Dental Schools Council response to the Academy of Medical Sciences Review of the regulation and governance of medical research

What are the principles that should underpin the regulation and governance of medical research?

The principles of the Declaration of Helsinki are well recognised and universally accepted. The key principles relate to patient safety, consent, confidentiality, respect and public trust. These issues are important to allow the public to have confidence in the system and respect for clinical researchers.

Research must also be underpinned by integrity and scientific quality. It is reasonable that, as in all other areas of clinical practice, clinical researchers are expected to have undergone some training in clinical research (e.g. GCP) and should be able to produce good documentary evidence of their intentions (e.g. a robust research protocol)

With regards to regulation and governance, it is essential that issues of risk and proportionality should underpin the regulatory process.

What are the most significant regulatory and governance impediments to medical research in the UK? In each case, is the impediment caused by: the underpinning regulation (or absence of regulation); its implementation at national or local level; the guidance and support provided for researchers (or lack of it)?

The overall most significant impediment is a massive, and shifting, bureaucracy that has developed around the governance process. This, in large part, has been aggravated by risk averse local processes managed by administrative staff who themselves have insufficient understanding of all the complex issues.

It is generally felt that the regulatory processes, especially around low risk research, (e.g. use of archival tissues, tissue sampling, questionnaires, case note review) have become overly complex and that the costs of this micro-management are disproportionate to the need to prevent malpractice and protect the public. Indeed there is evidence that the complex governance framework may inhibit clinical research generally with the potential to do great harm to the advancement of knowledge and hence to the advancement of patient care.

Examples include:

- Overly bureaucratic and complicated classification systems for research projects, resulting in lack of understanding and conflicting advice to researchers from R&D officers. Sometimes resulting in refusals and the researcher having to 'start again'.
- Failure to distinguish adequately between projects that may have no significant ethical issues (e.g. a review of datasets or cases notes) and those with complex ethical and patient safety considerations which should be subject to rigorous ethical review of proposals (and the many projects which might fall someway in between these two extremes);
- The inconsistency of local reviews of multi-centre studies (see for example Mallick AA & O'Callaghan FJ J Royal Soc Med 2009 102 : 195 – 8)
- A negative culture amongst regulators (both internal R&D departments and externally) of obstruction rather than facilitation, often reflecting a risk-averse mindset which is particularly prevalent in NHS management. R&D officers and others are quick to point out what is not acceptable etc but are rarely actively involved in

writing an ethics application or facilitating an approval. Ethics Committees are often very slow, unresponsive and inconsistent, and often feel obliged to make amendments to applications however trivial, sometimes even contradicting themselves over previously approved wording or practices.

- The governance process has resulted in a culture of 'policing' rather than facilitating research. Overly zealous R&D administrators can be officious and intimidating. We have reports of unpleasant experiences during inspections of site-files and checking of paperwork. Fear of reprimand by R&D officers may prevent young researchers from even attempting to start the process.
- The bureaucracy of regulation de facto provides a very long time lag in initiating and pursuing projects.
- It is pointed out that the regulatory mechanisms now in place have almost completely stopped clinical research at an undergraduate level. Previously it was common for all UGs to undertake a small research project involving patients, for example a questionnaire based project, case-note reviews to correlate factors, or retrospective analysis of pathology samples or radiology. This is now all but impossible in the timescales needed within an undergraduate curriculum with increasing numbers of students. This is a huge lost opportunity to introduce undergraduates to research and to inspire a future generation of clinical academics. This, at a time when recruitment to academic posts is still in crisis.
- This problem is also aggravated by the fact that some NHS R&D offices are charging universities for the governance approval of all projects which are not within the NIHR portfolio. This includes almost all student-led research (at UG and PG level).
- Finally – Money. The increasing costs of gaining regulatory approval could be significantly reduced if the process were proportional and streamlined. Almost all research organisations now employ staff to assist with the complex bureaucracy of the approvals process.

Which parts of the regulatory and governance framework are working well and why?

It is difficult to identify those elements which are working well. The responses received varied, and this seemed mostly to reflect the ways in which guidelines had been implemented locally. Again this was related to the locally introduced bureaucratic processes.

All respondents recognised the need for a robust regulatory and governance framework and all wished it to work well.

In general there is a view that the ethics process has improved over recent years, first through COREC and now with IRAS and NRES.

HTA licensing has the potential to work well.

When appropriate, public and patient involvement in research works well. However there have been times when an insistence on PPI when not necessarily appropriate or desirable (e.g. a retrospective analysis of tissue samples for potential new biomarkers, an analysis of contamination of instruments) has inhibited, delayed or prevented local approval of projects.

What initiatives to reduce the burden of the regulatory and governance framework are currently in progress, both here and abroad?

NIHR have initiated a bureaucracy-busting initiative, the outcomes of which are not yet apparent.

We are aware that a number of Universities and Trusts are working together to try to reduce bureaucracy and streamline processes. At present, university researchers often have to duplicate paperwork and processes to satisfy two pay-masters – e.g. finance approval forms, preparation of protocols in two formats for separate peer-review or approval processes. This may be even more complicated when the project involves a (PhD) student.

