheless analyzed the evidence relating to the potential contribution of thimerosal as a cause of autism spectrum disorders.

[6] As evidence that the measles virus can persist in the biological material of autistic children, petitioners relied primarily on the following articles: H. Kawashima, et al., Detection and Sequencing of Measles Virus From Peripheral Mononuclear Cells From Patients With Inflammatory Bowel Disease and Autism, Dig. Dis. Sci. 45(4): 723–29 (Apr. 2000) (co-authored by Dr. Wakefield); V. Uhlmann, et al., Potential Viral Pathogenic Mechanism for New Variant Inflammatory Bowel Disease, Mol. Pathol. 55(2): 84–90 (Apr. 2002) (co-authored by Drs. Wakefield, O'Leary, and Sheils); and C.M. Martin, et al., Detection of Measles Virus in Children With Ileo-Colonic Lymphoid Nodular Hyperplasia, Enterocolitis and Developmental Disorder, Mol. Psychiatry 7 Suppl. 2: S47–48 (2002) (co-authored by Drs. Uhlmann, O'Leary, and Sheils). In addition, petitioners cited the preliminary results of the Walker group purporting to find the existence of the measles virus in the bowel biopsies of autistic children. S.J. Walker, et al., Persistent Ileal Measles Virus in a Large Cohort of Regressive Autistic Children With Ileocolitis and Lymphonodular Hyperplasia: Revisitation of an Earlier Study, poster presentation at the International Meeting For Autism Researchers (IMFAR), University of California, Davis (June 2006).

litigation, Drs. O'Leary and Sheils of Trinity College in Dublin formed the Unigenetics laboratory, a non-accredited, for-profit institution that used a technique called PCR (polymerase chain reaction) to test for the presence of the measles virus in biopsied tissue.[7] The positive findings reported by the Unigenetics laboratory[8] were later the focus of the Walker group, whose preliminary testing purported to replicate Unigenetics' results.

The special master observed, however, that Dr. Wakefield's work has been widely discredited by the scientific community,[9] and that the testing conducted at

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[7] PCR testing is a standard technique for detecting and identifying particular gene sequences in tissue samples by exponentially replicating strands of DNA. Hazlehurst, 2009 WL 332306, at *95.

[8] The methods used by Unigenetics formed the basis for the research in the 2002 Uhlmann article, one of the articles on which petitioners primarily relied. Cedillo Tr. at 1938A. In addition, Unigenetics tested tissue and cerebrospinal fluid samples from—and purported to detect the presence of the measles virus in—the vaccinees in the other two test cases, Michelle Cedillo and Colten Snyder. Yates, by contrast, underwent no such testing.

[9] Dr. Wakefield published an article in 1993 positing a causal connection between the measles virus and infarctions of small blood vessels in the gut wall leading to Crohn's disease. A.J. Wakefield, et al., Evidence of Persistent Measles Infection in Crohn's Disease, J. Med. Virol. 39(4): 345–53 (Apr. 1993). The special master noted that in response to the public "furor" created by the 1993 Wakefield article, the Medical Research Council of the United Kingdom reviewed Dr. Wakefield's work and concluded that Dr. Wakefield had performed his experiments with reagents that were not specific for the measles virus and without important controls that the manufacturer of the testing equipment recommended. Hazlehurst, 2009 WL 332306, at *87. The special master additionally observed that following a series of methodologically sound studies conducted in the late 1990s, the scientific community ultimately dismissed Dr. Wakefield's hypothesis as having little scientific merit. Id.

Dr. Wakefield published two additional articles in 1998 and 2000, the first advancing the hypothesis that the MMR vaccine leads to the development of autism spectrum disorders with gastrointestinal manifestations and the second reporting the finding of enterocolitis in children with developmental disorders. A.J. Wakefield, et al., Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children, Lancet 351(9103): 637–41 (Feb. 1998); A.J. Wakefield, et al., Enterocolitis in Children With Developmental Disorders, Am. J.

(continued...)

both the Unigenetics and Wake Forest laboratories contained procedural flaws that compromised their reliability. The special master thus found that the studies on which Dr. Corbier relied were "scientifically flawed or unreliable" and that Dr. Corbier's opinion regarding that aspect of petitioners' causation theory (positing the existence of persisting measles virus in the gut tissue of autistic children) "could not be credited as sound or reliable." Hazlehurst, 2009 WL 332306, at *13. The special master accordingly concluded that petitioners' theory of causation was "premised upon a series of biological implausabilities" and was "at variance with the known science." Id. at *148–49.

Following the issuance of the special master's decision denying compensation, petitioners now ask the court to address three issues on appeal. Specifically, petitioners object to: (1) the special master's consideration of evidence discrediting Unigenetics, the laboratory that detected the measles virus in the tissue of autistic children; (2) the special master's failure to consider evidence demonstrating the reliability of results obtained by the Walker group, also purporting to find the presence of the measles virus in the tissue of autistic children; and (3) the special master's failure to decide whether regressive autism is a distinct phenotype from classic autism. We address these issues in turn below.

DISCUSSION

When deciding a motion for review of a special master's decision under the Vaccine Act, the court may:

> (A) uphold the findings of fact and conclusions of law of the special master and sustain the special master's decision,
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> (B) set aside any findings of fact or conclusion of law of the special master found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law and issue its own findings of fact and conclusions of law, or
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> (C) remand the petition to the special master for further action

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[9](...continued)
Gastroenterology 95(9): 2285–95 (2000). Both articles were the subject of extensive criticism, however, and the special master ultimately found them to be "scientifically unreliable." Hazlehurst, 2009 WL 332306, at *90. In addition, the special master observed that ten of Dr. Wakefield's 12 co-authors on the 1998 article later retracted the study's conclusion that a potential causal link exists between the MMR vaccine and autism. Id. at *90–92.

in accordance with the court's direction.

