

**The CDC finances, writes and helps publish Danish research
Another useless CDC-supported autism study**

Study & Year	Lead Author	Subject	CDC-Funded	CDC-Authored
DS 2002	Madsen	MMR	YES	YES
DS 2003 A	Madsen	Thimerosal	NO	NO
DS 2003 B	Hviid	Thimerosal	NO	NO
DS 2004	Lauritsen	Incidence	NO	NO
DS 2005	Larsson	Causes	YES	YES

Reviewed Danish Studies (DS)

On May 16, 2005, an official request that I had submitted to Dr. Harvey V. Fineberg, President of the Institute of Medicine (IOM) was made public: To retract the report of the Immunization Safety Review Committee Meeting of February 9, 2004, to form a new committee and to reconvene meetings on vaccines and autism. (1, 2)

Also on May 16, the Centers for Disease Control and Prevention (CDC) posted on its website a press release entitled “**Parent, Pregnancy, and Birth Factors Found Possible Associations with the Risk of Autism**” to report the findings of yet another CDC - supported study from Denmark. **[Exhibit I]** Both the press release and the latest “National study” have garnered little attention so far. It is entirely possible that by now people in the United States, where 1 in 166 children has been diagnosed with an autism / autism spectrum disorders (ASD), are bored and rightfully upset at seeing their hard-earned tax dollars wasted to gather irrelevant information about **698** Danish children with autism born after 1972 and diagnosed before 2000.

Denmark’s present population is 5 to 5.5 million, approximately the population of Maryland where in school year 2003-2004, there were 3,536 students age 6 to 21 and 548 students aged 3 to 5 with autism and ASD. (3, 4)

Of these 4,084 children registered with the Maryland Department of Education (DOE) last year, it is likely that about one third or approximately **1360**, had autism (299.00) based on an Institute of Medicine (IOM)-accepted review that estimated that among 194,650 US students under age 18 in 2000, there were 70,782 with autism, 17,696 with Asperger’s syndrome and 106,173 with PDD-NOS or Pervasive Developmental Disorders- Not Otherwise Specified. (5)

Only 595 and not all 698 Danish subjects were included in the “adjusted analysis”. In other words, the total number of individuals with autism born over a quarter century and reported in the latest CDC-sponsored “Danish National Study” was about half the number of students with autism (299.00) who attended school in Maryland in 2004.

The following figures from the California Department of Developmental Services (DDS) help place the scope of the recent Danish study even more in perspective (6): *“From December 1998 to December 2002, the population of persons with autism in California's Developmental Services System nearly doubled. This unprecedented 97 percent increase in four years did not include children less than three years of age, persons classified with less common forms of autism, or persons who are suspected of having autism but are not yet diagnosed. The total number of persons with autism served statewide increased from 10,360 in December 1998 to 20,377 in December 2002.”*

In the recent press release, José Cordero MD, MPH, Director of CDC's National Center on Births Defects and Developmental Disabilities was quoted as saying: *“This study is a helpful step forward in identifying possible risk factors for autism...It also indicates there may be some children for whom we need extra vigilance in watching for signs of developmental delay. In recent years, many programs and studies have found that early recognition of autism and other developmental disabilities is important because early treatment can significantly improve a child's development.”* Without once mentioning the Measles, Mumps and Rubella (MMR) vaccine and Thimerosal, a mercury preservative, Dr. Cordero who had recently moved from the CDC's National Immunization Program (NIP) cleverly ruled them out by focusing attention on familial and perinatal findings in Denmark since the seventies that he deemed relevant to the present US situation.

The causes of Regressive Autism will eventually be revealed and MMR vaccination and Thimerosal will be listed among the many environmental factors that can precipitate autistic regression in certain genetically predisposed children who have deficient or defective detoxification mechanisms. Most people at the IOM and the CDC are or should be well aware that like a pregnancy, that fact is getting harder to hide - for much longer. Obviously until then, the cover-up will go on, total denial will be the rule and much effort will be spent to publish irrelevant studies.

Because there are so many epidemiological studies from Denmark and to avoid confusion, this recent study will be referred to as **DS 2005** for Danish Study 2005.

A previous CDC-supported Danish study published in the New England Journal of Medicine (NEJM) on November 7, 2002 (7) had been received with much more fanfare and referred to, at the time, as “The Big Study from Denmark” and the “Definitive Madsen MMR study”. It will be referred to here as **DS 2002**. The study, like **DS 2005**, was co-authored by the CDC's own Dr. Diana Schendel. When that study manuscript was submitted for consideration, it was accompanied by a cover letter signed by Dr. Madsen and each of his co-authors [**Exhibit II**] in which they said in part:

1. “So far, no study has had sufficient power to address this topic”– i.e. Earlier studies by Dales, Kaye, Peltola, Taylor and others “could not have ruled out” an MMR-autism connection in spite of all the publicity they had received, mostly by the CDC. Dr. Robert Chen, who had praised these studies as they were published, did not take issue with Dr. Schendel's statement, so far.

2. “It has been suggested that the measles-mumps-rubella (MMR) vaccine may cause autism. If true, this could jeopardize the MMR vaccine program in children.” Intimated: “The MMR vaccination program must be safeguarded even if Wakefield is right and MMR vaccination indeed precipitates some cases of Regressive Autism.”

3. “We declare that there is no conflict of interest in connection with this paper”. It is hard to understand how a conflict of interest does not exist when the study was financially supported by the CDC, the US Agency that promotes vaccination, when a co-author was a CDC employee and when the Danish authors either worked for a vaccine manufacturer or in related agencies. Of note is the fact that in 2004, the editor of the Lancet was harassed and urged to retract a 1998 publication by Andrew Wakefield because a one-time grant to the Royal Free Hospital, where Wakefield worked, gave the “appearance” of a potential conflict of interest.

Madsen’s statistical analysis in **DS 2002** was immediately questioned by Dr. S. Suissa, a respected McGill epidemiologist. Unfortunately her letter to the NEJM was never published and the Madsen MMR study enjoyed a prolonged period of acceptance: It influenced the outcome of the IOM Immunization Safety Review Committee Meeting of February 9, 2004 and helped sabotage the MMR litigation in the United Kingdom.

In September 2004, an original investigation by Goldman and Yazbak (8) in the Journal of American Physicians and Surgeons highlighted some concerns and deficiencies pertaining to the Madsen MMR study. A statistically significant increase in autism had, in fact occurred from 1990 to 1992 after the introduction of the triple vaccination and prior to the advent of a new classification and changes in enrollment in the Denmark registry.

Because of its design--not separating those children born with autism from those that developed late-onset autism, the Madsen study was unable to really measure autism in the latter cohort. Additionally, Madsen could not have included all the children with autism who had received the MMR vaccine, as autism is diagnosed in Denmark around the age of 5 and many children enrolled in the study were followed for a shorter period.

In an invited commentary in the same issue of the Journal, Stott, Blaxill and Wakefield (9), revealed for the first time that Professor Suissa’s epidemiological analysis had disagreed with Madsen’s conclusions. Dr. Stott and associates also supported the fact that autism had increased in Denmark--corresponding to increasing coverage following the introduction of MMR vaccination in that Country.

In still another letter to the editor in the following issue of the Journal of American Physicians and Surgeons, Trelka and Hooker systematically discussed additional problems with the Madsen methodology and analysis that severely limited any conclusions drawn by such analysis. (10)

Though invited, Dr. Madsen chose not to respond.

