

APPENDIX 7, 8: Dr. Lewis Commentary; GSK Dubious Record & risks of multi-valent vaccines

APPENDIX 7:

Commentary with original pathologists' diagnostic evaluation of Lancet children's biopsy slides submitted for publication by David L. Lewis, Research Microbiologist, National Whistleblowers Center, September, 2011

Brian Deer concluded that Andrew Wakefield misrepresented the results of a blinded analysis of biopsy slides by pathologists Amar Dhillon and Andrew Anthony in order to conclude in Table 1 of the Lancet article that 11 of the 12 children exhibited signs of non-specific colitis. To create Table 1, Wakefield relied on Dhillon's and Anthony's grading sheets where they recorded their observations of various architectural features in the children's colonic tissue samples and assessed inflammation levels. [1,2]

Based on interviews with various experts, Deer concluded that pathology grading sheets "don't generate clinical diagnoses such as colitis." He argued, therefore, that Wakefield mistranslated the pathologists' inflammation scores to create the diagnosis of non-specific colitis. However, Deer wrote, the "ultimate proof" lies in the biopsy slides, which are missing. Editors at The Lancet retracted Wakefield's article in 2010 when the General Medical Council (GMC) pursued Deer's previous allegations and found Wakefield and one of his coauthors guilty of professional misconduct.

In January of this year, National Whistleblowers Center (NWC) director Stephen Kohn spoke at a vaccine safety conference in Jamaica, West Indies, where Wakefield discussed his research. [3] I was invited as an outside observer. My responsibilities at the NWC include investigating "institutional research misconduct" in which government, industry and academic institutions use false allegations of research misconduct and other means to suppress scientific research to protect certain government policies and industry practices.

During the conference, news coverage of Deer's latest allegations published in the BMJ broke in the international media. In response to my request for more information, Wakefield allowed me to review his personal files concerning the Lancet article, which contained key documents that have never been published. They included the GMC's copies of Dhillon's grading sheets for all but Child 11, plus photomicrographs of the missing slides for some of the children (2-5, 9). Child 11 was a U.S. citizen, and therefore was not subject to the GMC's investigations.

The GMC's hearings began almost nine years after the Lancet article was published; and many of Anthony's grading sheets were no longer available. Anthony testified that he examined the children's biopsy slides both before and after the Lancet study was published;² however, the GMC's records included only his post-publication results. Almost all of these were dated in 1998, just months after the Lancet article was published.

Since Table 1 was based on the pathologists' grading sheets, and Deer alleged that Wakefield misinterpreted them, it follows that the grading sheets--not the missing slides--are the ultimate proof of whether Wakefield fabricated the diagnoses in the Lancet article. As indicated in Deer's article, scientists disagree over the significance of different architectural features and inflammation levels in colonic tissue samples. Such disagreements do not represent research fraud.

Dhillon's grading sheets (Attachment 1) included boxes to check, which characterized various conditions that are widely recognized as different forms of colitis, including Crohn's disease, ulcerative colitis ("UC"), and infectious, ischemic, and non-specific colitis. In one case (Child 7), Dhillon left the boxes blank, meaning none of these forms of colitis were present. For the remaining 11 children, he checked "non-specific."

Similarly, Anthony described various stages and types of colitis on his forms (Attachment 2). For all but Child 7, he specifically noted active, mild, or moderate "colitis" and/or indicated specific changes diagnostic of colitis, e.g. "chronic inflammation." Photomicrographs of the missing biopsy slides (Attachment 3) exhibit the architectural features described in Dhillon's and Anthony's grading sheets. Surprisingly, Wakefield's files included a report by Professor Ian Booth, the GMC's expert pediatric gastroenterologist, which mirrors Deer's allegations of research fraud.⁴ Prior to the GMC holding hearings, Booth compared routine pathology reports from the Royal Free Hospital with Table 1 of the Lancet article and found that on-duty pathologists had indicated that most of the children's biopsies were normal. He reported to the GMC that the "altered" diagnoses in the Lancet article suggested "an exaggerated view of the histology," and concluded that "scientific fraud" could not be ruled out.

Using this same approach four years later, Deer concluded that Wakefield changed most of the diagnoses from normal to non-specific colitis. "These changes--from normal to abnormal, or from healthy to diseased--had also raised concern in the mind of at least one of the paper's authors [histopathologist Susan Davies]." Davies, as Deer noted, testified at the GMC's hearings that her concerns were allayed when she discussed them with Dhillon and others.