42 U.S.C. § 300aa-12(e)(2). The Federal Circuit has interpreted 42 U.S.C. § 300aa-12(e)(2)(B) as setting forth three distinct standards of review: (1) the special master's findings of fact are to be reviewed under the arbitrary and capricious standard; (2) the special master's discretionary rulings are to be reviewed under the abuse of discretion standard; and (3) the special master's legal conclusions are to be reviewed de novo under the not in accordance with law standard. Turner v. Secretary, Dep't of Health & Human Servs., 268 F.3d 1334, 1337 (Fed. Cir. 2001). Reversible error is extremely difficult to establish, however, so long as the special master has "considered the relevant evidence in the record as a whole, drawn plausible inferences from that evidence, and articulated a basis for [the] decision which is rational." Hines v. Secretary, Dep't of Health & Human Servs., 940 F.2d 1518, 1527 (Fed. Cir. 1991).

There are two methods for establishing entitlement to compensation under the Vaccine Act. If the vaccinee suffered one of the injuries identified in the Vaccine Injury Table within the prescribed time period (42 U.S.C. § 300aa-14(a) (initial Table) and 42 C.F.R. § 100.3 (updated Table)), a petitioner may assert what is commonly referred to as a "Table injury," with a rebuttable presumption that the injury was caused by the vaccine. 42 U.S.C. § 300aa-11(c)(1)(C)(i); Pafford v. Secretary, Dep't of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). If the vaccinee suffered an injury not identified in the Vaccine Injury Table, however (as in the present case), no such presumption exists and a petitioner must show that the vaccine "caused" or "significantly aggravated" the injury in question (commonly referred to as a causation-in-fact claim). 42 U.S.C. § 300aa-11(c)(1)(C)(ii)(I); Pafford, 451 F.3d at 1355.

In order to demonstrate that Yates's injury was caused in fact by the challenged vaccine, petitioners must prove their claim by a preponderance of the evidence, a standard that is satisfied by showing that it is "more probable than not" that the vaccine at issue caused the vaccinee's injury. Althen v. Secretary, Dep't of Health & Human Servs., 418 F.3d 1274, 1279 (Fed. Cir. 2005). To make a prima facie case for causation under Althen, petitioners must provide: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Id. at 1278.[10] Although petitioners are not required to present "epidemiologic studies,

[10] Even if petitioners are successful in making a prima facie case for causation, the special master may nevertheless deny compensation where the respondent has shown by a preponderance of the evidence that the injury is due to (continued...)

[evidence of] rechallenge, the presence of pathologic markers or genetic disposition, or general acceptance in the scientific or medical communities," to establish causation, Capizzano v. Secretary, Dep't of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006), they must nevertheless provide a "reputable medical or scientific explanation" for their claim, Althen, 418 F.3d at 1278. The determination of whether a proffered theory of causation is "reputable" may "involve an assessment of the relevant scientific data." Andreu v. Secretary, Dep't of Health & Human Servs., No. 2008-5184, 2009 WL 1688231, at *9 (Fed. Cir. June 18, 2009). "Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." Id.

In the instant suit, petitioners assert that the measles component of the MMR vaccine can cause an immune dysfunction in certain children that impedes their systems from clearing the measles virus. According to this hypothesis, the persisting measles virus leads to chronic inflammation in both the gastrointestinal system and the brain. The inflammation in the brain, petitioners maintain, causes neurological damage that manifests as autism.

In analyzing petitioners' medical theory under the Althen standard, the special master identified two cardinal flaws in petitioners' case. First, the special master explained that petitioners' experts based their opinions on the characteristics of the "wild-type" measles virus rather than on the characteristics of vaccine-strain measles, despite the fact that the measles vaccine is distinguishable from the wild-type measles virus in several key respects.[11] Second, the special master observed that petitioners' experts further based their opinions on studies (detecting the presence of the measles virus in the gut tissue of autistic children) that the special master found to be unreliable. As a result of these deficiencies, the special master held that

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[10](...continued)
factors unrelated to the administration of the vaccine. Walther v. Secretary, Dep't of Health & Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007).

[11] Citing the testimony of several expert witnesses (among them Dr. Diane Griffin—an acknowledged authority on measles), the special master observed that the vaccine-strain measles virus, in contrast to the wild-type measles virus, is much less virulent, has been specifically designed not to replicate well in the human body, and does not exhibit the most significant complications associated with the wild-type measles virus. Hazlehurst, 2009 WL 332306, at *149–50. The special master additionally noted that in the "rare circumstance" that the wild-type measles virus persists in the body and causes disease, the resulting injuries are distinguishable from the impairments associated with autism and include neurological deterioration that results in death. Id. at *149.

petitioners had failed to satisfy the first two prongs of the Althen standard because their medical theory was premised upon a series of biological implausibilities and the presented evidence did not support a logical sequence of cause and effect between the vaccine and the injury. Hazlehurst, 2009 WL 332306, at *149–50.[12]

In reaching her conclusion, the special master described the finding of persistent measles virus in the gut tissue of autistic children as the "linchpin" of petitioners' theory. Id. at *171. The special master went on to describe that proposition, however, as "glaringly unreliable" based on her assessment that the studies on which petitioners' experts based their conclusions were "critically flawed and scientifically untenable." Id. In particular, the special master devoted extensive discussion to an analysis of the testing methods of the Unigenetics laboratory, explaining that petitioners' reliance on those test results, coupled with respondent's criticism of them, made it necessary for her to analyze Unigenetics' practices "with more scrutiny than generally occurs in vaccine proceedings." Id. at *126. It is this scrutiny that serves as the first ground for petitioners' appeal.

I. The Special Master's Reliance on Evidence That Should Not Have Been Considered

The special master based her assessment regarding the reliability of the testing conducted at Unigenetics in part on the testimony of Dr. Stephen A. Bustin, a molecular biologist who appeared as an expert witness both for the vaccine manufacturers in the UK litigation and for respondent in the omnibus proceeding. As part of the UK litigation, Dr. Bustin was charged with evaluating the 2002 Uhlmann article and examining the testing methods used by the Unigenetics laboratory. Dr. Bustin later testified that he spent 1,500 hours analyzing data from the laboratory, including two site visits, and billed approximately $400,000 for his efforts.