Because **DS 2002** had been published in the New England Journal of Medicine, it was appropriate to respond to it in the same journal. When Dr. Goldman submitted our manuscript for publication in 2003, it was promptly turned down and we were told that: *“The decision here was on editorial grounds, not on the methodology or conclusions of your analysis.”*

On November 25, 2003, I faxed a personal letter to Edward W. Campion, MD, Senior Deputy Editor of NEJM asking him to reconsider [**Exhibit III**]. I wrote in part: “By publishing the Madsen paper, The New England Journal of Medicine endorsed its findings, and your support immediately granted the study recognition as credible research...I respectfully submit that both your editorial fairness *and* search for the truth on this important debate will be better served should you accept to reconsider your decision...Wouldn’t you like to be part of the solution rather than part of the problem?”

As a Massachusetts physician and because the NEJM is owned and published by the Massachusetts Medical Society, I expected at least a response or some acknowledgement. I never received either.

José Cordero MD, MPH, Director of CDC’s National Center on Births Defects and Developmental Disabilities, who is now publicizing **DS 2005**, was intimately involved with **DS 2002**, the Madsen **MMR** Study, literally since its “conception”.

In an e-mail on Tuesday, May 30, 2000 at 2:36 PM, (**Exhibit IV**) Dr. Marshalyn Yeargin-Allsopp, a CDC epidemiologist wrote to Dr. Cordero, at the time the Deputy Director of the National Immunization Program (NIP) of the CDC:

“Jose,

As we discussed on Friday, we have become aware through Poul Thorsen of an exciting opportunity to study the role of MMR vaccine and autism using several registries/existing studies and the repository of biologic specimens and laboratory capabilities in Denmark. Attached below is a proposal for such a study. Poul will be leaving on Thursday to travel to Denmark where he will be meeting with the PIs for the proposed study on June 6th. We would like to be able to have Poul say whether it is likely that CDC (NIP) can fund the study, if NIP is interested. The proposed budget is included; there may be additional sources of funding (in addition to NIP) but we are not certain at this time. Unfortunately, the DD Branch does not have much (if any) \$\$ to fund the study, but we do have the expertise that we have developed due to the autism surveillance in Atlanta and the MMR/autism case-control study. I will be out of the office tomorrow, but you may contact Diana or Poul if you have questions. Thank you so much for considering this proposal. Marshalyn.”

Monday May 29, 2000 was Memorial Day. “PIs” refers to Principal Investigators. The CDC describes the National Immunization Program *“Leading the way to healthy lives”* as follows: *“As a disease-prevention program, NIP provides leadership for the planning, coordination, and conduct of immunization activities nationwide”*.

The NIP Mission is described in 145 words that do not include the word autism. (11)

It is evident from the above e-mail that:

- The “proposed” study had already been planned and discussed in Denmark, at the DD (Developmental Disabilities) Branch of the CDC and with key NIP people
- Dr. José Cordero had the authority to promptly approve NIP funding of the “autism” study
- Dr. Cordero who was responsible for the “*planning, coordination, and conduct of immunization activities nationwide*” could not possibly appropriate funds - or in any way support a study - that COULD potentially have compromised the MMR vaccination program
- Before the study was started, it was guaranteed NOT to find any connection between MMR and regressive autism.

Drs. Diana Schendel, a CDC epidemiologist (Diana) and Dr. Poul Thorsen (Poul) went on to co-author the study in question.

It is no wonder at all then that **DS 2002** that was

1. Funded by the CDC
2. Co-authored by a CDC epidemiologist
3. And evidently supported by the CDC’s “*expertise that we have developed due to the autism surveillance in Atlanta and the MMR/autism case-control study*” did indeed conclude that MMR did not cause autism in Denmark and did justify the CDC’s financial investment.

The “additional source of funding” in the US was the National Alliance for Autism Research (NAAR). The organization has asserted: “To be clear, our unrestricted donation of \$25,000 from Merck in 2000 was not used to fund the Danish study – or any other vaccine-related studies.” (12)

In a follow-up e-mail on June 1, 2000 at 12:41 PM [Exhibit IV] Dr. Frank Destefano wrote: “**I hadn’t seen it but it looks like a good opportunity. The availability of data from pregnancy, as well as blood specimens, is particularly attractive. The blood spot component would be very valuable just by itself to try to confirm the exciting findings from the small NIH study. If these are true biomarkers for autism, it would be great to see if they identify high risk groups of kids for a vaccine-autism association. In addition to MMR, the study should include all infant and childhood vaccines to look at issues of multiple antigens, vaccine additives, etc. Serologies for measles and rubella in the maternal and cord blood might also be worth considering.**”

In these few lines, written in June of 2000 and revealed here for the first time, Dr. Destefano enumerated succinctly the important aspects of **clinical autism-related MMR and vaccine research, as it should have been done with the support of the CDC**. If others at the CDC had listened to him then, we could have had – by now - an answer to

the mystery of regressive autism. Instead, in order to exonerate the MMR vaccine, the CDC invested time and money to finance an irrelevant and flawed epidemiological study forgetting that even the BEST epidemiological study – which the Madsen study was not - could not prove a negative: That MMR does not cause autism.

A few days after the Destefano e-mail, on June 12 and 13, 2000 to be exact, the American Academy of Pediatrics (AAP) held an important conference “New Challenges in Childhood Immunizations” in Oak Brook, Illinois to which many CDC representatives, including Dr. DeStefano were invited. (13) Dr. Wakefield could not attend and forwarded his information to the conference. My presentation, a preliminary report, was entitled “Maternal vaccination before, during or after pregnancy predisposes to Autism: A hypothesis”. That research was later peer-reviewed and published. (14, 15)

Marie Bristol-Power PhD, Co-ordinator, Network of the Neurobiology and Genetics of Autism, National Institute of Child Health and Human Development, National Institutes of Health could not personally appear but she addressed the Conference by telephone and was kind enough to comment favorably on my research. On June 18, 2000 she also testified before the Committee on Government Reform, U.S. House of Representatives on the controversy surrounding MMR, IBD and autism. Dr. Bristol-Power said in part: *“Recent reports in the literature and testimony before this Committee have raised the possibility of a link between vaccines, especially the MMR vaccine, and regressive autism, a particular concern given the importance of vaccines to the health of America’s children. A related concern has been raised about the possibility of a link between mercury and autism resulting from exposure to preservatives such as thimersol in cumulative infant vaccinations.”* Dr. Bristol-Power then described the planned NIH research: *“Group comparisons (early onset autism, regressive autism, and normal development) will include presence/absence/duration of normal development, age at regression, vaccination histories of children and of mothers (i.e., maternal vaccination before, during, or after pregnancy), measles antibody levels, and association of vaccine additives and autism. The study provides for independent, blind assessment of laboratory samples.”*(16)

Unfortunately, Dr. Bristol-Power’s proposed research of the environmental factors of regressive autism came to a screeching halt when she became unable to fight for its survival. The generously- supported “genetic” research went on as usual with no one realizing that genetics do not cause epidemics. A multitude of marginal epidemiological studies supporting vaccinations, were ordered and produced at a dizzying speed, applauded for a few weeks before being discarded. Meanwhile Wakefield’s study of twelve was surviving and its findings were duplicated by many other scientists.

