

APPENDIX 1: The UK High Court Decision in the appeal by Professor John Walker-Smith was issued on March 7, 2012.

Professor Walker-Smith was the senior clinician and senior author of the *Lancet* article. The High Court decision covered all of the most serious medical ethics charges that were brought against both Professor Walker-Smith and Dr. Andrew Wakefield – and Justice Mitting repudiated them. The entire GMC case against the doctors, the charges and findings rest on the pivotal unsubstantiated assumption that the *Lancet* case series was Project 172-96, a study undertaken on behalf of the Legal Aid Board to provide support for a class action lawsuit. The panel’s conclusion rested on unspecified “available evidence”:

"The Panel has heard that ethical approval had been sought and granted for other trials and it has been specifically suggested that Project 172-96 was never undertaken and that in fact, the Lancet 12 children's investigations were clinically indicated and the research parts of those clinically justified investigations were covered by Project 162-95. In the light of all the available evidence, the Panel rejected this proposition."

Justice John Mitting summarized the GMC’s untenable charges and conclusions:

"The Panel rejected Professor Walker-Smith’s contention that Project 172-96 was never undertaken. Professor Walker-Smith was involved in research on young, vulnerable children, without the appropriate ethical approval; he caused them to undergo in the pursuit of that research, invasive procedures that were not in their best clinical interests; he was irresponsible in his reporting in a scientific journal of a study which he knew, or ought to have known, had major public health implications. Furthermore he caused a child to be administered Transfer Factor for experimental reasons... the Panel concluded that the description of the referral process was irresponsible, misleading and in breach of Professor Walker-Smith’s duty to ensure that the information in the Lancet paper was accurate.

The Panel concluded that...the findings are not only collectively such as to amount to serious professional misconduct, but also when considered individually, constitute multiple separate instances of serious professional misconduct."

- Justice Mitting applied an impartial, forensic methodology to evaluate the credibility, relevance, and truthfulness of the testimonies and documented evidence.

The decision explicitly repudiated the entire conduct of the GMC proceedings and the manner in which the panel reached its factually unsubstantiated “findings.” Justice Mitting examined in detail the clinical documents pertaining to each of the 12 children in the *Lancet* case series study; he evaluated the documented evidence and testimonies of the expert witnesses on both sides; and he evaluated the GMC panel’s reasoning and interpretations in reaching its findings.

"It is in its findings on the clinical issues in the individual cases of the Lancet children that the most numerous and significant inadequacies and errors in the determination of the panel occur. In no individual case in which the panel made a finding adverse to Professor Walker-Smith did it

address the expert evidence [sic], except to misstate it. The issues to which this evidence went were of fundamental importance to the case against him. Universal inadequacies and some errors in the panel's determination accordingly go to the heart of the case. They are not curable." [par. 150]

(a) *"The children's diagnostic investigations were carried out pursuant to Project 172-96"—is wrong.* Justice Mitting points out that an application for a research project 172-96 titled: "A new paediatric syndrome: enteritis and disintegrative disorder following measles/rubella vaccination" was approved September 16, 1996.

"Professor Walker-Smith, Dr. Murch and Dr. Wakefield were named as responsible consultants. Dr. Harvey, a Consultant Neurologist and Dr. Berelowitz, a Consultant Child Psychiatrist, signed as heads of collaborating departments. The hypothesis which it was designed to test was that in genetically susceptible children, measles vaccination is associated with persistent enteric (and possibly CNS [Central Nervous System]) infection, enteritis and mal-absorption of vitamin B12.

Two working hypotheses were set out for the possible link between measles/rubella vaccine in a previously healthy child and the subsequent development of enteritis, Cbl deficiency and disintegrative disorder. Disintegrative disorder – Heller's disease – occurred when normally developing children show marked behavioural changes and developmental regression after age 2 often in association with bowel or bladder problems. Project 172-96 was drafted by Dr. Wakefield." [Par. 4]

On February 3, 1997 Dr. Wakefield wrote to Professor Walker-Smith to explain why he thought it right to become involved in what he described as "the legal aspect of these cases" – i.e. the litigation then being proposed by Dawbarns, pursuant to which the Legal Aid Board had provided £25,000."