Based on his analysis of Unigenetics'procedures, equipment, and laboratory notebooks, Dr. Bustin concluded that the Unigenetics researchers had failed to follow the laboratory's own standard operating procedures, failed to adhere to certain standard laboratory practices, and failed to comply with the standards set forth by the manufacturer of the testing equipment, all of which diminished the reliability of the test results purporting to show the presence of the measles virus in the gut tissue of autistic children. Dr. Bustin speculated that the Unigenetics researchers had detected

[12] The special master additionally held that petitioners had failed to establish a temporal association under the third prong of Althen because the vaccine-strain measles virus does not replicate well in the human body and the only evidence petitioners offered for measles persistence—the Uhlmann article—was discredited. Id. at *150.

DNA contamination rather than the measles virus in the biopsied tissue.

Dr. Bustin was subsequently identified as an expert in the Cedillo case in late May/early June 2007 in support of a motion in limine by the respondent unrelated to the testimony presently at issue. On June 7, 2007, two business days before the commencement of the hearing in Cedillo, the respondent sought to introduce two expert reports by Dr. Bustin obtained from the UK litigation (Cedillo Resp. Exs. WW and XX), along with Dr. Bustin's testimony regarding his evaluation of Unigenetics' procedures, equipment, and laboratory notebooks. The petitioners objected to the last-minute filings and disclosure, but the exhibits were nevertheless provisionally admitted into evidence on June 8, 2007. (The presiding special master deferred ruling on whether he would rely on the reports, but allowed either party to question Dr. Bustin.) By order dated June 11, 2007, however, the special masters assigned to the three test cases advised that they would "favorably consider joining in a request for release of relevant reports" if the steering committee filed a formal application with the British court.[13]

Dr. Bustin was the subject of a similar challenge in the present case. In a motion filed on September 4, 2007, petitioners objected to the admission of Dr. Bustin's reports regarding Unigenetics under the theory that consideration of that evidence in the absence of the other expert reports prepared in the UK litigation would be prejudicial. In addressing petitioners' motion, the special master noted that petitioners had been afforded a "generous" period of time to obtain the release of additional expert reports from the British court but had declined to do so. Hazlehurst v. Secretary, Dep't of Health & Human Servs., No. 03-654V, 2009 WL 332258, at *8 (Fed. Cl. Feb. 12, 2009).[14] Observing that both parties had been given "an opportunity, procedurally, to obtain and to present relevant information for consideration in deciding this case," the special master concluded that petitioners were indeed prepared to address the reliability of the Unigenetics results, and thus,

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[13] Prior to their admission in the Cedillo case, Dr. Bustin's reports, like all of the exhibits in the UK litigation, had been under seal by the British court. Dr. Bustin additionally had been the subject of a court order prohibiting him from testifying about Unigenetics' procedures, equipment, and laboratory notebooks in any other case. Both Dr. Bustin's reports and his testimony were made available, however, following the respondent's successful application to the British court.

[14] The special master explained that the steering committee had informed the special masters hearing the three test cases of its decision not to seek the release of additional documents from the British court because its efforts to do so likely would have been unsuccessful given the steering committee's inability to get the requisite consent from the experts whose reports they sought. Hazlehurst, 2009 WL 332258, at *8.

more than a year and a half after the hearing in Cedillo, denied petitioners' motion to strike the testimony of Dr. Bustin. Id. at *8–9.

Petitioners now argue, however, that the special master's consideration of Dr. Bustin's testimony and reports was fundamentally unfair and was inconsistent with the purpose and nature of the Vaccine Program in violation of both the Vaccine Rules and the relevant case law.[15] Specifically, petitioners maintain that the special master's reliance on Dr. Bustin's analysis violated the Vaccine Rules' requirement that the consideration of evidence in the Vaccine Program be "governed by principles of fundamental fairness to both parties." Vaccine Rule 8(b)(1).[16] The admission of Dr. Bustin's testimony and reports was fundamentally unfair, petitioners argue, because the material was submitted a mere two working days before the beginning of the Cedillo hearing, severely impairing the ability of the Cedillos' attorney to mount an effective cross-examination of Dr. Bustin or to prepare an adequate response to his analysis. Further compounding this inequity, in petitioners' view, is the fact that petitioners could not have countered Dr. Bustin's analysis without spending large sums of money, something they were unable—and should not in the spirit of the Vaccine Program have been required—to do. Finally, petitioners maintain that even if they had received adequate notice of Dr. Bustin's analysis and had sufficient funds to address it, they nevertheless would have been unable to counter Dr. Bustin's testimony because the Unigenetics laboratory no longer exists and Unigenetics' equipment and laboratory notebooks are no longer available for review. Such prejudice, petitioners maintain, can only be remedied by excluding Dr. Bustin's testimony and reports.

In addition, petitioners contend that the admission of Dr. Bustin's testimony and reports converted the proceeding into "full blown tort litigation," thereby contravening Congress's intention that individuals injured by vaccines receive compensation "quickly, easily, and with certainty and generosity." Knudsen v. Secretary, Dep't of Health & Human Servs., 35 F.3d 543, 549 (Fed. Cir. 1994) (quoting H.R. Rep. No. 99-908, at 3 (1986), as reprinted in 1986 U.S.C.C.A.N.

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[15] Petitioners challenge only that portion of Dr. Bustin's analysis pertaining to his review of the Unigenetics laboratory: Cedillo Resp. Ex. WW, "Summary Report on Real-Time RT-PCR Assays Carried Out by Unigenetics, Ltd.," (Nov. 10, 2004) (prepared in the course of the UK litigation); Cedillo Resp. Ex. XX, "Report on MMR/MR Vaccine Allegations," (June 30, 2003) (also prepared in the course of the UK litigation); Cedillo Resp. Ex. 13, "PCR and Reliability of the Unigenetics Laboratory," (PowerPoint presentation introduced at the Cedillo hearing); and Cedillo Tr. at 1962A– 2069.

[16] The Vaccine Rules were amended on July 13, 2009, renumbering Vaccine Rule 8(c), to which the parties refer, as Vaccine Rule 8(b)(1).

6344). Petitioners assert that admitting evidence inconsistent with the purpose and nature of the Vaccine Program is an error of law and thus urge the court to review the special master's reliance on such evidence de novo under the not in accordance with law standard.