A month after the publication of the Madsen MMR study in the NEJM, and apparently gratified with its immediate and immense success, Dr. Jose Cordero, now the Director of the National Center on Births Defects and Developmental Disabilities, the CDC division responsible for autism research, decided that it was time to demolish the “other vaccine-autism issue”: Thimerosal.

In a personal letter to Jerold F. Lucey, MD, FAAP, Editor in Chief of PEDIATRICS, dated December 10, 2002, [Exhibit V] Dr. Cordero wrote:

“Dear Dr. Lucey

I am writing in support of an expedited review and consideration of the enclosed manuscript that examines the association between thimerosal, an ethyl mercury containing preservative, and autism. As you may know, there has been considerable interest by parents, clinicians, educators and policy makers for an explanation of the marked increase in the rate of autism in recent years... One factor hypothesized to have a causal role is childhood vaccinations. Specific aspects of vaccinations that have been subject to inquiry include the MMR vaccine and thimerosal. There are now numerous epidemiologic studies to suggest that the MMR vaccine is not associated with the risk of autism; an Institute of Medicine review that was published in 2000 concluded that the weight of the scientific evidence did not support a link between MMR vaccine and autism. For thimerosal, however, there are limited data to evaluate this factor.”

Dr. Cordero ended his letter by stating: **“I feel this is a very important study that deserves thoughtful consideration by the Journal. Its findings provide one strong piece of evidence that thimerosal is not causally linked to autism. Thank you for your timely consideration.”** The letter was signed José.

The Madsen Thimerosal study in question (**DS 2003 /A**) was published in PEDIATRICS in September 2003 (17). It was co-authored by M.B. Lauritsen, C.B. Pedersen, P. Thorsen, A.M. Plesner, P.H. Andersen, and P.B. Mortensen. It essentially concluded that thimerosal could not possibly be the cause of autism because in Denmark *“From 1991 until 2000 the incidence (of autism) increased and continued to rise after the removal of thimerosal from vaccines, including increases among children born after the discontinuance of thimerosal ...The discontinuation of thimerosal-containing vaccines in Denmark in 1992 was followed by an increase in the incidence of autism.”*

MMR vaccination was introduced in Denmark in 1987 and became widely used by 1991-1992. The argument used by Madsen to rule out a thimerosal connection, the sustained increased incidence of autism after 1991, could certainly suggest an MMR connection, as later demonstrated by Goldman and Yazbak. While Madsen asserted that neither MMR (2002) nor Thimerosal (2003) caused autism, he did not volunteer an alternate cause for the increase in autism in Denmark in the nineties.

On September 2, 2003, SafeMinds Director Mark Blaxill, described **DS 2003/A**, the Madsen Thimerosal study, as misleading and uninformative. He started: *“A report by Madsen et al. published by the American Academy of Pediatrics in their journal Pediatrics claims to provide evidence against a link between autism rates and the mercury in thimerosal, a preservative used in childhood vaccines. Unfortunately, the study analysis is full of flaws and inaccuracies, invalidating the conclusions regarding*

thimerosal. The study adds little of value to the scientific literature on autism and mercury.”

Blaxill went on to describe all the mercury study problems carefully and ended by stating *“In summary, the report by Madsen et al. appears to be an attempt to present selectively chosen data that provide support for policy choices in which the authors and their collaborators are involved. Once again, rather than seriously evaluating the autism-mercury hypothesis and carrying out the research agenda specified by the Institute of Medicine in 2001, public health authorities (now teamed with a Danish vaccine manufacturer) have chosen to issue another piece of propaganda masquerading as science, with the only possible outcome being that legitimate research and discussion might be suppressed. We sincerely hope that well-informed scientists and public officials will note the flaws in this report and be motivated to conduct the recommended investigations into the autism-mercury connection, which still await completion.”* (18)

In spite of Blaxill’s accurate review, the IOM Immunization Safety Review Committee at its February 9, 2004 meeting ruled out a thimerosal-autism connection on the basis of that particular Madsen publication and four other - just as questionable - epidemiological studies.

At the Autism One Conference on May 29, 2004, Congressman Dave Weldon MD (19) commenting on **DS 2003/A** by Madsen stated: *“...Again, the relevance of the Danish experience to the U.S. experience is limited in that the Danish population is genetically homogenous and had significantly lower thimerosal exposures than children in the U.S.*

Let’s consider the conflicts of interest with this study. First of all, two of Madsen’s coauthors are employed by the Staten Serum Institute. Additionally, like Hviid, two of Madsen’s coauthors work directly for the Staten Serum Institute (SSI) – the Danish vaccine manufacturer which exports vaccines and vaccine components to the U.S. and which faces liability if an association is found. Madsen works for the Danish Epidemiology Science Center – which is affiliated with SSI.

This study, like Hviid, added outpatient cases into the number of cases of autism after 1995. The authors acknowledged that this addition might have exaggerated the incidence of autism after the removal of thimerosal. The IOM acknowledged that this limits the study’s contribution to causality.”

DS 2003/B, the thimerosal study by Hviid to which Dr. Weldon alluded was published in the October issue of JAMA, the Journal of the American Medical Association. (20). The Danish studies had now “made it” to all three major and most read US Medical Journals. To have essentially the same information by the same group, based on the same conflicted foreign data published back to back in Pediatrics and JAMA may be the CDC’s most remarkable “coup de force” yet.

Hviid, Wohlfahrt and Melbye, who had co-authored two MMR studies with Madsen, **DS 2002** and a follow-up study published in a Danish Journal in December 2002, stayed

away from the PEDIATRICS **DS 2003 /A**, passing under the radar screen and making it to JAMA (**DS 2003 /B**) just a month later.

In **DS 2003 / B**, Hviid found that: *“The risk of autism and other autistic-spectrum disorders did not differ significantly between children vaccinated with thimerosal-containing vaccine and children vaccinated with thimerosal-free vaccine...Furthermore, we found no evidence of a dose-response association...The results do not support a causal relationship between childhood vaccination with thimerosal-containing vaccines and development of autistic-spectrum disorders.”*

Always alert, the Safeminds parents promptly demolished the Hviid JAMA study, its methods, inconsistencies and results. They concluded: *“The **Hviid et al** finding of lower autism rates with thimerosal exposure is likely due to errors in record keeping in the registry data set. Another approach to analyzing the same data, which adjusts for lack of outpatient records, has found a **3-fold increase** in autism incidence with thimerosal exposure. The Denmark autism registry has large variability in the nature of its records and utilization of the data set for epidemiological analysis is prone to bias. Use of this data to investigate the role of vaccines in autism should be conducted by researchers unconnected to vaccine manufacture or promotion.”* (21)

Commenting on **DS 2003/B**, Congressman Weldon (19) said: *“Let’s consider first the conflict of interest of the principal author. Hviid works for the Danish Epidemiology Science Center which is housed at the Staten Serum Institute (SSI) the government owned Danish vaccine manufacturer. Also, all of his coauthors either work with him at the Center or are employed by SSI. Staten Serum Institute (SSI) makes a considerable profit off the sale of vaccines and vaccine components and the U.S. is a major market for SSI.SSI has \$120 million in annual revenues and vaccines are the fastest growing business segment accounting for 80% of its profits. Both the U.S. and U.K. are important export markets for SSI’s vaccines and vaccine components...Yet even with these serious limitations, the committee concludes that this study has a ‘strong internal validity,’ finding an increase in autism after removal of thimerosal.”*

It is unlikely that the readers of PEDIATRICS and JAMA realized the significance of Madsen’s and Hviid’s conflicts (more on that later). On the other hand, it is more than likely that the CDC and the Chairperson of the ill-fated IOM Immunization Safety Review Committee Meeting of February 9, 2004 were well aware of every detail of the situation.