Conclusions

Dhillon's and Anthony's grading sheets are consistent with the results Wakefield reported for the children's histologies in Table 1 of the Lancet article. Namely, Child 7 was the only child whose biopsies showed no evidence of colitis in Dhillon's blinded expert analysis. Deer's results, on the other hand, are consistent with the expert report submitted by Professor Ian Booth, who concluded that most of the Lancet children exhibited no evidence of colitis. Since Booth and Deer both relied upon the same routine pathology reports, this finding was to be expected.

When I asked Booth why the GMC did not pay more attention to his analysis, given the fact that Deer's replication of it received so much attention, he replied: "My analysis of the case records of the children presented in the Lancet publication was carried out specifically at the request of the GMC's solicitors and it formed part of the basis of the case brought against Wakefield et al by the legal team acting on behalf of the GMC."⁵

As an expert in clinical studies involving the collection and examination of colonic biopsy samples [See, Attachment 4], I would have advised against publishing the 1998 Lancet article had the children's histopathologies relied upon routine pathology reports rather than a systematic, blinded expert analysis. It is extremely unlikely that all, or even most, of the on duty pathologists who created these reports were experts in pathological features associated with inflammatory bowel disease.

In conclusion, it should be no surprise that stringing together biopsy reports from on-duty pathologists with unknown credentials in intestinal pathology does not match a blinded analysis by Dhillon and Anthony, who systematically reviewed all of the biopsies together. Wakefield, in other words, did not fabricate the histopathologies of the 12 children reported in the Lancet article.

Final Note: Brian Deer objected to a preliminary analysis of Wakefield's documents, which I posted on the NWC website in June 2011. He asked Executive Director Stephen Kohn to remove it; and Mr. Kohn obliged. The NWC will refrain from commenting on Mr. Deer's allegations on its website until such time as funding is available for attorneys to review and approve any future postings. Among Mr. Deer's various complaints, he questioned my objectivity and whether I am qualified to comment on these matters. He also indicated that his allegations of research fraud do not rise or fall based upon mismatches in the histopathology records. These issues are addressed separately (Attachment 4).

References

1. General Medical Council, Statement of Professor Amar Dhillon. 28 July 2006.
2. General Medical Council, Statement of Dr. Andrew Anthony. 18 October 2006.
3. Vaccine Safety: Evaluating the Science. Jamaica, West Indies. 3-8 January 2011.
<http://www.vaccinesafetyconference.com/index.html>
4. Booth I. General Medical Council, Fitness To Practice Panel (Misconduct). Wakefield, Walker-Smith, Murch. Second Addendum to Overview Statement. 8 November 2006.
5. Personal communication [Email]. I. Booth, University of Birmingham, to D. Lewis, University of Georgia. 10 August 2011.

Attachments:

1. Professor Amar Dhillon's grading sheets
 2. Dr. Andrew Anthony's grading sheets
 3. Photomicrographs of biopsy slides (Fig. 1)
 4. Brian Deer's objections to the NWC website
- Competing interests: None declared

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#### **APPENDIX 8:**

##### **GlaxoSmithKline's long dubious corporate record of concealing its products' serious risks**

- In 1999, GSK (then known as SmithKline Beecham) completed a clinical trial that revealed that its diabetes drug, Avandia (rosiglitazone) posed a greater risk of cardiac problems than its competitor, Actos. However, an internal email stated baldly: "*These data should not see the light of day to anyone outside of GSK*" The company spent the next 11 years trying to cover up the cardiac risk.<sup>1</sup>
- GSK (and Eli Lilly and Pfizer) denied for years the suicide risk of their SSRI antidepressants and concealed the data documenting suicides during their clinical trials, and disparaged researchers who pointed out that risk. GSK also concealed the data showing that Paxil (paroxetine) was addictive even though their original license application confirmed that 30% of patients had withdrawal reactions. GSK derided scientists' analyses of these risks as "scientifically invalid".<sup>2</sup>

