MMR and the development of a research governance framework in UCL

1. Introduction

In May 2010, the General Medical Council found Dr Andrew Wakefield guilty of serious professional misconduct and erased his name from the medical register[i]. The GMC's findings related mainly to his clinical misconduct, notably through unnecessarily causing three young and vulnerable children to undergo the invasive procedure of lumbar puncture; and through collecting blood from a group of young children at a birthday party. However, the GMC Panel also raised a range of issues relating to Dr Wakefield's research conduct.

A journalist working for the Sunday Times suggested in a series of articles published in the BMJ in January 2011 that the GMC's findings amount to evidence of research fraud[ii]. The BMJ called on UCL to investigate these claims. UCL was conscious that any such investigation should be independent, robust, fair both to the initiator of the complaint and to the respondent(s), and conducted according to a transparent process. To that end, detailed advice was sought from the UK Research Integrity Office in respect of the scope, remit and processes for such a review. That advice in turn prompted a range of further concerns about the feasibility of any such inquiry, given the passage of time since the initial allegations. Independent advice was sought from a senior legal figure and the prospect of a detailed inquiry into alleged research fraud rejected for a number of reasons.

In essence, it was concluded that UCL would lack sufficient authority to require respondents or potential witnesses to contribute to any hearing or to provide evidence to inform the inquiry's processes, as the majority of the main characters are no longer in UCL's employ. Lacking any legal powers of compulsion, UCL would likely encounter reluctance or refusal to contribute from one or more respondents. Secondly, there is no formal complaint or complainant to trigger the formal UCL process. Thirdly, an inquiry at this distance in time from the events themselves may be resented by those most closely involved and oral evidence may be affected by failing memory. Although there is a good body of written evidence relating to the events in question still available (not least the documents made available to the GMC inquiry), documentary and laboratory materials relating to specific research projects and publications will be unlikely to be complete (or be obtainable by any such inquiry). The net result would likely be an incomplete set of evidence and an inconclusive process costing a substantial sum of public money.

However, the GMC's findings have serious implications both for UCL's own internal research governance and processes and for the research governance policies of health and higher education institutions across the UK and beyond. This paper will examine those issues and their implications for research governance policy and practice. It will look at how UCL has responded to date to the challenges of the incident and its aftermath and will attempt to draw some more general conclusions that may be of value to the wider scientific community.

2. Brief rehearsal of the incident

Dr Wakefield worked at the Royal Free Hospital Medical School from 1995 to 2003. He was a Senior Lecturer (and, from May 1997, a Reader in Experimental Gastroenterology) in the Departments of Medicine and Histopathology and an honorary consultant at the Royal Free hospital. The Royal Free Hospital Medical School merged with UCL in 1998 to form the

Royal Free and University College Medical School (RFUCMS). Dr Wakefield continued to be employed by RFUCMS until he left by mutual agreement in 2003.

In 1996 and 1997 Dr Wakefield's research sought to demonstrate a link between bowel disease and autism in children. His Early Report, *Ileal lymphoid nodular hyperplasia, non-specific colitis and pervasive developmental disorder in children,* published in the Lancet in February 1998 (partly retracted in 2004 and fully retracted in February 2010) claimed to report a new syndrome in 12 children, including an alleged temporal association between a type of autism and the measles, mumps and rubella (MMR) vaccine [iii]. The paper included a statement that the research team "did not prove an association between measles, mumps, and rubella vaccine and the syndrome described" and included an accompanying Comment that emphasised the safety and efficacy of the vaccine. However, the paper was subsequently promoted at a press conference where statements not included in, or supported by, the paper (or by other authors) were made, leading to a public health scare with far-reaching consequences for the uptake of MMR in the UK.

In February 2004, a journalist working as part of a Sunday Times investigation into the MMR health scare met with the editor and other senior staff at the Lancet. The Lancet asked the journalist to delay publication so that the allegations could be considered by the UK's Committee on Publication Ethics where a plan could be agreed for their proper investigation. When it became clear that this avenue for resolving the allegations would not be possible, the concern arose that the reputations of the doctors under scrutiny could be unfairly damaged in the media if there was no opportunity for some form of local inquiry, even if time pressures prevented a full and proper process.