DS 2004

There was indeed an indirectly-related Danish study published in Psychological Medicine in 2004: **“The incidence and prevalence of pervasive developmental disorders: a Danish population-based study”** (22). It was written by M.B.Lauritsen , C.B.Pedersen and P.B.Mortensen and reported that: *“A total of 2061 children younger than 10 years of age were identified as having childhood autism, atypical autism, Asperger's disorder, or*

PDD-NOS. From 1971 to 2000, 759 children (78% males) were diagnosed with childhood autism, and 285 (73% males) were diagnosed with atypical autism. From 1994 to 2000, a total of 419 children (94% males) were diagnosed with Asperger's disorder and 806 (82% males) with PDD-NOS." The authors found that "the estimated prevalences of the PDDs studied were probably underestimated..." Pedersen had co-authored **DS 2003 A** and Mortensen co-authored both **DS 2003 A** and **DS 2005**.

The same authors, Marlene Briciet Lauritsen, Carsten Bøcker Pedersen and Preben Bo Mortensen of the Centre for Basic Psychiatric Research, Psychiatric Hospital in Aarhus, Aarhus University Hospital, Denmark; National Centre for Register-based Research, University of Aarhus, Denmark published another related study (23) "**Effects of familial risk factors and place of birth on the risk of autism: a nationwide register-based study**" in the Journal of Child Psychology and Psychiatry in March 2005. In that study they concluded: "The highest risk of autism was found in families with a history of autism, or Asperger's syndrome and other PDDs in siblings, supporting the commonly accepted knowledge that genetic factors are involved in the etiology of autism."

Two months later, Preben Bo Mortensen with others was publishing **DS 2005** and relating autism to mental illness, breech delivery and APGAR scores.

The CDC-funded / co-authored Danish Study of 2005

The most recent Danish study is entitled "**Risk factors for autism: Perinatal Factors, Parental Psychiatrist History, and Socioeconomic Status**". It was published in the latest issue of the American Journal of Epidemiology, Volume 161 No. 10 copyright © 2005 by the Johns Hopkins Bloomberg School of Public Health.

Parting with tradition, the CDC press release did not once quote the lead author nor list the authors' names. They are: Heidi Jeanet Larsson, William W. Eaton, Kresteen Meldgard Madsen, Mogens Vestergaard, Anne Vingaard Olesen, Esben Agerbo, Diana Schendel, Poul Thorsen and Preben Bo Mortensen. Dr. Eaton is associated with the Department of Mental Health at the Bloomberg School of Public Health, Johns Hopkins University. As previously mentioned CDC's Dr. Diana Schendel together with Drs. Poul Thorsen and Mogens Vestergaard had also co-authored **DS 2002**, the CDC-NAAR funded Madsen MMR-study.

DS 2005 was received for publication February 6, 2004 and accepted August 11, 2004. It is possible that the study was commissioned and the funding promised by the National Center on Births Defects and Developmental Disabilities before the arrival of Director Gerberding to the CDC.

It is not known whether Dr. Cordero tried to get this latest epidemiologic essay published in a more "popular" journal and was turned down, before Dr. Eaton submitted it to the American Journal of Epidemiology at Johns Hopkins. Logically the CDC would have

wanted pediatricians, family practitioners and pediatric nurse practitioners - and not only epidemiologists - to know the results of its most recent “supported research”. Clinicians would be the ones who need to be convinced that breech presentation and the parents’ psychiatric health of a few children in Denmark in the seventies and eighties are relevant in the United States where there were 140,920 children aged 6 -21 years and 22,724 children 3 to 5 year-old registered in schools in 2004. (3, 4)

The latest CDC Danish study did not need to discuss vaccines and preservatives because the IOM special committee on vaccines and autism had declared the subject closed in February 2004 and certainly no one needed to be encouraged to revisit that subject again.

In his quiet press release, Dr. José Cordero, Director of CDC’s National Center on Births Defects and Developmental Disabilities was quoted as saying: *“This study is a helpful step forward in identifying possible risk factors for autism”*.

Interestingly, the authors of **DS 2005** concluded - in a statement that could even be understood by non-epidemiologists: *“Of the risk factors investigated in this study, parental psychiatric history was associated with the highest independent risk of autism. Parental psychiatric history was more common among the cases (17 percent) than the presence of one or more of the significant adverse perinatal risk factors: breech presentation, low APGAR score, and gestational age at birth of less than 35 weeks (13 percent). For only 2 percent of the cases, both risk factors were present. The results suggest that prenatal environmental factors and parental psychopathology are associated with the risk of autism and that these factors seem to act independently. Because none of the single significant risk factors found in this study were present in the majority of cases, we still have much to learn about the many different factors that contribute to autism and how they may potentially interact.”*

The authors’ above parting statement suggests that Dr. Cordero’s “helpful step forward” may just be a very small one and not a “giant step for mankind”.

It is interesting that the familial history of autistic disorders was not investigated and discussed in this study though Preben Bo Mortensen had just done so in the other Danish study that was published in the March 2005 issue of the Journal of Child Psychology and Psychiatry.

Study findings

Perinatal risk factors

Unadjusted analyses: There was an increased risk of autism with breech presentation, low APGAR score (7 or under) at 5 minutes, low birth weight (2500 grams or less), gestational age < 35 weeks and being small for gestational age. High parental age (mother 30 and older and father 35 and older) was also associated with increased risk.

Adjusted analysis: A total of 595 cases and associated controls (25 per case) were included in the adjusted analyses. The same perinatal factors were found to be associated with increased incidence of autism. An increased risk of autism was found in children born to mothers younger than 20.

Parental psychiatric history and socio-economic status

To be listed as having a psychiatric history, the parent must have had a psychiatric diagnosis recorded before the child had been diagnosed with autism. The involved parents were ranked with schizophrenia-like psychosis, affective disorder, substance abuse or other mental disorders.

Unadjusted analysis: There was an increased risk of autism associated with parental history of any psychiatric disease. Low parental income was associated with an increased risk of autism.

Adjusted analysis: There was a “substantial risk of autism” for children with parental psychiatric history of schizophrenia-like psychosis (RR = 3.44, 95% CI: 1.48, 7.95) and affective disorder (RR= 2.91, 95% CI: 1.65, 5.14). Parental wealth was not associated with a significant risk of autism.

Discussion of the findings by the authors

Usually in the discussion part of scientific papers, authors explain their findings and their relevance - in terms that can be understood.