In respondent's view, petitioners cannot contend that Unigenetics' testing is critical to their case and yet object when respondent offers evidence to challenge its reliability. Respondent argues that Dr. Bustin's reports are reliable evidence that is directly applicable to the issues in this litigation and are thus vital to assessing the correctness of petitioners' theory of causation. In addition, respondent maintains that the subject of Dr. Bustin's reports should have come as no surprise to petitioners because several of petitioners' expert witnesses had direct knowledge of the problems with Unigenetics' testing methods identified by Dr. Bustin. Indeed, respondent points out that four of petitioners' experts in the omnibus proceeding also served as expert witnesses in the UK litigation, and petitioners' expert Dr. Ronald Kennedy specifically testified about the Unigenetics laboratory during the Cedillo hearing. Finally, respondent endorses the special master's conclusion set forth in her denial of petitioners' motion to strike: "[F]airness to the parties has been achieved by affording both parties an opportunity, procedurally, to obtain and to present relevant information for consideration in deciding this case." Hazlehurst, 2009 WL 332258, at *8.

Vaccine Rule 8(b)(1) indeed requires that proceedings within the Vaccine Program be conducted in a manner that is fundamentally fair. And petitioners are correct that the program does not anticipate or encourage complex litigation. See Andreu, 2009 WL 1688231, at *4 (recognizing that Congress, in enacting the Vaccine Act, was "acutely aware that the traditional tort system had proven ineffective in providing redress for vaccine-injured individuals 'because it resulted in lengthy delays, high transaction costs, and sometimes no recovery,'" quoting Lowry v. Secretary, Dep't of Health & Human Servs., 189 F.3d 1378, 1381 (Fed. Cir. 1999)). We do not believe, however, that the special master violated either principle in the instant case.

It is evident, as an initial matter, that petitioners were given adequate time to address Dr. Bustin's analysis. Although petitioners were notified of the submission of Dr. Bustin's reports a mere two business days before the Cedillo hearing, the special masters nevertheless made every effort to accommodate petitioners and remedy any element of surprise by leaving the record open for more than a year following the Cedillo hearing to allow petitioners to recall witnesses (including Dr. Bustin) or to provide additional evidence. The special masters additionally offered to lend their names to a request for relevant reports filed in the UK litigation. Hazlehurst, 2009 WL 332306, at *93. Given these circumstances, we are unable to conclude that petitioners were unfairly prejudiced as a result of the timing of the

submission of Dr. Bustin's reports.

Nor do we believe that the special master's consideration of Dr. Bustin's analysis transformed the proceeding into complex tort litigation. Although Dr. Bustin's reports were created in connection with the UK litigation and funded by the vaccine manufacturers, the relevant consideration is not the cost of Dr. Bustin's reports but rather their purpose: to rebut critical evidence introduced by petitioners.[17] Petitioners themselves acknowledge that Unigenetics' results are central to their claim. Dr. Bustin's testimony speaks directly to whether that evidence has any merit. The proposition that "fundamental fairness" requires the special master to ignore evidence so crucial to the case—in effect to contend that respondent has no right to mount a defense—is untenable. Indeed, a special master's refusal to consider such "highly relevant and probative evidence" has been found to be an abuse of discretion. DeFazio v. Secretary, Dep't of Health & Human Servs., 40 Fed. Cl. 462, 467 n.5 (1998).

As the special master correctly noted in her decision, petitioners had no obligation to submit medical studies in support of their claim. But once petitioners had done so, the special master was duty-bound to assess the reliability of those studies. Hazlehurst, 2009 WL 332306, at *17 (citing Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 590 (1993)); see also Campbell ex rel. Campbell v. Secretary, Dep't of Health & Human Servs., 69 Fed. Cl. 775, 781 (2006) (interpreting the relevant case law as requiring a special master "to rely on reliable medical or scientific evidence not only in finding causation, but also the lack thereof").

The only difficulty we have then with Dr. Bustin's analysis is that it essentially goes unanswered in petitioners' case. Despite the special masters' best efforts to accommodate petitioners, the unfortunate fact remains that Dr. Bustin's testimony and reports reflect 1,500 hours of critical evaluation that petitioners have no way to replicate. While petitioners' experts Dr. Karin Hepner (a molecular biologist) and Dr. Ronald Kennedy (a professor and the chair of the Department of Microbiology and Immunology at Texas Tech University Health Sciences Center) each filed supplemental reports addressing Dr. Bustin's analysis and the validity of Unigenetics' testing, Cedillo Pet. Exs. 120 and 121, neither expert had the opportunity to review the primary materials on which Dr. Bustin based his conclusions. The closest either expert actually came to the Unigenetics laboratory, in fact, was Dr. Kennedy's participation in a meeting in which he and several

[17] Indeed, given the fact that respondent neither commissioned nor paid for the reports, it is difficult to distinguish them conceptually from any information existing in the public domain.

colleagues questioned Dr. Sheils about Unigenetics' research practices.[18] We do not, however, consider Dr. Kennedy's testimony a legitimate counterweight to Dr. Bustin's testimony regarding Unigenetics' procedures because the former spent a mere five hours interviewing Dr. Sheils while the latter spent 1,500 hours with full access to Unigenetics' facilities and records. Their experiences are simply not comparable.

Dr. Kennedy's supplemental report illustrates the significance of this imbalance. Addressing Dr. Bustin's criticism of the Unigenetics laboratory, Dr. Kennedy opined as follows:

> What becomes clear in a review of [Dr. Bustin's] testimony and his PowerPoint presentation is that while he readily identifies problems, he omits any explanatory references which would place the issue into context. By selectively highlighting only a few pages which he claims supports his criticism that the [Unigenetics] laboratory was less than diligent, it is unknown whether these laboratory notebooks also contain information which demonstrates that the laboratory took the appropriate action to resolve unexpected issues. The lack of access to the laboratory notebooks will, of course, affect my comments.