The Lancet's editor accordingly convened a meeting with those accused by the journalist, and reported the journalist's allegations to the Vice-Dean of the Royal Free and University College Medical School. No formal complaint of research misconduct was received, so the Vice-Dean was not in a position to trigger a formal investigation according to the requirements of the usual UCL research misconduct procedure. Nonetheless, because of the time pressure and the fear of an unfair news report without input from the accused parties, action was clearly required.

After consulting with more senior colleagues at UCL and the Royal Free Hospital Trust, the then Vice-Dean launched an informal inquiry which took the form of a meeting, led by the Vice-Dean, accompanied by the Lancet's Editor, interviewing two of the clinicians concerned. The meeting was a lengthy and difficult affair. The two doctors were questioned about the journalist's allegations, focusing on the issues of ethics approval, patient referral, and conflict of interest - namely, that funds received from the UK Legal Aid Board were used for clinical and scientific tests on 10 children involved in a lawsuit being prepared against MMR manufacturers.

Due to the informal nature of this process, no written note was taken of the meeting. In the week that followed, the Vice-Dean met again with staff engaged in the research in the department of Paediatric Gastroenterology where they examined the children's records and the relevant biopsy book and ethics committee records.

As this was an informal inquiry, the process lacked the usual features of an effective investigation of a complaint of misconduct. There were no terms of reference set out, no

defined investigatory panel, no gathering of documentary evidence, no formal presentation of allegations nor any representation from the complainant himself. Two of those accused of misconduct were involved in the process of gathering the evidence from the children's files, which would not now be permitted under UCL's formal procedures. The rapid, informal investigation culminated in written statements being provided by the staff involved and by the Vice Dean on behalf of the Medical School. These statements were subsequently published in the Lancet in March 2004 and confirmed that aspects of funding, ongoing litigation, and overlap of children with another Legal Aid Board funded pilot project were not, and should have been, disclosed to the journal.[iv]

3. UCL Research Governance Framework 2004 to the present

UCL Research Governance is enshrined in three documents: the *code of conduct for research*; the *procedure for investigating and resolving allegations of misconduct in academic research*; and the *declaration of interest policy*[v]. Although these or equivalent policies were in place by 2004, all three have also undergone significant revision since then.

Together, the documents constitute a framework to support UCL's research strategy and to ensure that research conducted by members of staff, honorary staff, students and individuals who collaborate with UCL conform to good practice and ethical expectations. The research misconduct procedure defines in detail the actions to be taken in the event that an individual is suspected or accused of research misconduct. Together, the three documents ensure an approach that is full, fair, thorough and robust while also protecting researchers from malicious or frivolous allegations.

The framework is overseen by the UCL Research Governance Committee (RGC) which did not exist at the time of the MMR incident. RGC originated in 2008 as a working group of the (then) Research Strategy Committee (RSC). The growing importance of research governance issues at UCL and sector-wide is reflected in the group's subsequent 'promotion' to a sub-committee of the RSC and, from August 2010, to a formal Standing Committee of UCL. Today, the UCL RGC is chaired by UCL's Vice-Provost (Research) and has a broad and weighty membership including the Vice-Provosts Health and Enterprise, the senior officers responsible for Registry and Academic Services, HR, and Research Strategy and Governance, a lay member of UCL Council and six academic representatives. Its terms of reference reflect the breadth of its activities, including the co-ordination of the operation of research governance processes and oversight of the operation of UCL's procedure for investigating and resolving allegations of misconduct in academic research.