The following portion of the “discussion” of **DS 2005** makes as much sense and has as much relevance to autism in the United States as the funding, design, research, results and reporting of the study: *“Although we observed a strong association between parental psychiatric history and autism, adding parental psychiatric history to the multivariable model had little impact on the association between the perinatal risk factors and autism, suggesting that these factors are independently associated with autism. In our data, the psychiatric diagnosis for the parents originated before the date of case diagnosis but not necessarily before the birth of the child; therefore the order of precedence in terms of etiology is uncertain. For example, autistic children of parents with a diagnosed psychiatric disorder may more likely to be identified and diagnosed than autistic children of parents without a psychiatric diagnosis. However, genetic links have been found between schizoid personality traits and autism (22, 36) and children of schizophrenic mothers are at increased genetic risk of schizophrenia and neurodevelopmental impairment (37, 38). The causal direction between autism and parental affective disorder, substance abuse, or other mental illness is less clear. Because genetic inheritance patterns may differ for mothers and fathers, it would be ideal to consider psychiatric history of the mother and the father separately. The number of affected parents was limited in this study, so we were unable to consider parental differences related to the risk of autism in the offspring. Genetic inheritance might be related to high parental age (39). However, our adjusted results showed no increased risk of autism*

associated with high parental age. We did not adjust for preeclampsia and smoking in our adjusted analysis; information on these factors was available for limited time periods only. Both of these factors are associated with reduced fetal growth (40, 41) and smoking may affect the behavioral outcome in childhood (42). The results from the unadjusted analyses showed only weak associations between autism and each of these two factors, which argues against a strong confounding effect. In contrast to previous studies, we were able to adjust for information about socioeconomic status. In the unadjusted analyses, the risk of autism was higher for those with less parental wealth; however after we adjusted for other variables, socioeconomic status-measured by either parental wealth or maternal education-did not have a significant effect. Adjustment for socio-economic status did not have any influence on the associations between perinatal factors and autism. Thus, socioeconomic factors play little or no role in the etiology of autism in Denmark, where access to the healthcare system is equally available for all and is free of charge.”

Relevance and comments

Parental psychopathology: Parents of children with autism have been blamed for everything: Mothers have been accused of being cold and distant “Refrigerator Mothers” and fathers were made to feel guilty because they were computer scientists, geeks and engineers. I am not an epidemiologist and I did not research the psychopathology of the many parents of children with autism whom I have met over the last few years but I am confident that very few if any had serious psychiatric problems prior to their child's birth or diagnosis and certainly nowhere near 17% of the total. I do not know how many parents Dr. Schendel has met personally but she could consider going to the next DAN meeting or Autism One Conference and finding out for herself how many parents had pre-existing psychiatric disturbances. Obviously parents who are living with and caring without respite for, one or two children with autism are understandably tired, frustrated, sad and sometimes depressed. Dr. Schendel should try spending a week or so with a seriously-affected child or an out-of-control young adult and find out for herself how easy it is to lose one's mind AFTER the child has regressed.

Parental socioeconomic status: We did not need to spend money and time in Denmark to know that in the United States autism is an equal opportunity offering and that African-Americans, Hispanics, Orientals, whites, the poor, the rich, those in the inner city and those in the up-scale suburbs are equally affected.

Perinatal factors

In the last few years in the United States, while autism was increasing dramatically, very few infants if any were delivered as a breech and almost all breech presentations were delivered by cesarean section. In addition, before Kanner, autism was unheard of, even in Denmark, regardless of the position at birth or the mode of delivery.

Prematurity is unfortunately increasing in the United States in spite of all efforts. According to Dr. Nancy S. Green, Medical Director of the March of Dimes (January 24,

2005) the number of women delivering prematurely in the United States increased by 29% between 1981 and 2002 when there were approximately 480,000 deliveries. Presently, about 12% of US deliveries are pre-term.

Dr. Green was quoted as saying: "Premature birth is now the number one health risk for America's newborns. It is the leading cause of death in the first month of life. Babies who survive often suffer lifelong consequences, including cerebral palsy, mental retardation, chronic lung disease, blindness and hearing loss". (24) It should be noted that Dr. Green did not mention autism.

Low APGAR scores indicate distress and compromise here, in Denmark and elsewhere.

There is no argument that any compromise around birth, whether the birth is pre-term or at full term, carries a developmental risk to the infant. The relevance of the very limited and antiquated Danish information can hardly be worth the effort and the whole exercise seems to be nothing but an expensive farce.

On the other hand, present clinical studies investigating the perinatal factors of autism - including and not limited to early clamping of the cord and the use of Pitocin - deserve the full support of the US Government.

Study references

To provide an aura of scientific value to their study, the authors of **DS 2005** listed 42 (Forty two) references. Except for a few, the references had little bearing to the findings.

In summary, the relevance of DS 2005 to the autism situation in the USA is nil.

General Discussion

The Danish numbers

It may or may not be intentional that epidemiological studies - including and particularly Danish ones - are so hard to understand: An example was quoted earlier. Numbers on the other hand should be clearly understandable and more importantly, they should match. In the autism Danish studies that were reviewed, they do not seem to.

In **DS 2002**, the MMR study, Madsen reported that among children born in Denmark from January 1991 through December 1998 (8 years- 537,303 children and 2,129,864 person-years), there were 316 with autism and 422 with ASD. His co-author Hviid stated in his own **DS 2003 / B** that among Danish children born from January 1990 through December 1996 (7 years – 467, 450 and 2,986, 654 person-years) there were 440 with

autism and 787 with ASD. Keeping in mind that even Madsen stated that the incidence of autism and ASD increased after 1991, it is difficult to explain how Hviid's earlier and smaller sample contained 39% more cases of autism and 86% more cases of autistic spectral disorders.

In October 2003, Madsen, Lauritsen, Pedersen, Mortensen et al reported in **DS 2003 A**: "*A total of 956 children ...had been diagnosed with autism during the period from 1971-2000.*"

In October 2004, Lauritsen, Pedersen and Mortensen stated, in **DS 2004**: "*From 1971 to 2000, 759 children were diagnosed with childhood autism...*" or 26% fewer children.

The above inconsistencies are significant. It is not clear how the same authors looking at the same data and using the same criteria of case selection can get such different results. What is evident is that, as they stand, these results are unacceptable. There is therefore an urgent need for an official investigation of the accuracy of the data extraction to find out which results were wrong or whether they were ALL wrong.

A review of other Danish studies reveals inconsistencies in the number of cases that may or may not be due to the studies' cut-off dates and the age range of the included cohort. They too should be reviewed by an independent panel.

The conflict of interest issue

The organizations

Danish Epidemiology Science Centre (DESC): A total of 50 (FIFTY) researchers are employed at or affiliated with the DESC. The main center is situated at Statens Serum Institut (SSI), Copenhagen. There are smaller centers at the Institute of Epidemiology & Social Medicine, University of Aarhus (Medicine) and at the Institute of Preventive Medicine, University of Copenhagen. (25, 26)

National Centre for Register-based Research at the University of Aarhus, Aarhus.

Statens Serum Institut (SSI): According to its "Mission Statement" SSI prevents and controls infectious diseases and congenital disorders. The Institute's expertise includes: "*-Monitoring, advising and teaching on the incidence, prevention and treatment of infectious diseases and congenital disorders - Specializing in the diagnosis of infectious, autoimmune, congenital and genetic diseases – Ensuring the supply of vaccines, other biological products and diagnostic services through production and procurement – Preparedness against biological terrorism - Research and development in the Institute's area of activity at an international level.*"

The "Institute", a state-owned for-profit enterprise with about 1100 employees, researches, produces, sells and exports vaccines and biologicals. Unlike vaccine manufacturers in the United States, it is not protected from litigation. Its 2004 Annual

Report (27) is 55 pages long and the financial statements can be found on pages 26 - 31. Between 2000 and 2004, the Institute's net revenues increased from 759.4 million to 979.9 million DKK (29 %) and its share of exports increased from 22 to 30% of total sales. Its 2004 net income was DKK 11.7 million, an increase of DKK 7.6 million (185%) over 2003 "*and higher than expected.*" The US Dollar is slightly more than six Danish Kroners.