Cedillo Pet. Ex. 121 at 2. Addressing Dr. Bustin's specific criticisms of the contamination issue, Dr. Kennedy additionally observed as follows:

> It is easy to rectify contamination of negative controls and does not invalidate positive results by any laboratory that is competent in PCR technologies. While Dr. Bustin identified the contamination problem, he attempted to use this one page to imply that contamination issues were never resolved, yet his PowerPoint presentation did not include

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[18] Dr. Kennedy described the meeting with Dr. Sheils as follows:

> [O]ver four-and-a-half to five hours, [Dr. Sheils] was asked a number of questions relative to the technology, the standard operating procedures, the immunohistochemistry that was shown, how she detected what were her primers, what were the sensitivity, how was isolation done, what were controls, what were positive controls, how did she know that this was not contamination, what was the samples. She was essentially taken apart by, I would say, three or four extremely good microbiologists.

Cedillo Tr. at 811A.

> any further support that contamination was an unremedied problem in the [Unigenetics] laboratory. He did not include any additional pages from the laboratory notebooks that indicate contamination issues were pervasive and unresolved. Since contamination is an ever present problem in laboratories, an isolated day of problems should not be used to impugn a reputation developed over a life time of achievement.

Cedillo Pet. Ex. 121 at 3 (citation omitted). Dr. Kennedy offered similar observations regarding Dr. Bustin's other criticisms, describing many of them as irrelevant or unverifiable without having access to the laboratory notebooks upon which Dr. Bustin relied. As Dr. Kennedy noted, "an isolated page from a laboratory notebook does not provide any context for the conditions associated with [a] particular experiment." Cedillo Pet. Ex. 121 at 3.

Given that the special master's critique of Unigenetics' practices reflects a greater level of scrutiny than generally occurs in vaccine proceedings, Hazlehurst, 2009 WL 332306, at *126, we find this disparity of access to Unigenetics' facilities and laboratory notebooks troubling. Few institutions, we suspect, can entirely withstand the level of scrutiny provided by Dr. Bustin, particularly without explicative or rehabilitative testimony. And we acknowledge, as Dr. Kennedy charges, that Dr. Bustin's criticisms may be taken out of context.

But while we are sympathetic to petitioners' concerns on this score, it would be an extraordinary remedy to exclude such relevant and probative evidence. The only solution, we believe, is the one the special master employed: mitigating any potential prejudice by affording petitioners the opportunity to seek relevant reports from the UK litigation and to recall Dr. Bustin for further questioning. The fact that petitioners did neither considerably weakens their position. See Snyder v. Secretary, Dep't of Health & Human Servs., No. 01-162V, 2009 WL 332044, at *27 (Fed. Cl. Feb. 12, 2009) (holding that petitioners waived any argument regarding the reports filed in the UK litigation because of their failure to seek their release).[19]

Most significant for the purposes of our analysis, however, is the fact that we believe that the special master would have reached the same conclusion regarding Unigenetics even in the absence of Dr. Bustin's analysis. As the special master

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[19] During oral argument, petitioners' counsel raised the issue whether his clients should be bound by procedural decisions made by the steering committee or by the counsel in Cedillo (i.e., the decision not to seek expert reports from the British court). Petitioners themselves, however, could have sought evidence filed in the UK litigation, particularly when it became clear at the Cedillo hearing that the reliability of the Unigenetics results would be an issue in dispute.

explained in her decision, she did not "rely solely on [Dr. Bustin's] testimony in evaluating the reliability of the test results obtained by Unigenetics," but also based her conclusions on "the testimony of other witnesses and the filed scientific literature addressing Unigenetics' testing techniques." Hazlehurst, 2009 WL 332306, at *93.[20]

Notably, the flaws identified by the special master in the challenged articles would have been evident even without the scrutiny given by Dr. Bustin to the Unigenetics laboratory. First, the "reported positive findings of measles virus have not been replicated by laboratories independent of [Unigenetics]," thereby "diminish[ing] the confidence of the scientific community in the validity of the reported findings." Id. at *124. Second, "the published articles on which petitioners rely do not include sufficient laboratory data to evaluate the conducted testing procedures and the validity of the test results," thereby "impair[ing] the scientific community's ability to scrutinize the reported findings for methodological errors." Id. Thus, even if we were to consider the admission of Dr. Bustin's testimony unfair to petitioners, the special master's consideration of that evidence would rise at most to the level of harmless error. Hines, 940 F.2d at 1526 (holding that it was harmless error for the special master to rely on a medical textbook, even if unfair to the petitioner, because "the special master's decision was based on a number of factors and [petitioner had] not shown that reliance on the . . . textbook was likely critical to the result").

II. The Special Master's Disregard of Relevant Evidence

In addition to the Unigenetics studies, petitioners also relied on the preliminary, unpublished findings of the Walker group reporting the existence of the measles virus in the bowel biopsies of children with regressive autism.[21] Petitioners argue that these findings not only offer independent support for their causation theory regarding measles persistence, but also provide clear evidence that the challenged

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[20] In particular, the special master identified the testimony of respondent's experts Dr. Brian J. Ward (an infectious disease specialist), Dr. Diane Griffin (an immunologist), and Dr. Bertus Rima (a virologist) as "the most persuasive on the subject of vaccine-strain measles virus persistence," Hazlehurst, 2009 WL 332306, at *7, and relied upon the testimony of those same experts in her discussion of the Unigenetics laboratory, id. at *128–32.

[21] Specifically, the Walker group contended that they (1) detected measles virus genomic material in the gut tissue of children with regressive autism using the PCR technology employed by Unigenetics, and (2) confirmed that the product identified as measles virus genomic material through PCR testing was in fact measles virus genomic material by matching its genetic sequence to that of the measles virus.

Unigenetics testing was reliable. Petitioners contend, however, that the special master failed to take into account evidence that the Walker group had verified their PCR testing through genetic sequencing,[22] thereby violating 42 U.S.C. § 300aa-13(b)(1)'s requirement that the special master consider all relevant evidence. Petitioners maintain that had such evidence been weighed properly, it would have confirmed the correctness of Dr. Corbier's hypothesis linking Yates's regressive autism to the MMR vaccine. Petitioners thus argue that the special master's finding that the Unigenetics and Walker group results were unreliable was arbitrary and capricious.