If Wakefield's case were to have emerged in 2012, UCL would expect the journalist's concerns to have formally been expressed as a complaint, triggering an investigation under the *procedure for investigating and resolving allegations of misconduct in academic research.* In brief summary, the procedure requires that any allegation of research misconduct should be submitted as a detailed statement, with any supporting documentary evidence, to the UCL Director of Registry and Academic Services (RAS)[vi]. The allegation is then considered initially by a Screening Panel consisting of two senior members of UCL's academic staff drawn from the Department or Faculty concerned of whom one should normally be the Chair, and an academic specialist in the general area within which the misconduct is alleged to have taken place, from outside UCL. There may also be representation from any partner organisation involved in the research.

The Screening Panel considers whether the matter is sufficiently serious to warrant a full, formal investigation. The full formal Panel consists of at least three members: an external specialist in the academic area in question (who normally chairs the Panel); a senior member of staff from the Faculty (but not the specific department) in which the alleged misconduct took place; and an academic member of the UCL Research Governance Committee. The procedure takes care to ensure that enquiries undertaken both by the Screening Panel and the full Panel are thorough and objective, follow a transparent process, and as far as possible, are confidential to the Panels. It enshrines the principle of no-detriment to both the initiator(s) of the complaint and the respondent(s).

4. UCL's subsequent response to the GMC findings

The GMC's 2010 Fitness to Practise Hearing highlighted a range of issues relating to research misconduct by Dr Wakefield, notably non-compliance with ethics procedures, an erroneous selection of patients and the non-declaration of a conflict of interest. These issues prompted a specific UCL review in 2010 led by the Joint UCL/UCLH Royal Free Biomedical Research Unit (now part of the School of Life and Medical Sciences Clinical Research Support Centre). The review looked in detail at the issues raised by the GMC's findings, tested them against UCL's existing research governance processes and procedures, identified ongoing procedural risks and made a series of recommendations for action.

The review's report was considered first by the UCL Clinical Research Governance Committee (CRGC) in November 2010 and then by the main UCL Research Governance Committee described above, to which the CRGC reports. The implementation of the report's findings has led to further improvements in UCL's governance processes. Specifically:

4.1 The GMC found that Dr Wakefield had been dishonest and misleading in applying for funding from the Legal Aid Board. The Review found scope for research grants from small scale, less sophisticated funding bodies to be administered in non-research accounts, outside the formal UCL grants administration system. The finding has prompted an audit of UCL grant income that falls outside the formal grants administration systems and a tightening of systems to prevent any future avoidance of the established processes.

4.2 The grant from the Legal Aid Board was used for purposes other than those originally agreed (for example, funds were used to support staff costs rather than, as stated, for diagnostic tests). Most grant funding bodies permit some defined, limited divergence in expenditure from the approved grant application, provided the change is justifiable and does not compromise delivery of the grant objectives. Nonetheless, the scope for unauthorised divergence was deemed greatest for awards held outside the formal grants administration system, and this issue was subjected to the audit set out in 4.1 above.

4.3 Wakefield violated conditions attached to his honorary contract of employment with the Royal Free Trust. This is an area where, nationally, procedures have been improved substantially since 2004. Nonetheless, the decision about conditions for honorary contracts is taken by NHS Human Resources departments and does not link to an understanding of the study protocol in question; nor can staff whose Trust honorary contract relates solely to research (rather than clinical) activity be readily identified. In response, UCL has set in

motion a review of job planning and appraisal arrangements for staff working in a clinical environment but without formal clinical responsibilities.

4.4 The GMC found that Wakefield had failed to disclose to the Research Ethics committee facts relevant to their consideration of the application, notably his potential conflict of interest. It also found that he did not disclose his potential conflict of interests to the Lancet editor. This finding prompted a review of UCL's Conflict of Interests policy that recommended a range of changes, including a revised 'declaration of interest' policy to mitigate the identified risk. The new policy is undergoing revision with a view to being implemented in 2012-2013.

4.5 The GMC also found that there was no ethics approval in place to cover the specific activities undertaken by Wakefield. Although UCL already has in place a regular research governance audit of its project portfolio, this issue is one that requires training and local monitoring within constituent academic Divisions and Institutes. The Chair of the UCL Clinical Research Governance Committee is leading the development of research training and the enhancement of departmental level accountability for research conduct.