The authors' affiliations

Madsen (DS 2002, 2003 A, 2005), Thorsen (DS 2002, 2003 A, 2005) Vestergaard (DS 2002, 2005) are employed at the Danish Epidemiology Science Centre (DESC), University of Aarhus where Jorn Olsen, MD is Director (DS 2002)

Hviid (DS 2002, 2003 B) and Wohlfart (DS 2002, 2003 B) work at DESC at the Department of Epidemiology Research, Statens Serum Institut (SSI) where Mads Melbye, MD (DS 2002, 2003 B) is in charge.

Mortensen (DS 2003 A, 2005) and Pedersen (2003 A) are employed at the National Centre for Register-based Research at the University of Aarhus.

Andersen (DS 2003 A) and Plesner (DS 2003 A) are members of the Department of Medicine at SSI where Michael Stellfield, MD (DS 2003 B) is the Department Head.

Dr. Diana Schendel is an employee of the National Center on Births Defects and Developmental Disabilities, Centers for Disease Control and Prevention.

The Danish studies and Autism Research

As incredible as it sounds, Danish studies 2002, 2003 A and 2003 B were efficiently used to directly convince some, including the IOM Special Committee on Immunization, to decree that a vaccine – autism connection did not exist, that MMR and Thimerosal research should cease and that further research should be directed elsewhere.

The IOM special committee did not need much convincing.

The Centers for Disease Control and Prevention and the National Institutes of Health **commissioned** the Institute of Medicine to review vaccines safety concerns relative to autism. A special committee was formed under the chairmanship of Marie McCormick, M.D., Sc.D., of the Harvard School of Public Health and met at regular intervals with the last meeting being that of February 9, 2004. (1) The reports of the "open meetings" of the committee are available on the IOM web site.

As early as January, 2001, Dr. McCormick asserted at a closed meeting: "*We are not ever going to come down that it is a true side-effect.*"

At the same closed meeting, Kathleen Stratton, Ph.D., of the IOM and the Study Director, Immunization Safety Review Committee stated: *“We said this before you got here, and I think we said this yesterday, the point of no return, the line we will not cross in public policy is to pull the vaccine, change the schedule. We could say it is time to revisit this, but we would never recommend that level. Even recommending research is recommendations for policy. We wouldn’t say compensate, we wouldn’t say pull the vaccine, we wouldn’t say stop the program.”* Later, Dr. Stratton added: *“Chances are, when all is said and done, we are still going to be in this category. It is just a general feeling that we probably still are not going to be able to make a statement.”* (28)

In other words, as of January 2001, the marching orders were:

- The committee will never concede that a vaccine-autism connection exists, even if it does
- The committee will appease the parents and the public for a while: Exactly what happened from 2001 to 2004
- The committee will eventually reject the possibility of a vaccine-autism connection altogether: Again, exactly what happened in 2004.

The only way to achieve the last goal was to ignore Congressman Weldon’s request to the CDC Director and proceed with the February 9, 2004 meeting, accepting shabby and biased studies and ignoring reliable and convincing research supporting a vaccine connection. (1)

The pressure to publish and not to publish

Medical practitioners and other health professionals receive some of their continuing medical education from information provided in medical / nursing publications and lectures. When these are sponsored by drug and vaccine manufacturers or full of publicity ads, the readers and attendees expect some of the information to be slanted and exercise caution (or at least should) concerning what to or what not to believe.

When an article is published in leading medical journals, the readers are inclined not to question its contents because they are convinced that after all, peer review must have been careful and all conflicts must have been clearly divulged.

One expects to see the CDC discussing, planning and plotting damage control at a private meeting such as that at Simpsonwood. (29) One does not expect the CDC to be twisting the arms of the editors of our leading medical journals.

Whether Dr. Madsen, a Danish Epidemiology Science Centre employee at the University of Aarhus in Denmark wrote his cover letter to the NEJM on his own or not, the message from the CDC to the editor was clear: “We paid for this study and it must be published because if it is not, the MMR vaccination program will suffer and that must not happen - even if the MMR vaccine sometimes causes autism.”

Because of the exposure it received in the prestigious New England Journal of Medicine, the Madsen MMR study was universally acclaimed. Its national and international celebration was then perpetuated by the editors of the Journal refusing to publish Professor Suissa's timely, valuable and justified criticism. A year later, the investigation by Goldman & Yazbak was also summarily rejected "*on editorial grounds*" although the Journal frequently publishes critiques and discussions of published articles and provides the authors the opportunity to rebut.

It is unlikely that any article or research perceived to be critical of vaccination will be considered for publication in a major medical or nursing journal. The logic of such a blackout is hard to understand when the CDC urges pediatricians and family physicians to report reactions to the Vaccine Adverse Event Reporting System (VAERS) and inform parents of injured children that a National Vaccine Injury Compensation Program exists.

Dr. Jose Cordero's pressure on PEDIATRICS in regards to **DS 2003 A** appears even more problematic. By his strong support of that study -a non CDC funded or authored foreign scientific investigation that could not be adequately checked, Dr. Cordero who had left NIP to become the Director of the National Center on Birth Defects and Developmental Disabilities compromised himself as well as the distinguished Editor of PEDIATRICS and the American Academy of Pediatrics. As a Fellow of the Academy since 1963, I find that disturbing.

The role of the CDC

It is now evident that:

- At the Centers for Disease Control and Prevention in 2000, appropriation of funding for foreign research did not require a meeting, a discussion or a vote but could be secured via a short e-mail to the Deputy Director of the National Immunization Program.
- A blanket approval of any research was in place as long as funds were spent to safeguard the MMR vaccination program and deny an MMR-autism connection - even if such existed
- The CDC supported and requested the publication of a Danish study that was neither funded by US dollars nor co-authored by a US researcher because "*Its findings provide one strong piece of evidence that thimerosal is not causally linked to autism.*"
- An Epidemiologist from the National Center on Births Defects and Developmental Disabilities contributed to and co-authored **DS 2002**, the MMR study.
- The same epidemiologist co-authored the just released **DS 2005**, that was also supported by a grant from the CDC and investigated few, old and irrelevant factors, in a small Scandinavian country, that were unjustifiably perceived to be relevant to the present tragedy that is faced by the United States.

By financing, writing, encouraging and helping to publish said Danish studies, the Centers for Disease Control and Prevention through its employees, became responsible for their contents. If the involved CDC experts did not realize that these studies were flawed and irrelevant, we all have a problem. If they did, then we all have an even bigger problem.

Anyone in and out of the CDC who supported **DS 2002**, **DS 2003 A**, **DS 2003 B** and **DS 2005**, should accept the fact that they may have set autism research back and contributed to the misery of the many affected American children and their families since 2000.

If indeed a cover-up existed, at any level, it should be made public.

Conclusion

Full-scale investigations by the appropriate committees of the Senate and the House of Representatives are urgently needed to examine the present autism crisis, recommend corrective measures and support honest and ethical research into the many causes of autistic regression. No greater national emergency exists.