- In 2004, New York State Attorney General Eliot Spitzer uncovered GSK's clinical trial 329 documents showing that (a) the antidepressant, Paxil (Seroxat) failed to demonstrate effectiveness, and (b) that GSK had [concealed the suicide data](#) by the euphemism "emotional lability". GSK was charged with consumer fraud. GSK agreed to a settlement requiring it to pay \$2.5 million and to make individual patient data available. GSK failed to honor the data disclosure agreement until 2012, when Dr. Peter Doshi contacted NYS Attorney General.
- Hepatitis B Vaccine Infant deaths – four Hep B vaccines withdrawn between 2000 – 2009 in the EU and UK; but authorities deny connection to deaths. "The safety of the vaccine is not in question, but it is suspected to be ineffective." Professor Kent Woods, Chief Executive, MHRA.<sup>3</sup>
- In 2008, Professor Jens Lundgren of Denmark presented a paper at an international AIDS conference in Mexico City, in which he showed that GSK's drug Abacavir almost doubled the risk of cardiac arrest.<sup>4</sup> At the end of the presentation Prof. Lundgren had to be escorted to the airport with 8 body guards, having received a death threat.<sup>5</sup>
- In 2009, James Murdoch was appointed non-executive director of GSK to serve as a member of GSK's corporate responsibility committee, where he will help to review "*external issues that might have the potential for serious impact upon the group's business and reputation*".
- In 2011 – 2012, the Murdoch corporate brand of "gutter journalism" was laid bare in extensive Parliamentary hearings. Under the stewardship of James, more than 27 different journalists ordered more than 1,000 illegal searches.<sup>6</sup>
- In 2012, GSK pleaded guilty to fraud in a suit filed by the U.S. Justice Department, resulting in a \$3 billion fine, the biggest fine in corporate history.
- In May 2014, Mark Reilly, the former head of GSK Chinese operations was found guilty of operating a "massive bribery network". Internal emails confirmed that the company bribed Chinese doctors and government regulators. GSK was fined \$488.8 million. ([Inquisitor](#))
- In 2011, GSK suspended the supply of Tritanrix-HB+Hib, a pentavalent vaccine against diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenza type b(Hib) due to contamination. ([World Health Organization](#))
- In 2012, [GlaxoSmithKline](#), submitted a [confidential report](#) Re: *Infanrix hexa*, its hexavalent (6 in 1) vaccine to the European Medicines Authority. *Infanrix* combines Diphtheria Tetanus and Acellular Pertussis (DPT), Hepatitis B, inactivated Poliomyelitis and Haemophilus influenza type B vaccine; it is administered in 3 doses within the first 180 days of life.
- The report acknowledges that during the vaccine's clinical trials, five cases of autism were reported. GSK received 1,742 reports of adverse effects, of which 503 were serious effects not listed and 56 were serious adverse effects listed. The events registered included 36 deaths (over the two-years period), most of which occurred within three days after the child received the *Infanrix Hexa* vaccine. (p. 626)
- GSK's disregard for the safety of babies is demonstrated by GSK's risk/benefit assessment: "[t]he benefit/risk profile of *Infanrix hexa* continues to be favourable," even as GSK cites the

following reported severe adverse events during clinical trials:

*“anaemia haemolytic autoimmune, thrombocytopenia, thrombocytopenic purpura, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, haemolytic anemia, cyanosis, injection site abscess, Kawasaki’s disease, important neurological events (including encephalitis and encephalopathy), Henoch-Schonlein purpura, petechiae, purpura, haematochezia, allergic reactions (including anaphylactic and anaphylactoid reactions),”* and death (see page 9)

The confidential GSK report<sup>7</sup> was made public in 2014, following an order by the [Italian Court of Justice](#). Nicola Di Leo who was overseeing a [case](#) involving a child whose autism was triggered following the third Infanrix dose in 2006. When the Italian Ministry of Health rejected the parents’ claim, they sued the Ministry in a court of general jurisdiction – an option not available either in the UK or the U.S.

- The court determined that autism and brain damage was likely caused by the mercury (thimerosal) contained in Infanrix Hexa at the time.

In 2015, Dr. Jacob Puliyel,\* head of pediatrics, St. Stephen’s Hospital, New Delhi, analyzed the data in the confidential GSK report, which covers a two year period. He concluded that of 69 sudden infant deaths within 10 days after vaccination, 65 were caused by Infanrix Hexa, and another three who died during the following 10 days. Dr. Puliyel’s analysis is published [here](#) and on PubMed Commons.