4.6 The GMC found that Wakefield should have taken account of the potential significance for public health of the 1998 Lancet paper[vii] and taken greater care to ensure the accuracy of his data and findings. It also found that when challenged at scientific meetings, Wakefield provided inaccurate and misleading answers. This major finding prompted a significant review of UCL's research governance framework, resulting in the revised *procedure for investigating and resolving allegations of misconduct in academic research* which was also finalised and released in January 2012.

In summary, UCL's response consisted of a range of internal reviews that refreshed its policy framework and committee structure for research misconduct and conflicts of interest. It was deemed vital to ensure that its governance mechanisms enable UCL to meet all the necessary regulatory and governance requirements, without stifling research by any excessive controls on the approval process. That same balance is one that challenges every UK organisation involved in biomedical research.

5. Good practice lessons

UCL's specific experience of the MMR issue reflects the general need for all institutions engaging in biomedical research to have in place a robust and effective research governance infrastructure. Some of the key lessons prompted by UCL's experience include:

5.1 The need for policies and procedures to be clear and comprehensive, setting out in detail the notification of concerns, preliminary vetting of allegations and the escalation of complaints to a relevant second-stage panel (or other body). That panel requires a membership that is appropriately skilled to consider the detailed subject matter of the particular case while sufficiently distanced from the specifics of the allegation to bring true impartiality to bear. The panel should include external representation to ensure an alternative perspective on matters of potential public interest. The policy should flag the need to ascertain at an early stage whether a formal complaint is being made so that the appropriate subsequent procedure may be expedited.

5.2 The need for the consequent research governance framework to be firmly embedded in the quotidian research processes of the organisation. The processes must be well understood, not only by officers charged with their implementation, but by academic/scientific departmental heads and by individual principal investigators. It follows that the institution must provide for its staff, affiliates and students effective education and training in the importance of best practice in research governance. Institutions must develop a culture of research integrity that values transparency, welcomes whistle-blowing on instances of misconduct, and has in place clear and well understood policies on conflicts of interest.

5.3 Research activity is increasingly carried out across organisational divides. Clinical research almost always involves at least one higher education institution and at least one NHS Trust. It is critical that the processes governing clinical procedures are aligned with those that govern academic research activity. UCL's experience suggests that a Research Office that is run jointly between Trust and university can contribute significantly to the mitigation of risk in such joint research projects.

5.4 Formal collaborations, alliances and mergers are increasingly commonplace in the higher education sector, with UCL itself in the last twenty-five years having formally merged (on the biomedical front alone) with two medical schools, four postgraduate institutes and a School of Pharmacy. Alongside the many benefits of such mergers come risks that require careful mitigation. The merging organisations will have different experiences of research governance best practice that might usefully prompt a review of the framework adopted by the new, joint institution. Once revised, the new policies will need careful and clear communication to all stakeholders and further embedding into culture and practice at departmental level.

5.5 New scientific discoveries are regularly embraced by – and contribute to the welfare of – our society. It follows that society has a significant stake in the ethics and activities of its scientists. Particularly at the frontiers of science, public involvement is critical to the building of greater trust between society and its researchers and academic institutions ignore that involvement at their peril. It is incumbent on institutions to embed into their governance procedures a clear and prominent role for the consideration of matters of public interest and to subject such matters to particularly careful and focused scrutiny.

5.6 Institutions have a second responsibility which is to the wider promotion of science. Governance procedures must be clear, robust and well communicated, but they must also avoid any inhibition of legitimate scientific investigation. The designers of process must steer clear of the pitfall of overly bureaucratic or intrusive procedure. If processes are viewed by researchers as obstructive, compliance will inevitably fall away and the risks of misconduct will increase. Administrators must strike a careful balance between the complex and demanding requirements of statute and good practice against the legitimate and necessary promotion of scientific excellence.