Exhibit I

<http://www.cdc.gov/od/oc/media/pressrel/r050516.htm>

Press Release

For Immediate Release
May 16, 2005

Contact: CDC Media Relations
404-639-3286

Parent, Pregnancy, and Birth Factors Found Possible Associations with the Risk of Autism

Pregnancy factors, parental psychiatric history, and preterm delivery may be associated with the risk of autism, according to a recent study supported in part by the Centers for Disease Control and Prevention (CDC). The study, "Risk Factors for Autism: Perinatal Factors, Parental Psychiatric History, and Socioeconomic Status," appears in the most recent issue of the American Journal of Epidemiology.

The research, which involved national study of all 698 Danish children with autism born after 1972 and diagnosed before 2000, focused on perinatal risk factors (i.e., delivery and newborn characteristics, pregnancy characteristics, and parental characteristics), parental psychiatric history (i.e., did a parent have a diagnosed psychiatric illness before the date that autism was diagnosed in the child) and socioeconomic status (i.e., the mom's formal education and parental wealth at the child's birth). Previous research had suggested each category may represent or include risk factors for autism.

"This study is a helpful step forward in identifying possible risk factors for autism," said Dr. José Cordero, director of CDC's National Center on Birth Defects and Developmental Disabilities. "It also indicates there may be some children for whom we need extra vigilance in watching for signs of developmental delay. In recent years, many programs and studies have found that early recognition of autism and other developmental disabilities is important because early treatment can significantly improve a child's development."

Some of the specific factors that the study found to be associated with the risk of autism included: breech presentation at birth, delivery before 35 weeks, a parent who had a diagnosis of schizophrenia-like psychosis before the date that autism was diagnosed in the child, and low birth weight at delivery. The study also found many of these factors were independently associated with autism. For example, there was an association between adverse pregnancy events and autism, regardless of whether one of the parents had a diagnosed psychiatric illness.

"We need to further investigate the role of events during pregnancy, including their possible interaction with genetic factors, to learn more about potential causes of autism," said Diana Schendel, CDC epidemiologist and one of the authors. "We also need additional research to determine if the factors identified here really play a role in causing autism. Right now, we have only identified possible associations. But if we can find a cause-and-effect relationship, it may help our efforts to prevent autism."

Autism spectrum disorders (ASDs) are a group of developmental disabilities that are caused by unusual brain development. People with ASDs tend to have problems with social and communication skills. Many people with ASDs also have unusual ways of learning, paying attention, or reacting to different sensations. ASDs begin during childhood and last throughout a person's life. CDC funds projects on autism spectrum disorders (ASDs) in several states. These projects track the number of children who have an ASD, conduct studies to find out what factors make it more likely that a child will have an ASD, and offer education and outreach programs for researchers, families, and other people affected by ASD. Large representative studies are needed to answer questions necessary to determine the potential causes of autism and develop prevention strategies for this disorder.

Exhibit II

The Editor
The New England Journal of Medicine
10 Shattuck St.
Boston
MA 02115
USA

Dear Editor,

Please find enclosed a manuscript entitled “**MMR vaccination and autism - A population based cohort study**” which we would like you to consider for publication in the *New England Journal of Medicine*.

It has been suggested that the measles-mumps-rubella (MMR) vaccine may cause autism. If true, this could jeopardize the MMR vaccine program in children.

The debate was initiated by research in Britain providing suggestive evidence of an association between the MMR vaccine and autism. Wakefield and colleagues described how 12 children developed behavioral problems, including autistic disorder, shortly after receiving the MMR vaccine. In addition, Uhlmann and colleagues recently published a study where they found measles virus in the gut in patients with developmental disorders but not in developmentally normal pediatric controls. These findings, combined with the more general concern that the introduction of wide-scale use of MMR coincides with an apparent increase in the incidence of autism, has led WHO and IOM to request further research into the association.

So far, no study has had sufficient power to address this topic nor had a population-based design.

We evaluated the suggested association based on a population-based cohort design comprising all children in Denmark born from 1991 through 1998. The study gave no support for an association between MMR vaccination and autism or autism-like conditions. Taking into account the size and nature of the study, which ruled out potentials for bias effects, we believe that these results may significantly contribute to the public health debate on this issue.

These results are not being considered for publication elsewhere. All authors have contributed substantially, and have approved the final version of this paper. We declare that there is no conflict of interest in connection with this paper.

Sincerely yours,

Kreesten Meldgaard Madsen, M.D.

Jan Wohlfahrt, M.Sc

Anders Hviid, M.Sc.

Poul Thorsen, M.D.

Mogens Vestergaard, M.D.

Jørn Olsen, M.D.

Diana Schendel, Ph.D.

Mads Melbye, M.D.

Correspondence and negotiations concerning the manuscript should be addressed to:
Kreesten Meldgaard Madsen, The Danish Epidemiology Science Centre, Department of
Epidemiology and Social Medicine, Vennelyst Boulevard 6, DK-8000 Aarhus C, Denmark
Telephone number: + 45 8942 6149 e-mail: kmm@dadlnet.dk

Exhibit III

**F. Edward Yazbak, MD, FAAP
TL Autism Research
70 Viewcrest Drive
Falmouth, Massachusetts 02540
Tel (508) 540 5060 Fax (508) 457 9814
e-mail TLAutStudy@aol.com**

**Edward W. Champion, M.D.
Senior Deputy Editor
New England Journal of Medicine**

November 25, 2003

Dear Dr. Champion,

I am writing to you to comment on your response to Dr. Gary Goldman, about our article, entitled "An Investigation of Association between MMR Vaccination and Autism in Denmark", and why it was rejected for publication in the New England Journal of Medicine.

You wrote:

Dr. Goldman --

The decision here was on editorial grounds, not on the methodology or conclusions of your analysis. We are a general journal that publishes on a wide range of topics, and we can publish only a limited amount of the research in any one area. For any major database many analyses on a given question are possible. We are in the difficult position of having to decline over 92 percent of the manuscripts that we receive. You should certainly be able to find an appropriate place to publish your manuscript elsewhere. I am sorry that it was declined here, but we wanted to let you know that promptly to avoid delay.

Thank you.

**Edward W. Champion, M.D.
Senior Deputy Editor
New England Journal of Medicine
(617)-734-9800; fax (617)-739-9864
ecampion@nejm.org**

Since 1998, I have devoted my energies to autism research and have presented my findings at an American Academy of Pediatrics conference attended by many top CDC investigators.

By publishing the Madsen paper, The New England Journal of Medicine endorsed its findings, and your support immediately granted the study recognition as credible research. When I decided to look at the data eight weeks ago, I was dismayed to find out that the study had a serious statistical flaw, and this flaw has not been publicly noted previously. I was sure that you would have had the same shocked reaction and would not have endorsed the Madsen paper had you known that the wrong sample was selected.

I contacted Dr. Goldman and asked him to analyze the data that I had obtained. The result was the paper we submitted to you, which was also reviewed by 3 independent experts. I'm pleased to see that you had no problems with our methodology and our conclusions. Our research and findings are sound.

Autism is, at this time, the most pressing pediatric epidemic in the United States. I have attached two graphs for your review. The first is based on the annual reports of the U.S. Department of Education to Congress and shows the increase in the number of children with autism aged 6 to 21 in U.S. schools. There were 5415 children with the diagnosis in 1991-1992 (the first year that autism was listed as a separate diagnostic category) compared to 118,603 students in the 2002-2003 school year.