Professor Walker-Smith responded on 20th February 1997: "My position as with measles, MMR and Crohn's disease is that the link with MMR is so far unproven. It is clear that the legal involvement by nearly all the parents will have an effect on the study as they have a vested interest. I myself simply will not appear in court on this issue.

I would have been less concerned by legal involvement if our work were complete and we had a firm view. Never before in my career have I been confronted by litigant parents of research work in progress. I think this makes our work difficult, especially publication and presentation.

I am very excited by this work and it is very worthwhile. Simon Murch and I met today and have drawn up a draft for patient selection for your comment please." [Par. 6]

The study reported in the Lancet (1998) was NOT Project 172-96, which was never carried out:

"Between 21st July 1996 and 16th February 1997 eleven children were admitted to the Malcolm Ward at the Royal Free Hospital for investigation under Professor Walker-Smith and his team.

The case histories of those eleven children plus a twelfth child were subsequently summarised in a paper published in the Lancet under the heading "Early report..." [Par.7]

"None of the five clinicians involved in the investigation of the Lancet children who gave evidence to the panel considered that they were following Project 172-96. None of the children fitted the hypothesis to be tested under Project 172-96, in that none of them had both received a single or double vaccine and had developed disintegrative disorder. The great majority had received MMR vaccine and been diagnosed with autism." [Par. 19]

Justice Mitting dismissed this pivotal GMC conclusion in the absence of evidence to support it:

"Its conclusion that Professor Walker-Smith was guilty of serious professional misconduct in relation to the Lancet children was in part founded upon its conclusion that the investigations into them were carried out pursuant to Project 172-96. The only explanation given for that conclusion is that it was reached 'in the light of all the available evidence'. [] that was an inadequate explanation." [Par. 20]

(b) "the research was not clinically motivated and it lacked ethics approval":

"their [GMC] case was that [Professor Walker-Smith] was in fact undertaking research, which required Ethics Committee approval, without realising that he was doing so. This is an untenable proposition, as the analysis of the letter of 11th November 1996 above demonstrates. In consequence, not only was the panel invited by the GMC not to determine Professor Walker-Smith's intention, it was also invited not to determine his truthfulness in his dealings with the Ethics Committee." [Par. 18]

"No parent was required to sign a consent form submitted to the Ethics Committee [under 172-96] the only consent forms signed were for diagnostic colonoscopy and the additional research biopsies approved in September 1995." [Par. 19]

"Dr. Pegg was not the only responsible person to whom Professor Walker-Smith stated that the investigations were clinically indicated; he told Mr. Else, Chief Executive of the Royal Free NHS Trust that they were, as Mr. Else confirmed to Dr. Wakefield on 4th September 1996; he gave a lecture at the Wellcome Trust on 20th December 1996 in which he spoke of the investigations and gastrointestinal diagnoses of the first seven Lancet children; on 6th February 1997, he wrote to Dr. O'Connor, a Consultant in Public Health Medicine responsible for funding the referrals of children 6 and 7 to him, enclosing a five page explanation of the rationale, aims and potential therapeutic implications of the investigations, in which he and Dr. Wakefield set out the clinical justification for them." [Par. 19]

In a letter dated May 29th 1997, to child JS' skeptical pediatrician he wrote:

"The success that we have had with treating autistic children is an unexpected secondary aspect of our study, we had expected improvement with the gastro-intestinal symptoms with use of 5

ASA derivatives and salazopyrine, but we had not expected the parents to tell us that there had been such an improvement in behaviour. We are in fact with the help of Dr. Mark Berelowitz, planning a further study to analyse the successes but our work at the moment has been to provide a diagnostic service to determine the gastro-enterological manifestations of these children....

