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By Federal Express

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Re: Alleged Research Misconduct - falsification by omission of material results in the publication of: "Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta. 2004;113:259-266 [The Paper; Exhibit 1]

Dear Drs. Jaffe and Wright,

We write to provide you with supplemental information in support of our earlier complaint regarding alleged research misconduct by senior investigators within the National Immunization Program (NIP), Battelle Memorial Institute at the Centers for Public Health Evaluation (CPHE), and the National Center on Birth Defects and Developmental Disabilities (NCBDDD).

We have heard back from Dr. Jaffe. Dr. Wright, we have yet to receive any response to our earnest reporting of this most serious matter, either from you or your office.

Supplemental points.

The central element to the alleged misconduct is that The Group deliberately and willfully concealed a significantly increased autism risk associated with receipt of MMR vaccine according to the CDC's recommended schedule (by 18 months) in vulnerable subgroups of children i.e. African American boys and children with "isolated" autism

who were essentially previously developmentally normal. As a consequence, millions of American children have been put in harms way.

1. Isolated autism (IA).

1.a. Having limited the Isolated Autism subgroup to those without mental retardation, The Group presented results for the entire group in what they described in The Paper as an “unadjusted analysis.” Comparing autism risk in those vaccinated with MMR before and after 36 months, the Odds Ratios (OR) are significant at 2.45 (1.20-5.00). [Exhibit 1, page 263; Table 4]

1.b. When the analysis was confined to the birth certificate cohort, with adjustment for birth weight, multiple gestation, maternal age, and maternal education, the same comparison yielded a non-significant increased OR of 3.55 (0.74-17.07). This was presented in The Paper as the “adjusted” analysis [Exhibit 1, page 263; Table 4].

1.c. However, adjustment for birth weight, multiple gestation, maternal age, and maternal education was unnecessary since, in their own words:

Although the birth certificate sample results in Table 3 were adjusted for maternal and birth characteristics, the OR’s were not different from the unadjusted results for the birth certificate sample (data not shown) indicating that there was little or no confounding effects by these factors.

[Exhibit 1, page 261]

1.d. The adjusted analysis was superfluous and the valid result for the “Isolated” subgroup is the significant risk of 2.45 (1.20-5.00) described in the unadjusted analysis in 1.a. above. The authors knew this, and they also knew that this effect was being driven specifically by those vaccinated by 18 months – data they chose to conceal. Those vaccinated on schedule (i.e. 12-18 months) were the one group that, from repeated analysis of the data over time, consistently showed a significant increased autism risk. See table 1 (revised).

1.e. In the Abstract of The Paper, in referring to children vaccinated with MMR before 18 and 24 months the authors state,

No significant associations for either of these age cutoffs were found for specific case subgroups, including those with evidence of developmental regression.

[Exhibit 1, page 259] The authors deliberately omitted reference to their subgroup analyses using the 36 month cutoff, which showed highly significant risks for at least three groups of children, as shown in Exhibit 7,

Table 5, including: “isolated” autism vaccinated at 12-18 months, African American children vaccinated at 12-18 months, and African American children with isolated autism vaccinated at 16-18 months.

1.d. The Group’s original intention to analyze and present the data by age categories at first MMR vaccination is evident in their finalized Analysis Plan, as set out in Table 1 (revised), enclosed with this supplemental complaint. The authors failed to do this.

2. Omission of gender-related data.

The final Analysis Plan states the following:

3) Analyses examining Gender Effects

Males are at substantially higher risk for autism and may be more vulnerable to the exposure associated with the MMR vaccine. We will analyze males and females separately and replicate the main objectives of the primary analyses as well as examine the potential confounders available from Georgia birth certificates.

[Exhibit 3 of original Complaint, page 9] The original intention is clearly stated. However, in The Paper and in the presentation to the IOM there is an ominous absence of data on gender-specific risk. For example, results from reanalysis of African American boys in the whole group, comparing those receiving MMR before and after 36 months, reveals a increased autism risk (Odds Ratios and Confidence Intervals) for MMR not only before 36 months of 3.36 (1.50 – 7.51), but also 24 months of 1.73 (1.09 – 2.77).

While there was no justification for confining their race analyses to the Georgia birth certificate subgroup, for reasons set out in the original complaint, having done so they should (and likely did) have followed through on their stated intention, as set out above, of replicating the primary analyses separately for males and females in this birth certificate subgroup. When this was reanalyzed the risk for autism in African American boys was 2.75 (1.05-7.22). If these analyses were performed according to the Analysis Plan, they have been concealed. Thompson has not provided them and we will urge Congress to access them as part of its enquiry.

Omission of gender-specific data was essential to maintaining The Group’s alleged deception. A significantly greater risk in boys but no significantly increased risk in girls – exactly what was found - would have confirmed (and does confirm) the validity of the association.

3. The residual significant 49% excess autism risk.

Department of Health and Human Services document, “Public Health Service Policies Research Misconduct; Final Rule. para. 93.103 of. 42 CFR Parts 50 and 93, states that:

Falsification in science includes manipulating research processes, or changing, or omitting data or results such that the research is not accurately represented in the research record.

There is an additional aspect to The Paper by DeStefano et al that falls under this definition of falsification by virtue of the willful misrepresentation of the findings in order to conceal the MMR-autism risk.