Petitioners' expert Dr. Hepner indeed cited her own work with the Walker group as evidence of the reliability and reproducability of the Uhlmann article's results. Cedillo Pet. Ex. 120 at 1. According to Dr. Hepner, although other studies—most notably by researchers M.A. Afzal and Yasmin D'Souza[23]—had attempted to replicate the Uhlmann results, the Walker group investigators were the first to do so successfully, in part because of their use of gut tissue. (Dr. Hepner explained that the Afzal and D'Souza studies, by contrast, each used other biological material. Cedillo Tr. at 629A, 631.) Dr. Hepner testified that the Walker group's results, though preliminary, were nevertheless a "technical accomplishment," because they demonstrated that the primer sets[24] used in the Uhlmann article successfully amplified the measles virus and that vaccine-strain measles virus could indeed be found in the tissue of autistic children who suffer from gastrointestinal problems. Cedillo Tr. at 682; Cedillo Pet. Ex. 120 at 3.[25] Dr Hepner additionally noted—both

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[22] Sequencing is the process of confirming that the product obtained through PCR testing contains the proper nucleotide composition for the targeted product (here, the measles virus). "Sequencing is the only way to be certain that the amplified material is the targeted material." Hazlehurst, 2009 WL 332306, at *119.

[23] M.A. Afzal, et al., Absence of Delectable Measles Virus Genome Sequence in Blood of Autistic Children Who Have Had Their MMR Vaccination During the Routine Childhood Immunization Schedule of UK, J. Med. Virol. 78(5): 623–30 (May 2006); Y. D'Souza, et al., No Evidence of Persisting Measles Virus in Peripheral Blood Mononuclear Cells From Children With Autism Spectrum Disorder, www.pediatrics.org/cgi/doi/10.1542/peds.2006-1242.

[24] A primer is a "short piece of DNA or RNA [that is] complementary to a given DNA sequence and acts as the point from which replication proceeds during the process of polymerase chain reaction." Hazlehurst, 2009 WL 332306, at *112 (quoting Dorland's Illustrated Medical Dictionary 764, 1506 (30th ed. 2003)).

[25] Such an accomplishment is significant, Dr. Hepner explained, because a (continued...)

in her testimony and in her two expert reports—that the Walker group's results had been "verified using nucleotide sequencing analysis" which is universally recognized as the most rigorous of scientific standards in genetic testing.[26]

Respondent points out, however, that genetic sequencing is only one aspect of proper PCR technique and argues that the use of sequencing does not overcome the other shortcomings of the Walker group's study, most significantly the absence of proper controls.[27] Accordingly, respondent contends that the Walker group's

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[25](...continued)
chief criticism of the Uhlmann article is that its results could not be replicated and the Walker group had thus taken the first step in doing so. Cedillo Pet. Ex. 63 at 5.

[26] In her initial expert report filed on May 25, 2007, Dr. Hepner advised that the Walker group had confirmed "[v]accine strain specificity . . . in a percentage of [their] samples using nucleotide sequencing." Cedillo Pet. Ex. 63 at 5. In her supplemental report filed on October 22, 2007, Dr. Hepner further advised as follows:

> Dr. S. Walker has confirmed that various primer sets used in the Uhlmann study successfully amplify [measles virus] and his PCR results were further verified using nucleotide sequencing analysis. . . . The conclusion drawn is simply this: Using the Uhlmann assay conditions, a product corresponding to the target gene is amplified and verified in a manner considered to be the most rigorous by all standards. If [a measles virus] target sequence is amplified and verified by sequencing using the Uhlmann primer sets, it is necessarily true that these Uhlmann primer sets are capable of amplifying the predicted [measles virus] target.

Cedillo Pet. Ex. 120 at 1–2. In addition, Dr. Hepner's testimony contains several references to the Walker group's sequencing of their results. See, e.g., Cedillo Tr. at 662A, 667. Finally, the abstract itself noted that 14 of the 82 patients who had tested positive for the presence of measles virus had their results "verified by DNA sequence." Cedillo Pet. Ex. 120, Tab C at 1.

[27] As the special master explained in her decision, proper PCR testing requires the use of four controls—positive, negative, experimental, and control samples—to be run every time an experiment is conducted. The special master described the necessity for positive and negative controls as follows:

> A positive control is a sample that contains the measles virus. The
>
> (continued...)

results are not reliable because there is no internal consistency in the study and the positive findings could very likely be due to contamination. Respondent additionally notes that Dr. Hepner herself acknowledged that the preliminary data from the study was "not useful at this time" (Cedillo Tr. at 682), declined to draw any conclusions about the biological significance of the Walker group's findings (Cedillo Tr. at 682), and identified what respondent describes as several significant drawbacks to the study, including that the experiments had not been "blinded"[28] and had lacked negative controls (Cedillo Tr. at 658, 681).[29] Respondent thus argues that the special

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[27](...continued)
sample must be positive every time the experiment is run. If the positive control is negative, there is a flaw in the experimental design, and no information can be obtained. A negative control . . . is a sample in which measles virus is not present. The sample must be negative every time the experiment is run. If the negative control is positive, there is either a flaw in the experimental design (such as a primer that is not sufficiently specific to the desired target) or cross-contamination between the negative control and the measles virus. The negative samples within the experiment function as a control for contamination. . . . [W]hen the controls do not function true to designation, confidence in the results obtained from the experiments diminishes.

Hazlehurst, 2009 WL 332306, at *120 (citations omitted). The special master additionally described the need for experimental and control samples as follows:

> The second level of control includes experimental subjects and the normal controls. . . . By design, the control group has to be similar to the experimental group but has to differ by the variable of interest.
>
> In running an experiment, the investigator must run all four controls (the positive, negative, experimental and control samples) at the same time. The controls must be run every time an experiment is conducted. That is standard laboratory practice.

Id. (citations omitted).

[28] A blinded experiment is one in which the researcher does not know whether he is working with a positive control, a negative control, or the sample in question so as to avoid introducing the researcher's subjectivity into the analysis.

[29] Respondent, we believe, overreads Dr. Hepner's testimony on these points. (continued...)

master correctly determined that the Walker group's preliminary, unpublished, and unconfirmed findings do not support the validity of the Unigenetics test results.