My own position in this work is entirely responsive, when I transferred from Barts to the Royal Free I was quite sceptical about the research work of Dr. Andy Wakefield, but since I came here it is absolutely obvious to me that there is a large unmet need of children with autism who have a variety of GI symptoms ranging from quite mild symptoms to quite major ones. The unexpected outcome of this research has led us to being very interested in the treatment of these drugs...[Par. 175]

As for ethics approval, Justice Mitting points out:

“Professor Walker-Smith had no rational motive to begin research before it was authorised, carry it out in breach of the requirements of the Ethics Committee after it was authorised or deliberately to mislead the Ethics Committee and others about his intention.” [Par. 19]

"The panel has heard that ethical approval had been sought and granted for other trials and it has been specifically suggested that Project 172-96 was never undertaken and that in fact, the Lancet twelve children's investigations were clinically indicated and the research parts of those clinically justified investigations were covered by Project 162-95 [the general permission given to Professor Walker-Smith in September 1995]...the panel rejected this proposition." [par. 20]

Justice Mitting acknowledged that: *“because it was a clinically driven investigation which did not require Ethics Committee approval, the wording in the published paper ‘Investigations were approved by the Ethical Committee of the Royal Free Hospital NHS Trust was [not necessary, but technically] untrue and should not have been included in the paper.” [Par. 153]*

Most likely, Justice Mitting was referring to the blinded biopsy re-analysis which was a research component of the observational study. The blinded re-analysis by Dr. Dhillon and Dr. Anthony, compared the intestinal biopsy specimens of the Lancet children to the biopsies of the controls. A summary of this re-analysis is reported in Table 1 of the Lancet. Dr. Wakefield testified that he believed that the re-analysis was covered under 162-95.

It can be argued that additional, formal ethics approval for the re-analysis component would have been prudent -- even though it did not in any way affect the children or subject them to any additional tests or procedures. Given that approval had been granted for various invasive diagnostic tests under 172-96, approval for a data analysis would have certainly been granted. In any case, it would be unreasonable to argue that this constitutes a serious ethics violation.

(c) *“the children underwent clinically inappropriate invasive diagnostic tests for research purposes”*

Justice Mitting gave serious consideration to the importance of a physician's *intent* when determining whether an activity falls under the definition of research or clinical care. [Par. 9 – 16] He described in detail the clinical case of each of the 12 children in the *Lancet* paper; and determined that their treatment had been "*clinically justified.*" To underscore the fact that the 12 children described in the *Lancet* had received medical care, he cited several letters written by Professor Walker-Smith. One letter dated January 1996, to Dr. Pegg, the Chairman of the Ethics Committee:

"Professor Walker-Smith expressly stated that he and his team had so far investigated five children with gastrointestinal symptoms who also suffered from a disease categorized as cerebral disintegrative disorder "on a clinical need basis" with a measurable benefit for them: establishing a diagnosis and excluding metabolic disorder and commencing a therapeutic regime. He could not have honestly written that statement if his primary purpose was to test a hypothesis for the benefit of others." [par. 17] "A colonoscopy offers the opportunity to demonstrate if there is any ongoing infection in the gastro-intestinal tract which could in some way be causally related to his present problems". [Par. 65]

Another letter, dated Nov. 7, 1996, to the Community Pediatrician, Professor Walker-Smith wrote:

"Through Dr. Wakefield we have been looking at a group of children with autistic symptoms related to MMR vaccine and have found that a significant number of children have had gastrointestinal symptoms."

And in a letter dated November 10, 1997, to the Contracts Manager of the Royal Free Hospital, he stated:

"I think it is essential that this child does have a colonoscopy. This kind of service is just not available elsewhere for children with autism and for the special investigations which Dr. Wakefield can offer" and the panel also noted the admission note dated 13 November 1997 which notes an "elective admission for colonoscopy".

Justice Mitting ruled that the GMC panel finding that the colonoscopy was:

"for the purpose of yours and Dr. Wakefield's research" is odd and the reasons given for it unsustainable... it is unlikely that child JS would have been admitted for the purpose of a joint research project in reaction to parental pressure[...] As child JS's mother's letter to Dr. Wakefield dated 5th July 1997 made clear, although she felt that he had been damaged by MMR vaccine, her purpose in seeking Dr. Wakefield's help was to "explore every possibility to help our son" who, otherwise, "has no future at all – other than being sedated and confined to an institution". [182]

(d) "the diagnosis of inflammatory bowel disease (IBD) identified in Table 1 of the *Lancet* article misrepresented the medical records and pathology grading sheets."

[This GMC charge was amplified by BMJ's editor-in-chief into a malignant accusation of fraud.]