In addition, UCL has received valuable advice from the UK Research Integrity Office (UKRIO) on the revision of its research misconduct procedures and the promotion of good practice in research. UKRIO has highlighted three related, key lessons to be learned from the MMR issue:

i) that institutional procedures enable and require the commitment of senior staff to the leadership roles set out in the Department of Health's *Research Governance Framework for Health and Social Care*[viii], and other relevant guidelines;

ii) that systems for investigating allegations of misconduct are in working order, so that institutions can deal confidently with rare and difficult events if they arise;

iii) that institutions look carefully at the collaborative mechanisms that will allow them to live up to *The Concordat to Support Research Integrity* and other good/ best practice guidance, whether regulatory, from funding/ professional bodies or organisations such as UKRIO and COPE.

6. Conclusions

There is broad recognition of the need to raise the profile of research governance issues across the sector. In January 2012, the BMJ and the Committee on Publication Ethics (COPE) jointly held a meeting on research misconduct in the UK which attracted national leaders across the health and university sectors. The meeting reflected that the impact of individual cases of misconduct can range far beyond any individual institution. It also agreed that that the UK's mechanisms for ensuring good research conduct and investigating research misconduct need to be strengthened[ix].

UCL has learned a great deal from its involvement in the MMR issue and has now introduced a research governance framework that is robust and fit for purpose. The test now for UCL – and for the sector more widely – is twofold. First, to ensure that research governance processes and procedures are properly embedded into the management infrastructure of the organisation.

Secondly, to test and re-test those procedures (whether called upon in practice or not) to ensure that they are robust and workable (without impeding legitimate academic research aspirations), and reflect best practice from other organisations. To that end, institutions should be encouraged to think self-critically about their own framework, to review processes and procedures annually, and to share anonymised cases with other related organisations. Only by consciously and actively raising the profile of research governance issues across - as well as within – institutions, will the UK biomedical sector develop a framework that is truly fit for purpose. UCL is committed to working with the research community - including our NHS partners, other universities and UKRIO - to achieve this.

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[i] GMC, Andrew Wakefield: determination on serious professional misconduct and sanction, 24th May 2010

[ii] Deer, B, How the Vaccine Crisis was meant to make money, BMJ 2011:342:c.5258

[iii] Wakefield AJ, Murch SH, Anthony A, Linnell, Casson, Mailk, Berelowitz, Dhillon, Thomson, Murray, Walentice, Davies SE, Walker-Smith "Ileal-Lymphoid-Nodular Hyperplasia, non-specific Colitis and Pervasive Developmental Disorder in Children". *Lancet Journal* 351 Feb 28th 1998 p.637

[iv] Horton R, A statement by the editors of the Lancet, Lancet 2004: 363:820 ff; A statement by the Royal Free Hospital Medical School and the Royal Free Hampstead NHS Trust, Lancet 2004: 363:824-825; A statement by Dr Andrew Wakefield, Lancet 2004: 363:823-824; A statement by Professor John Walker-Smith, Lancet 2004, 363:822-823; A statement by Dr Simon Murch, Lancet 2004, 363:821-822

[v] UCL, ;http://www.ucl.ac.uk/ras/acs/resgov/code-of-conduct-research; http://www.ucl.ac.uk/ras/acs/resgov/research-misconduct-procedure.pdf http://www.ucl.ac.uk/finance/finance_docs/doi_policy.html.
[vi] UCL, http://www.ucl.ac.uk/ras/acs/resgov/research-misconduct-procedure.pdf
[vii] Wakefield AJ, Murch SH, Anthony A, Linnell, Casson, Mailk, Berelowitz, Dhillon, Thomson, Murray, Walentice, Davies SE, Walker-Smith "Ileal-Lymphoid-Nodular Hyperplasia, non-specific Colitis and Pervasive Developmental Disorder in Children". *Lancet Journal* 351 Feb 28th 1998 p.637
[viii] Research Governance Framework for Health and Social Care, Department of Health, 2005
[ix] A consensus statement on research misconduct in the UK, BMJ 2012: 344:e1111