We have anecdotal evidence that NIH (USA) have similar problems – that clinical research (especially trials) have become over-regulated and overly complex, and that this is being addressed. In USA this has also fostered a burgeoning (private sector) industry in clinical trials management. This is not a route that we would wish to see followed in the UK.

What can we learn from the regulatory and governance framework in the different nations of the UK and from outside the UK?

We are aware that some R&D offices in the UK operate a system of proportionality. That is, they assess the risk and then apply appropriate governance procedures. In this way, low risk projects are 'fast-tracked'.

Conversely we have reports that some R&D offices DO NOT use any form of proportionality and apply the guidelines stringently to all forms of research. This means that a simple non-invasive evaluation or case note review has to go through the same process as an RCT of a newly introduced medication.

We are aware that some R&D offices do not accept paper-work or approvals from other regions or organisations and insist on duplicated paperwork (e.g. from their local University, or in the case of multicentre studies) and a repeat of the process locally. Conversely we have reports of offices who do facilitate research by accepting paperwork prepared elsewhere.

There is clear scope here for learning from and applying good practice.

What changes to the regulatory and governance framework would provide the greatest improvement to the progress of medical research, without putting patients at unnecessary risk?

All respondents ask for reduced bureaucracy, a reduction in the sheer volume of forms and paperwork, and a system which more overtly facilitates, rather than polices research.

All NHS organisations should use common procedures and processes and organisations should accept each other's paperwork. We have an example of a multicentre study involving 17 NHS trusts. The requirements for approval for a researcher to visit each site varied from Trust to Trust. For example differences in need, or processes, for honorary contracts, research passports, CRB checks etc.

The overwhelming view is that a system of proportionality must be introduced. In such a scheme the approval pathway for each project should be based on risk.

How might the medical research process evolve in the future? Does this raise any additional issues for the regulatory and governance framework?

There is a need for more general prospective consent from (NHS) patients for the use of their data or records (including archived radiology, and pathology samples) to be used for research.

All NHS patients should know about clinical research and should realistically expect to contribute to the research effort.

To facilitate this there needs to be a public awareness campaign to raise the profile of the amazing and good clinical research done in the UK, mostly through the NHS. Patients and the public should think of themselves as stakeholders and contributors to the UK clinical research effort and should be sufficiently informed of its success to be able to share the pride we have in the fact that UK biomedical research punches above its weight internationally.

At present, the adverse publicity surrounding UK biomedical research and the knee-jerk changes to the regulatory framework have significantly undermined public (and professional) trust and confidence in clinical research and in the professions generally.

Is there a need for a more risk-based approach to medical regulation and how might this be developed and adopted?

Overwhelmingly, respondents wish for a system of risk assessment and proportionality.

All research proposals should be assessed for the element of risk and the approval process steered accordingly. Much research which uses patient material or records has no risk at all for the patient or the public (only benefit), yet is subject to a one-size-fits-all governance process which, by and large, has been designed to protect patients from harm in clinical trials.

This approach is needed to facilitate more research and to address the issues raised above relating to costs,

proportionality and the adverse affects on research training opportunities, especially at UG level.

Examples of no- or low-risk research include:

- Simple questionnaire studies.
- Case-note reviews – for example to correlate smoking to disease, or to determine the prevalence of a clinical finding. We have a report of complex and long processes for approval of a study to determine the prevalence of supernumerary teeth in a retrospective review of panoral radiographs.
- Use of waste tissue or material. In dental research there is much work on the bacterial aetiology of disease and on the pursuit of potential biomarkers in fluids. This involves the collection of material (bacterial plaque, saliva or gingival crevicular fluid) which is normally discarded in the course of normal routine treatment. Yet we have many reports of complex approval process which have prevented or significantly inhibited research on these materials. There are cases where potential (industrial) funding has been lost because of this barrier.
- Studies to evaluate already available interventions. For example to compare patient preferences between two commercially available products (eg. toothbrushes, filling materials, mouthwashes).
- Studies to determine outcomes from the use of different materials – e.g. in terms of caries prevention, or longevity. We have an example where a study to evaluate the efficacy of two already widely used orthodontic appliances has been delayed for TWO years, because the Trust treats it as a RCT of interventional medicines for governance purposes.
- Studies using archived material. This applies especially to use of archived pathology specimens. Simple retrospective biomarker studies and even analyses for large case series are very difficult because of the approval process.

An approval process based on risk could use a system of 'accountable officers'. Simple no-risk projects could be approved internally within a single organisation by an accountable officer, who was approved by and accountable to the local R&D office and the ethics committee. There could be levels of accountability depending on perceived risk – both to patients and the public but also to the organisation.

A departmental or School officer for example may approve student led studies involving anonymous case-note review, simple questionnaires.

A Directorate-based officer might approve use of records – for example review of radiographs or pathological material, or use of archived material. Approval at his level might also apply to use of waste material or tissue normally discarded in the process of routine care.

Approval and governance of interventional trials would need more robust approval processes similar to those already in place, but even here there is proportional risk. RCTs of new drugs for example bring varying risks to patients. Studies of new drugs in general may need a more robust process than evaluation of a simple intervention – for example a new device (a new toothbrush, a new filling material, a novel design of a denture)

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