The second graph shows the increase in new cases of Type I Autism (299.00) accessing services in California since 1994 when the new and present diagnostic criteria of DSM-IV were introduced. The increase, in less than a decade, from 2 new cases per day *to 10 new cases per day in that State alone* should shock you as it has shocked everyone.

If Madsen's paper was published with its possible biases and deficiencies, certainly our paper, based on the same data, leading to an opposite conclusion should equally be considered. An important question is: If increases in autism in Denmark are not, in part, caused by MMR vaccination, then what is causing them?

Madsen's data was biased in that 0.81 million person-years of observation time in his study were among children aged less than 1.5 years who likely had not as yet received MMR vaccine. The balance of observation time involved less than 10 cases of autism per year in the study cohort, which is too rare of an occurrence to make meaningful statistical inferences. These facts, combined with the young cohort that Madsen inspected using person-time data, produced a biased and probably faulty conclusion.

While the Denmark data are subject to inconsistencies in later years, especially 1993-1994 due to the classification change and 1995 due to the addition of outpatients, extrapolation of data from the period of 1990 to 1992 among children aged 5 to 9 years indicates that in the absence of these later effects, incidence of autism had started to rise. The increase of autism by a factor of four in 2000 is an entirely plausible outcome based on linear regression analysis of the trends existing in 1990-1992.

Dr. Champion, as you mentioned in your e-mail to Dr. Goldman, we will find a journal to publish our very important findings. When we do, there will be many questions scientists and parents alike will be asking:

1. Why was the Madsen study published in the prestigious New England Medical Journal in the first place?
2. Why was a good study rejected, especially one which is co-authored by a Massachusetts physician, deals with a most pressing pediatric problem, and reveals critically important findings directly contradicting Madsen's?

I respectfully submit that both your editorial fairness *and* search for the truth on this important debate will be better served should you accept to reconsider your decision.

Wouldn't you like to be part of the solution rather than part of the problem?

I would be glad to discuss this request further by telephone or in person at your office in Waltham.

Should you decide to reconsider, I will be glad to e-mail you a new submission with minor improvements.

Sincerely yours,

F. Edward Yazbak, MD.

Exhibit IV

Williams, Lisa (NIP)

From: Bernier, Roger
Sent: Wednesday, August 01, 2001 2:04 PM
To: Williams, Lisa (NIP)
Subject: FW: Proposal for study of MMR vaccine and autism in Denmark

Original Message

From: Destefano, Frank
Sent: Thursday, June 01, 2000 12:41 PM
To: Bernier, Roger
Subject: RE: Proposal for study of MMR vaccine and autism in Denmark

I hadn't seen it, but it looks like a good opportunity. The availability of data from pregnancy, as well as blood specimens, is particularly attractive. The blood spot component would be very valuable just by itself to try to confirm the exciting findings from the small NIH study. If these are true biomarkers for autism, it would be great to see if they identify high risk groups of kids for a vaccine-autism association. In addition to MMR, the study should include all infant and childhood vaccines to look at issues of multiple antigens, vaccine additives, etc. Serologies for measles and rubella in the maternal and cord blood might also be worth considering.

—Original Message—

From: Bernier, Roger
Sent: Tuesday, May 30, 2000 5:35 PM
To: Destefano, Frank; Chu, Susan
Subject: FW: Proposal for study of MMR vaccine and autism in Denmark

Have you folks heard of this or seen this? It is a short turnaround but can you weigh in on this.
Thanks

-----Original Message-----

From: Cordero, Jose
Sent: Tuesday, May 30, 2000 5:32 PM
To: Bernier, Roger
Subject: FW: Proposal for study of MMR vaccine and autism in Denmark

Roger:

I got this from Marshallyn. Would appreciate your comments.

José

Original Message-----

From: Yeargin-Alisopp, Marshalyn
Sent: Tuesday, May 30, 2000 2:36 PM
To: Cordero, Jose
Cc: Schende~, Diana; Murphy, Catherine; Boyle, Coleen; Decoufle, Pierre; Thorsen, Poul; Yeargin-Allsopp, Marshatyn; Sinks, Tom
Subject: Proposal for study of MMR vaccine and autism in Denmark

Jose, As we discussed on Friday, we have become aware through Poul Thorsen of an exciting opportunity to study the role of MMR vaccine and autism using several registries/existing studies and the repository of biologic specimens and laboratory capabilities in Denmark. Attached below is a proposal for such a study. Poul will be leaving on Thursday to travel to Denmark where he will be meeting with the PIs for the proposed study on June 6th. We would like to be able to have Poul say whether it is likely that CDC (NIP) can fund the study, if NIP is interested. The proposed budget is included; there may be additional sources of funding (in addition to NIP) but we are not certain at this time.

Unfortunately, the DD Branch does not have much (if any) \$\$ to fund the study, but we do have the expertise that we have developed due to the autism surveillance in Atlanta and the MMR/autism case-control study. I will be out of the office tomorrow, but you may contact Diana or Poul if you have questions. Thank you so much for considering this proposal.
Marshalyn

<<File: MMR_autism_PROP_02.doc>>

Exhibit V



Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30341-3724

December 10, 2002

Jerold F. Lucey, M.D.
Editor in Chief
PEDIATRICS
University of Vermont
College of Medicine
Pediatrics Editorial Office
89 Beaumont Avenue, GIVEN D201
Burlington, Vermont 05405 - 0068

Dear Dr. Lucey:

I am writing in support of an expedited review and consideration of the enclosed manuscript that examines the association between thimerosal, an ethyl mercury containing preservative, and autism. As you may know, there has been considerable interest by parents, clinicians, educators, and policy makers for an explanation of the marked increase in the rate of autism in recent years. A University of Davis study released in October of children identified through the California developmental disabilities service system, reemphasized the upward trend in autism and the lack of understanding as to the cause.

One factor hypothesized to have a causal role is childhood vaccinations. Specific aspects of vaccinations that have been subject to inquiry include the MMR vaccine and thimerosal. There are now numerous epidemiologic studies to suggest that the MMR vaccine is not associated with the risk of autism; an Institute of Medicine review that was published in 2000 concluded that the weight of the scientific evidence did not support a link between MMR vaccine and autism.

For thimerosal, however, there are limited data to evaluate this factor. Because mercury in its inorganic form is known to have serious neurologic effects, many parents have speculated that the increased number of vaccines (many of which contained thimerosal) may have been a significant factor in the recent rise in autism. The Danish study is a powerful epidemiologic study of this issue and capitalizes on the Danish health registry system that incorporates all health encounters into disease and exposure specific registries. In addition, a key strength of the study is the ability to examine rates of autism prior to and after the *discontinuation* of vaccines containing thimerosal in Denmark in 1992. Contrary to what would be expected if thimerosal was linked to autism, the authors did not observe a decline in the rate of autism with the removal of thimerosal containing vaccines.

Page 2 - Dr. Jerold F. Lucey, Editor in Chief, PEDIATRICS

I feel this is a very important study that deserves thoughtful consideration by the Journal. Its findings provide one strong piece of evidence that thimerosal is not causally linked to autism. Thank you for your timely consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "José", written in a cursive style.

José F. Cordero, M.D., M.P.H.
Assistant Surgeon General
Director
National Center on Birth Defects
and Developmental Disabilities

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