Despite the lengths to which DeStefano and his colleagues went in order to conceal the causal associations between on-schedule MMR and autism risk, in 2004 they were left to explain a residual significant 49% increased risk for children in the total group vaccinated before 36 months. This finding is described in The Paper as set out below [Exhibit 1].

Abstract

Vaccination before 36 months was more common among case children than control children, especially among children 3 to 5 years of age....[Exhibit 1, page 259]

Results

Using a 36-month cutoff, more case children (93%) than control children (91%) were vaccinated before 36 months of age (OR: 1.49; 95% confidence interval [CI]: 1.04- 2.14); the association was strongest in children 3-to-5 years of age (OR: 2.34; 95% CI: 0.99- 5.54) [Exhibit 1, page 261]

Conclusion

Case children, especially those 3 to 5 years of age, were more likely than control children to have been vaccinated before 36 months of age. [Exhibit 1, page 265]

The Group were to claim at both the IOM and in The Paper that the difference in vaccination coverage by 36 months of age between case and control children is likely to be an “**artifact**” of immunization requirements for preschool special education attendance in case children. This claim is set out in The Paper as shown below [Exhibit 1] and this significant finding was dismissed without further analysis or explanation.

Abstract

...likely reflecting immunization requirements for enrollment in early intervention programs. [Exhibit 1, page 259]

Conclusion

The difference in vaccination coverage by 36 months of age between case and control children is likely to be an artifact of immunization requirements for preschool special education attendance in case children. [Exhibit 1, page 265]

The argument makes little sense any way one examines it. For example, vaccine requirements for these children are no different from regular education pre-school children.

If there were no vaccine association with neurodevelopmental disorders, special education pre-schoolers, with an increased risk of neurological contraindications to vaccination such as epilepsy, would be less likely to be vaccinated on schedule.

A further flaw in this argument is that to receive special education services the child required a diagnosis of autism and while the average age of getting this diagnosis in Atlanta's Developmental Disabilities system was 61 months at that time, the great majority of children had received their MMR much earlier - on average, at 20 months. [Exhibit 2]

The "artifact" argument is also inconsistent with compelling additional data generated by The Group but never disclosed, i.e. a Survival Curve that presents "Age of 1st MMR vaccination by Case Status", an example of which is provided as Exhibit 3.

For autism "Cases" and non-autism "Controls", the graph plots "Percent Vaccinated" (y-axis) by "Age at First MMR Vaccination (months)" (x-axis). As confirmed by Dr. Thompson, the graph shows a continuously distributed difference between groups that emerges at around 15 months of age at MMR vaccination and is evident out beyond 60 months.

This graph confirmed that the real difference in age at first MMR emerged long before the children were enrolled in pre-school and is totally inconsistent with "artifact" as the explanation.

DeStefano's unsupported supposition was also open to further scientific testing rather than casual dismissal as "artifact". If it were an artifact, then this artifact should be found randomly across all groups; for example there is no scenario where boys would receive MMR earlier for special education but girls would not.

When we further analyzed the original study data - as The Group could and should have done - the significant risk is observed in boys (Hazards Ratio 1.69; CI 1.11 - 2.57) but not girls (Hazards Ratio 0.996). It was not an artifact.

But of course, Destefano and his colleagues were aware of this; they already knew that the significant autism risk was being driven by African American boys and children with “isolated” autism. We conclude that they knew their “artifact” argument was a deliberate deception.

4. The effect of the alleged misconduct.

The far-reaching effect of this alleged misconduct is evident in The Paper’s interpretation by an influential scientist, Dr. Wang of Autism Speaks. In interview with Rowan Farrow on MSNBC he represented The Paper’s findings as showing that:

[Wang] The part that nobody’s talking about is that in that study children who got the MMR vaccine on time, which is before 18 months, there was no increased risk....So it actually looked like the increased risk was in people getting it late.

This epitomizes the impact of the CDC’s alleged misconduct. Wang and others have been lead, deliberately, to the conclusion that children who got the MMR earlier were not at risk of autism whereas those getting it later may be at greater risk, the exact opposite of what DeStefano and his colleagues had discovered. This public message has the effect of encouraging more children to be put in the way of potential harm from MMR vaccination by 18 months, the identified period of risk. At no stage has DeStefano or any his colleagues other than William Thompson sought to correct the error in Dr. Wang’s interpretation. Indeed, publically DeStefano has continued to stand by the original paper and maintain the deception.

5. Revised Table 1

Table 1 of the original Complaint has been revised to make its meaning and significance more clear. The key data generated by The Group but excluded from The Paper and the IOM are color-coded (green).

6. Revised Exhibit 14

Exhibit 14 in the original complaint was provided in error. The correct exhibit is now included as Revised Exhibit 14.

We urge that these supplemental items be taken into consideration along with our original complaint and that this entire matter is given the priority and rigor that it clearly merits.

Yours sincerely,

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List of Exhibits

1	DeStefano et al Pediatrics 2004
2	Wiggins LD , Baio J, and Rice C. Developmental and Behavioral Pediatrics, 2006
3	Survival Curve that presents “Age of 1 st MMR vaccination by Case Status”
Revised Exhibit 14 to original Complaint	
14	Email to Melinda Wharton October 18, 2002