L'affaire Wakefield: Shades of Dreyfus & BMJ's Descent into Tabloid Science | Copyright © 2017 Alliance for Human Research Protection

Justice Mitting's judicious review of the evidence concerning each of the children's symptoms and detailed endoscopic and colonoscopy test results sheds light on the complex diagnostic process that was followed by a team of 5 clinicians, led by Professor Walker-Smith, who evaluated the children's medical condition, ordered the necessary diagnostic tests, and determined each child's diagnosis. The goal of the team was to identify the disease underlying the symptoms that each child suffered from; to enable the doctors to begin appropriate treatment.

"In every case investigations were followed by a discharge letter prepared by Dr. Casson which set out a diagnosis of the child's condition and by a recommendation for treatment. In some cases, the treatment produced an apparent marked improvement in gastrointestinal symptoms and behaviour." [Par. 19]

"on 20th December 1996, Professor Walker-Smith reviewed child 3's histology reports with Dr. Dhillon, at the same time as the other six children who had by then been investigated. As a result, they arrived at final diagnosis: lymphoid nodular hyperplasia and indeterminate colitis... The discharge notes were appropriately amended. He suggested that an anti-inflammatory drug might be of some therapeutic value." [Par. 68]

Professor Walker-Smith's evidence was that [a child's] condition could not just be explained by constipation – a symptom of an underlying disease rather than a disease. Rectal bleeding and anaemia, of sufficient severity to require his general practitioner to give iron, was untypical of constipation. A colonoscopy would offer the opportunity to demonstrate whether or not there was ongoing "infection" (i.e. inflammation) in the gastrointestinal tract. Dr. Miller supported his approach: constipation requiring regular enemas, rectal bleeding and anaemia meant that this was not a simple case of constipation. He said that he saw nothing wrong in Professor Walker-Smith's decision to undertake colonoscopy, even after the inflammatory markers came back normal." [Par. 69]

GMC's expert witnesses were: Professor Michael Rutter and Professor Ian Booth. Expert witnesses for Professor Walker-Smith were: Dr. Neil Thomas and Dr. Victor Miller. Justice Mitting evaluated the GMC panel's failure to justify why its accepted the opinions of GMC's experts rather than the far more reasoned opinions of the defendant's expert witnesses:

"It is a striking feature of the panel's decision that it expressed no view about the expertise and objectivity of the experts; and even more striking that, when their views were in conflict, it expressed no conclusion about which of them it preferred. This is a serious weakness in its reasoning, frankly acknowledged by Miss Glynn [GMC's prosecuting attorney].

I would go further. In the case of each child, the experts were asked to consider whether the investigations undertaken were clinically indicated and, if not, contrary to the clinical interests of the child. It was common ground that the Bolam test applied to both issues. When, as was in fact the case, Dr. Miller and Dr. Thomas expressed the view, respectively, that colonoscopy (and if appropriate barium meal and follow through) or lumbar puncture were clinically indicated and

were not contrary to the clinical interests of the child, a finding that their view was not one held by a responsible body of medical opinion would have been an essential pre-requisite to the dismissal of their evidence in respect of that child. The panel made no such finding. [Par. 23]

Miss Glynn, recognising the difficulty it creates for the GMC, has attempted to analyse the case of each child, to show that, despite the lack of an express finding, the panel must have preferred the opinion of Professor Rutter and Professor Booth to that of Dr. Thomas and Dr. Miller...

It would be necessary for her to demonstrate that the panel must have rejected the opinion of Dr. Miller and, in part, of Dr. Thomas, as being outside the ambit of responsible medical opinion. She has not attempted that task, sensibly recognising that the material which would permit it to be discharged cannot be found in that submitted to the panel." [Par 23]

Professor Ian Booth disagreed with the expert diagnostic evaluation of Professor Walker-Smith and Dr. Dhillon. In his opinion, *"the children were investigated for purposes of research."* Justice Mitting noted that Prof. Booth had been criticized as being *"opinionated and had become an advocate for everything for which the GMC contended, rather than an independent expert commenting objectively on the facts."* Prof. Booth's opinion was based on his review of *"medical notes"* and *"correspondence"* from non-specialists in either gastroenterology or histopathology.