Although the special master recognized sequencing as the "gold standard" for determining the reliability of PCR testing, Hazlehurst, 2009 WL 332306, at *116, she made no mention of the Walker group's sequencing in her decision. The special master relied instead on the testimony of Dr. Bustin, who explained that in the absence of both positive and negative controls, he could not have "any confidence" in the test results presented by the Walker group. Cedillo Tr. at 1959A. The special master thus dismissed the Walker group's findings as preliminary and concluded that she could not "place much weight" on such findings because "test results without the use of these controls during PCR experiments may not be reliable." Hazlehurst, 2009 WL 332306, at *125.

There is evidence in the record, however, that Dr. Bustin was not aware that the Walker group had sequenced their results. Seemingly without regard to this fact, Dr. Bustin expressed concern about several unidentified bands in the Walker group's poster presentation, explaining that he could not rule out the possibility of contamination in the absence of negative controls. Cedillo Tr. at 1959A. Dr. Bustin went on to testify that in order to address the possibility of contamination, a researcher must "do additional techniques to confirm the identity of that band," noting that the "best way" to confirm that the band is the target "is sequencing, is getting a DNA sequence." Cedillo Tr. at 1942A.

Dr. Bustin unfortunately was never cross-examined on this point so we have no way of knowing what conclusions he would have drawn from the Walker group's

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[29](...continued)
Dr. Hepner explained that the Walker group's data was "not useful at this time" because the results for the experimental group (i.e., children with autism) had not been compared to a control group (i.e., children without autism), so no biological conclusions could be drawn regarding the connection between the measles virus and autism. Cedillo Tr. at 657–58. Dr. Hepner repeatedly maintained, however, that the Walker group results were relevant to the omnibus proceeding because they showed primer-set specificity, thereby helping to validate the Uhlmann article's results detecting measles persistence in the gut tissue of autistic children. Cedillo Tr. at 682. Similarly, while Dr. Hepner acknowledged that the Walker study was not blinded, she testified that "there would be no point in being blinded because there [were] only experimental samples." Cedillo Tr. at 681. Finally, Dr. Hepner explained that while the Walker group had not yet found control samples they deemed suitable (i.e., developmentally normal children with gastrointestinal issues), they had nevertheless run no-template controls in every experiment to ensure against contamination. Cedillo Tr. at 658, 662A.

sequencing of their results.[30] Even if we were to assume, however, that the special master overlooked this evidence, we are unable to conclude that such an omission rises to the level of reversible error. On balance, we do not believe the fact that the Walker group sequenced a portion—albeit not all—of their results carries enough weight to overcome the special master's conclusion that the Walker group's results were preliminary, unpublished, and not entitled to substantial weight. As petitioners' experts acknowledged, poster presentations are not subject to peer review and as a result do not receive the scrutiny of the scientific community that confers an element of reliability on published test results.[31] Indeed, respondent's expert Dr. Brian Ward testified that based on his own experience, such abstracts often turn out to be wrong. Cedillo Tr. at 1865. We are therefore unwilling to disturb the special master's finding on this point. See Cox v. Secretary, Dep't of Health & Human Servs., 30 Fed. Cl. 136, 144 (1993) (describing as "harmless error" the special master's decision to strike an expert report because the report would not have changed the outcome of the case).

III. The Special Master's Failure to Decide a Critical Issue

Having found no evidence to conclude that childhood vaccines lead to the development of autism, the special master declined to reach the issue of whether

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[30] We are unable to assess with any confidence either the legitimacy of Dr. Bustin's criticism of the Walker group's procedures or the correctness of petitioners' response to that criticism. Dr. Bustin testified that he had no faith in the results of the Walker group's study because of the absence of negative controls. Cedillo Tr. at 1959A. Petitioners' counsel contended at oral argument, however, that despite Dr. Bustin's criticism, the Walker group in fact used negative internal controls in their experiments and Dr. Hepner testified that a no-template control, designed to "function[] as a control for contamination," was run with every sample. Cedillo Tr. at 658, 662. The record unfortunately provides no way to reconcile these statements.

Similarly, it is unclear from the testimony whether the use of sequencing—a process designed to ensure the integrity of the targeted material—would nevertheless have made up for the absence of a negative control—a device designed to ensure primer specificity and to guard against contamination. As Dr. Hepner testified, "if we sequence through the vaccine strain nucletide[,] that will distinguish it from any kind of potential contamination source." Cedillo Tr. at 667. Petitioners' failure to cross-examine Dr. Bustin on this point, however, essentially means his testimony went unchallenged.

[31] Indeed, respondent notes that the results of the Walker group's investigation still have not been published.

regressive autism is a distinct phenotype with different causes than classic autism.[32] As the special master observed:

> [T]he evidence presented and considered in this litigation does not support a finding, under the applicable preponderance of the evidence legal standard, that postnatal exposure to the vaccines of interest leads to the development of autism of any type. Unpersuaded that childhood vaccines lead to the development of autism, the undersigned need not decide whether the evidence supports a finding that regressive autism is a separate phenotype.

Hazlehurst, 2009 WL 332306, at *24.

Petitioners maintain, however, that the resolution of this issue is critical to their medical theory causally linking Yates's MMR vaccination to his regressive autism. Petitioners argue that in the absence of such a determination, the special master could not have made a rational assessment regarding the neuroanatomy of autism, Dr. Corbier's credibility, or the appropriate weight to be given Dr. Corbier's testimony. Petitioners thus urge the court to set the special master's decision aside on the ground that it is arbitrary and capricious.