- **Multi-valent vaccines are promoted and recommended by the WHO and GAVI** (which is bankrolled by the Bill and Melinda Gates Foundation). Soon after a pentavalent (5-in-one) vaccine was first introduced in Asian countries: Bhutan, Sri Lanka, Pakistan, India and others; reports of sudden infant death syndrome followed. In five countries, 70 deaths were associated with different brands of the pentavalent vaccine. <sup>8</sup>
- **The WHO maintained the fiction promulgated by GSK:** *“no fatal adverse event following immunization (AEFI) has ever been associated with this vaccine.”*<sup>9</sup>

The response of the WHO to the deaths following vaccination was to revise its classification of adverse events following immunization (AEFI) so that the deaths following vaccination—even those occurring within 1 to 10 days of vaccination—are not classified as AEFI, but as merely *“coincidental.”* Following the death of 12 babies who were vaccinated with a pentavalent vaccine in Vietnam (2010) the WHO report acknowledged non-fatal cases as corresponding to known vaccine reactions; but the WHO declared (irrationally) that the deaths were not related to the vaccine.

[“Sudden Infant Death Following Hexavalent Vaccination: a Neuropathologic Study”](#) (2014)

A report by researchers from the University of Milan who analyzed 110 reported cases of sudden infant deaths: *“In 13 cases (11.8%) the death occurred in temporal association with administration of the hexavalent vaccine (from 1 to 7 days).”*

- As of August 2016, there were 237 infant deaths reported within 72 hours of being injected with the pentavalent vaccine in Sri Lanka, Bhutan, Pakista, Vietnam and India.<sup>10</sup>

Despite evidence of the risk of sudden infant deaths, the UK Joint Committee on Vaccination and Immunisation (JCVI) chaired by Professor Andrew Pollard, has recommended that the UK switch to hexavalent vaccines for babies. This recommendation disregards the risks for babies, much as the JCVI had disregarded the MMR Plusarex risks in 1988. [See Appendix 3] Prof. Pollard is Director of the Oxford Vaccine Group, noted for its active role in vaccine development and testing on behalf of industry. He is also a Trustee of the Jenner Vaccine Foundation. Dr. Norman Begg, Vice-President and Chief Medical Officer of GSK Biologicals, manufacturer of Infanrix Hexa, is also a Trustee of the Jenner Foundation.

Update: a peer reviewed commentary by Dr. Puliyel and Dr. C. Sathymala, a public health physician and epidemiologist, [Infanrix hexa and Sudden Death: a Review of the Periodic Safety Update Reports Submitted to the European Medicines Agency](#), was published in the *Indian Journal of Medical Ethics*, Sept. 2017. The authors note that 83 % of the reported infant deaths have taken place within the first 10 days after vaccination with “Infanrix hexa” vaccine and only 17% occurred in the next 10 days:

*“If this were simply coincidental deaths then it would not all cluster immediately after vaccination but would have been distributed uniformly over the 20 day period.”*

\*Dr. Jacob Puliyel is one of the exemplary medical professionals selected by the Alliance for Human Research Protection for its [Honors Roll](#)

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<sup>1</sup> ([Diabetes Drug Maker Hid Test Data](#), Gardiner Harris, *The New York Times*, 2010).

<sup>2</sup> Response from GlaxoSmithKline. *British Journal of Psychiatry* 2002

<sup>3</sup> “Unexplained Cases Of Sudden Infant Death Shortly After Hexavalent Vaccination” B. Zinka et al, *Vaccine*, 2005; MHRA Recalls GSK’s Hepatitis B Vaccine, Regulatory Affairs – *Hays Pharma News*, 2009

<sup>4</sup> [Glaxo 'Downplayed' Warning on Heart-Attack Risk Fom AIDS Drug](#), *The Independent* 2008

<sup>5</sup> Researcher receives death threats, Brix SM. *Universitetsavisen* 2008 cited by Professor Peter Götzsche, [GSK Backs Campaign for Disclosure](#), *BMJ*, 2013;

<sup>6</sup> [Ofcom Has Concerns About Murdoch Power In UK If Sky Bid Allowed](#). Mark Sweney, *The Guardian*, 2017

<sup>7</sup> *Infanrix hexa*, [Confidential Report to Regulatory Authorities](#) (the European Medicines Authority), GlaxoSmithKline 1271 pp. report: December 2011/ The report documents infant deaths (Oct. 2009 to Oct 2011). The report and the deaths were concealed from the public until an Italian court ordered it to be disclosed in 2014.

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<sup>8</sup> “Antivaccine Lobby” Replies to the BMJ, Dr. Jacob Puliyel, [Rapid Responses](#), 2013

<sup>9</sup> [AEFI and the Pentavalent Vaccine](#): Looking for a Composite Picture, Editorial. Jacob Puliyel, *Indian Journal of Medical Ethics*, 2013

<sup>10</sup> [237 Deaths By Pentavalent Vaccine And Still Counting](#), *Sunday Guardian*, Nov. 2016