"Professor Booth's firm view that this was research appears to have been based on the correspondence...[he] concluded, without hesitation, that the colonoscopy [sic] was a research investigation...As in the case of several of the other children, the correspondence is equivocal... The medical records provide an equivocal answer to most of the questions which the panel had to decide." [Par. 47; 70; 180; 184; 186]

Justice Mitting was not persuaded by Prof. Booth's single-minded argument. The detailed evidence submitted by Professor Walker-Smith and Dr. Murch, and the reasoned opinions by the expert witness, Dr. Miller, persuaded Justice Mitting who ruled:

"Professor Walker-Smith and Dr. Murch gave detailed evidence about the results of the investigation which, in their view, confirmed the presence of bowel inflammation, suggestive of Crohn's disease. Their evidence was unequivocally supported by Dr. Victor Miller who said that he was "absolutely certain that this child had active disease that required clinical management". He also gave unequivocal support to Professor Walker-Smith's decision to admit him for the investigations, because of child 2's long history of undiagnosed troublesome clinical symptoms: 'It is, I think, a responsibility of such a doctor to investigate that child as fully and comprehensively as he can, to try and determine what is wrong with him'". [Par. 43]

The panel] did not begin to address the serious debate between Professor Booth and Dr. Miller about this issue. Unless it was able, rationally, to dismiss Dr. Miller's firm view as outwith the spectrum of reasonable medical opinion, it could not sustainably have reached the conclusion that colonoscopy and barium meal and follow through were not clinically indicated." [50]

“Dr. Miller identified the very difficult question at the heart of the case against Professor Walker-Smith: determining what was, and was not, permissible as medical practice in a specialist field, by an acknowledged expert academic clinician, in a case in which the aetiology of the disorders he was investigating was uncertain.” [Par.73]

Professor Walker-Smith said in evidence that on the basis of what he knew from the clinical records and discovered at the outpatients clinic on 18th October 1996, colonoscopy was not clinically indicated. He wanted to await the results of the blood tests before making a decision. Both Professor Booth and Dr. Miller agreed with his decision. He said that it was the abnormal CRP result which changed his mind. He explained that the reference to that result as "slightly abnormal" in his letter to child 12's mother was gentle language used to avoid alarming her.

Dr. Murch considered that the result meant that they had "reached a tipping point", in favour of investigation. Dr. Miller agreed: an abnormal marker was precisely that and a clinician was entitled to act upon it, in particular, one who had already gained considerable experience from previous cases. At the hearing before the panel, Mr. Miller drew attention to evidence in the literature stressing the importance of diagnosing inflammatory bowel disease as early as possible. Professor Booth's opinion was that the fact that one of several inflammatory markers was raised "to the smallest possible degree" did not justify colonoscopy, without further prior investigation. Professor Rutter said that the documents and circumstances suggested research not clinical investigation.[117]

Justice Mitting notes that in the case of child JS, the correspondence:

“supports Professor Walker-Smith's case that his purpose was clinical investigation and treatment. His letters to Dr. Mills of 23rd April 1997 and 9th May 1997 are of particular significance: they were the letters of a clinician who believed that he had discovered something of therapeutic value for his patients. He may, or may not, have been wrong about that; but the letters exclude the proposition that his purpose was research. The terms of the letters are reinforced by the five page explanation of the protocol under which Professor Walker-Smith and his team were operating, which was sent both to Dr. Mills and to Dr. Shore.”[Par. 184]

Child 9 was one of the children whose histology reports were reviewed by Dr. Dhillon and Professor Walker-Smith in December 1996. Their diagnosis was indeterminate colitis. Professor Walker-Smith wrote to Dr. Spratt setting out his conclusions: endoscopy had revealed a marked increase in the size and number of prominent lymph nodes in the terminal ileum. Histology revealed an increase in chronic inflammatory cells throughout the colon. His diagnosis was indeterminate colitis with lymphoid nodular hyperplasia. [par. 85]

Professor Walker-Smith said in evidence that on the basis of what he knew from the clinical records and discovered at the outpatients clinic on 18th October 1996, colonoscopy was not clinically indicated. He wanted to await the results of the blood tests before making a decision. Both Professor Booth and Dr. Miller agreed with his decision. He said that it was the abnormal

CRP result which changed his mind. He explained that the reference to that result as "slightly abnormal" in his letter to child 12's mother was gentle language used to avoid alarming her. Dr. Murch considered that the result meant that they had "reached a tipping point", in favour of investigation. Dr. Miller agreed: an abnormal marker was precisely that and a clinician was entitled to act upon it, in particular, one who had already gained considerable experience from previous cases.