In support of this point, petitioners note that approximately 80 percent of individuals with autism suffer from classic autism. Petitioners observe, however, that the majority of the evidence considered by the special master concerning the neuroanatomy of autism—particularly the testimony of respondent's expert Dr. Rust and the articles on which he relied—fail to distinguish between classic autism and regressive autism. Petitioners thus posit that this evidence may apply only to persons with classic autism and not to individuals with regressive autism. According to petitioners, the special master therefore could not have assessed the relevance of such

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[32] The special master defined phenotype as "the entire physical, biochemical, and physiological makeup of an individual as determined both genetically and environmentally, as opposed to genotype [(meaning the "genetic constitution" of the individual)]." Hazlehurst, 2009 WL 332306, at *24 (quoting Dorland's at 1421). The special master went on to explain:

> Inherent in the definition of a "phenotype" is the combined effect of genetic and environmental influences on an individual. Underlying petitioners' argument that regressive autism is a distinct phenotype is their theory that this type of autism is caused, in part, by environmental factors that include childhood vaccines.

Id.

evidence without first determining whether regressive and classic autism have the same causes.

Nor, in petitioners' view, could the special master have rationally assessed Dr. Corbier's credibility or the appropriate weight to be given his testimony without first determining whether regressive autism is a separate phenotype from classic autism and correspondingly whether Yates's regression after receiving the MMR vaccination implicated environmental causes. Petitioners explain that if regressive autism is a separate phenotype with environmental causes, Dr. Corbier correctly characterized the fact that Yates regressed about a month after receiving the MMR vaccine as having "paramount" importance and the special master accordingly should have given his testimony considerably more weight. As petitioners observe, "treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" Capizzano, 440 F.3d at 1326 (quoting Althen, 418 F.3d at 1280).[33]

According to respondent, petitioners' contention that regressive autism is distinct from classic autism necessarily depends upon a finding that regressive autism has a distinct cause from classic autism. The problem with petitioners' argument, in respondent's view, is that it is circular: petitioners offered no credible evidence, either through their own expert witnesses or on cross-examination of Dr. Rust, to limit the applicability of Dr. Rust's testimony to classic autism and offered no

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[33] The Federal Circuit reached a similar conclusion in Andreu, a decision issued one week after the oral argument in this case. Andreu, 2009 WL 1688231. In Andreu, the court found that the special master had erred by failing to give sufficient weight to the testimony of a treating physician. Id. at *5. (Like Dr. Corbier, Yates's treating neurologist, the treating physician in Andreu concluded that a link existed between the vaccine and the asserted injury because no other causes were found and a close temporal relationship existed between the vaccination and the onset of the injury. See Hazlehurst Tr. at 299; Andreu, 2009 WL 1688231, at *6.)

Although the Andreu holding would appear to strengthen petitioners' case, the decision is distinguishable in at least one key respect: while the respondent in Andreu acknowledged that the petitioner had presented a biologically plausible medical theory (i.e., satisfying the first prong of the Althen standard), respondent in the instant case has made no such concession. Indeed, respondent's expert Dr. MacDonald, when asked about the plausibility of petitioners' medical theory, testified that it was "fantastic, improbable and . . . most importantly not based on any data." Hazlehurst Tr. at 643A . Similarly, Dr. Griffin, when asked whether measles virus in the gut tissue could move through the blood into the brain as petitioners theorized, responded: "I just don't see why that would be happening." Cedillo Tr. at 2782A.

reliable evidence of distinct causes of regressive autism. Respondent thus contends that petitioners fault the special master for failing to draw a distinction about the neuroanatomy of regressive autism that the scientific community has not recognized and petitioners have not proved. Finally, respondent asserts that whether regressive autism is a separate phenotype has no bearing on Dr. Corbier's credibility or on the weight to be given his testimony. In respondent's view, the special master gave Dr. Corbier's opinion little weight because she had concluded that the evidence underlying it was unreliable.

The special master addressed this issue as follows:

> Petitioners argue that because the body of epidemiological evidence to date has focused on autism in general and not on the regressive form of autism in particular, the conclusions of the discussed and cited studies have limited relevance to petitioners' [omnibus proceeding] claims.
>
> The undersigned finds petitioners' contention unavailing. . . . [M]ultiple epidemiological studies of different populations by different researchers using different study designs have failed to show an association between the MMR vaccine, thimerosal-containing vaccines, the onset of autism, and the development of gastrointestinal symptoms. That the collective body of epidemiological evidence has consistently failed to show any association makes petitioners' claims of a causal relationship less likely. Moreover, even if many of the conducted studies were not designed to examine whether an association exists between regressive autism and the vaccines of interest in this litigation, at least two of the conducted studies specifically looked for an association between the MMR vaccine and the development of regressive autism and found none.

Hazlehurst, 2009 WL 332306, at *39.

Contrary to petitioners' assertion, Dr. Rust in fact distinguished between classic and regressive autism,[34] but did not attribute the significance to this distinction that petitioners urge. Asked about Dr. Corbier's theory regarding the effect of environmental factors on the development of regressive autism, Dr. Rust testified that "the emerging view of autism as I've described is the working out of a genetic development of brain that doesn't develop properly, and the degree of that

[34] Dr. Rust testified that classic and regressive autism were "not entirely distinct from each other," but are "distinguished from one another very reliably by the fact that children [with regressive autism] are not so severely impaired as those children [with] classic autism." Hazlehurst Tr. at 543A–44A.

abnormality helps to differentiate the time of the onset of subtypes of autistic disorders." Hazlehurst Tr. at 527A–28A. Further, when asked directly if there are different genetic or environmental factors involved in the causation of classic versus regressive autism, Dr. Rust responded that he did not "think that environmental factors are involved at all in any way." Hazlehurst Tr. at 550A.

Given the above, we can find no fault with the special master's declining to draw a distinction between classic and regressive autism that the scientific community itself has not identified and for which petitioners have offered no proof. The special master found that petitioners had failed to offer persuasive evidence that the MMR vaccine causes any type of autism and therefore did not need to determine whether regressive autism has a different cause than classic autism. That conclusion, we believe, was entirely proper.

CONCLUSION

In hearing this appeal, the court is not without sympathy for Yates, the Hazlehursts, and the other children and families dealing with autism and autism spectrum disorders. And this court, like the special master, acknowledges both the burdens many of these families have faced and the tremendous love and support they have shown their children. The facts, however, do not support petitioners' appeal and we have no choice but to deny their motion. Accordingly, for the reasons set forth above, the special master's decision of February 12, 2009, is AFFIRMED.

s/John P. Wiese
John P. Wiese
Judge