At the hearing before the panel, Mr. Miller drew attention to evidence in the literature stressing the importance of diagnosing inflammatory bowel disease as early as possible. Professor Booth's opinion was that the fact that one of several inflammatory markers was raised "to the smallest possible degree" did not justify colonoscopy, without further prior investigation. Professor Rutter said that the documents and circumstances suggested research not clinical investigation.

"The findings [sic] that the referrals of four children were not routine because the referring doctors did not mention intestinal symptoms in their referral letters was factually accurate as to the contents of the referral letters, but of no significance. In each case, Professor Walker-Smith elicited gastrointestinal symptoms at his outpatients clinic. The finding [sic] that all four children "lacked a history of gastrointestinal symptoms" is wrong unless the panel intended only to refer to the contents of the referral letters.[par. 158]

Justice Mitting's determination that medical records by doctors who have no expertise in diagnosing a complex newly identified syndrome, are "of no significance," was validated by a [Wake Forest Study](#) (2013) that reported:

"Prospective controlled studies suggest that as many as 70% of autistic children exhibit chronic GI-related symptoms, including diarrhea, constipation, abdominal distension, failure to thrive, weight loss, feeding problems, and abdominal pain related to extreme irritability, aggression, and self-injury...[However] retrospective chart review studies have shown no increase in GI symptoms in ASD children. In ASD children who undergo endoscopic and histologic examinations, inflammatory pathology is reported with high frequency." (SJ Walker, PLoS One, 2013)

(e) GMC declared the phrase "consecutively referred" was "a dishonest representation of patient selection." Justice Mitting dismissed GMC's misinterpretation of the term:

"This [Lancet] paper does not bear the meaning put upon it by the panel. The phrase "consecutively referred" means no more than that the children were referred successively, rather than as a single batch, to the Department of Paediatric Gastroenterology. The words did not imply routine referral."[par. 157]

Justice Mitting commended the author's cautionary acknowledgment in the Lancet article:

"We describe a pattern of colitis and ileal-lymphoid-nodular hyperplasia in children with developmental disorders. Intestinal and behavioural pathologies may have occurred together by chance, reflecting a selection bias in a self-referred group; however the uniformity of the intestinal pathological changes and the fact that previous studies have found intestinal

dysfunction in children with autistic-spectrum disorders, suggests that the connection is real and reflects a unique disease process."

"Taken together with the comments already cited about the temporal coincidence of the onset of symptoms and MMR vaccination in the case of eight children, the author has made it clear that this was not a routine referral. It was a referral generated by the concerns of parents about a possible link. The statement made by the panel that [sic] Professor Walker-Smith had described the referral process in the Lancet paper as "routine" was wrong. It put its stretched meaning of the wording of part of the paper into his mouth and then found that it was irresponsible and misleading." [par. 157]

Justice Mitting noted that Dr. Wakefield's co-authors "were convinced that the investigations into the twelve 'Lancet children' had been of diagnostic value for all of them and therapeutic value for most of them." [par. 8] He cited a letter written by Professor Walker-Smith (October 1997) to Dr. David Salisbury, Principal Medical Officer and Director of Immunisation at the Department of Health, after the Lancet study had been completed:

"On the issue of autism, I am completely astounded by the clinical features of these children with autism and bowel inflammation. Very often the gastrointestinal symptoms have been ignored by a succession of the doctors and the findings on ileo-colonoscopy appear to be quite distinctive. This seems to me a whole new syndrome which is in urgent need of clarification". [Par. 8]

"That," Justice Mitting observed, "was the conclusion of the published paper."

Justice Mitting's Conclusion: *"both on general issues and the Lancet paper and in relation to individual children, the panel's overall conclusion that Professor Walker-Smith was guilty of serious professional misconduct was flawed...[there was] inadequate and superficial reasoning and, in a number of instances, a wrong conclusion... the medical records provide an equivocal answer to most of the questions which the panel had to decide. The panel had no alternative but to decide whether Professor Walker-Smith had told the truth to it and to his colleagues, contemporaneously. The panel's determination cannot stand. I therefore quash it." (March 7, 2012)*