



FACULTY OF PHARMACEUTICAL MEDICINE
OF THE ROYAL COLLEGES OF PHYSICIANS
OF THE UNITED KINGDOM

1 St Andrews Place, Regent's Park, London. NW1 4LB
Telephone + 44 (0)20 7224 0343 – Fax +44 (0)20 7244 5381
Email: fpm@fpm.org.uk Website: www.fpm.org
Registered in England & Wales as
a Company (No.6870644) and a Charity (No. 1130573)

28 May 2010

**FACULTY OF PHARMACEUTICAL MEDICINE RESPONSE TO THE REVIEW OF THE
REGULATION AND GOVERNANCE OF CLINICAL RESEARCH**

The Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the UK (FPM) welcomes the opportunity to respond to the Academy of Medical Sciences Review of the Regulation and Governance of Clinical Research set up by Andy Burnham MP, the then Secretary of State for Health. The FPM hopes that the final report of Prof. Sir Michael Rawlins' review will be given due cognisance by the new coalition government.

The FPM's Mission Statement is to advance the science and practice of Pharmaceutical Medicine for the benefit of the public. The FPM is a professional membership organisation with approximately 1400 members who are practising or retired Pharmaceutical Physicians or those with an interest in the specialty. Two thirds of the membership practise in the UK either within pharmaceutical companies or as consultants to those companies. About 60 members work within the Regulatory Authorities i.e. the Medicines and Healthcare products Regulatory Agency (MHRA) or the European Medicines Agency (EMA). A significant number of our members are directly involved in the clinical research process in the UK. A number of our members are Fellows of the Academy of Medical Sciences.

What are the most significant regulatory and governance impediments to medical research in the UK?

Clinical research in the UK is under considerable threat and is diminishing mainly because of the increase in bureaucracy associated with governance at NHS Trust level. When Prof. Sir John Pattison introduced NHS R&D Governance in 2001, he did so because non-commercial clinical research was of variable quality in the NHS. Much of it was very good but a significant amount was of poor quality and not of benefit to patients. Also at that time the UK research ethics system was inefficient and being heavily criticised by researchers and sponsors. The Health and Social Care Act of 1998 had given autonomy to NHS Trusts and as a result, the new NHS Research Governance Framework, when introduced, was interpreted in many different ways by NHS Trusts leading to a very bureaucratic and inefficient system with sponsors of multi-centre trials having no real idea when their trials would begin in each individual centre.

The transposition of the European Clinical Trials Directive into UK law in May 2004 provided one major benefit in that both the Competent Authority (the MHRA) and research ethics reviews had to be completed within statutory timelines. Unfortunately, the legislation did not cover NHS Research Governance and the long delays in NHS R&D review were thus exposed. The situation has not greatly improved in the six years since the introduction of the Directive for NHS review. The MHRA provides a Clinical Trial Authorisation (CTA) generally in less than 30 days, the National Research Ethics Service averages around 40 days for approval of a clinical trial but NHS review still takes several months in many Trusts. Timelines do vary from Trust to Trust as some are able to complete their review in a few days. This variation has had a serious adverse effect on recruitment to commercial trials in the NHS. The Centre for Medicines Research International (CMRI), an

independent body set up by the Association of the British Pharmaceutical Industry (ABPI) to develop and publish global comparative data on many aspects of pharmaceutical company activity showed in 2007 that there had been a threefold reduction in patient recruitment to commercial clinical trials in the UK between 2000-2006 (6% to 2% of global recruitment). This does not mean that the number of commercial trials in the UK has fallen as implied by the AMS report – Reaping the rewards: a vision for UK medical science. Indeed the MHRA statistics for CTAs since the introduction of the Clinical Trial Directive show a considerable rise after the first year which was maintained through 2006/7 and 2007/8 followed by very small reductions in 2008/9 and 2009/10 (see table and ref 1).

Year	Healthy volunteer CTAs	Patient CTAs Phase I-IV	Total CTAs
2004/5	270	561	831
2005/6	305	899	1204
2006/7	267	940	1207
2007/8	287	950	1237
2008/9	235	953	1188
2009/10	183	689	872

Notes: 2004/5 was only an 11 month year as the Directive only came into force in May 2004

2009/10 is only a 9 month year as the data for Jan – March 2010 is not yet available.

CTAs provided at the same rate would give an annual total of 1163 for 2009/10

There are a number of reasons for the reduction in patient recruitment to trials:

- Primarily the delay in getting trials started due to NHS R&D Governance review has meant that the window of opportunity for recruitment is shortened considerably in those centres that have taken several months to approve the trial
- Many UK affiliate pharmaceutical companies have reduced their target for patient recruitment because of the difficulties in getting trials started. At a global level it is far better to have recruitment running close to 100% of target in a country than 50% or lower
- Global HQs no longer see the UK as an essential centre for clinical trials. An increasing number of multi-national trials do not have a UK site. This is mainly due to the inefficiency in recruitment of patients as a result of NHS Governance. However another factor in active comparator trials is the lack of the active comparator being available because it hasn't been approved for use in the NHS by the relevant Health Technology Assessment body e.g. NICE. This latter situation means that UK patients do not get access to some new innovative treatments within clinical trials.

The NHS R&D Directorate and latterly the National Institute for Health Research (NIHR) has introduced some important initiatives to try and improve the situation with regard to patient recruitment numbers and timelines. The development of research networks and research passports has been helpful and there is no doubt that the leadership of the networks is determined to improve the situation but still the block is at local level. One very important development has been the introduction of the Integrated Research Application Service (IRAS) which has made the application process for trials much easier and more efficient. The NIHR Coordinated System for gaining NHS Permissions (CSP) theoretically should make a difference but its introduction has been slower than desired and it has not been helped by statements in the latest guidance document on Participant Identification Centres as follows: “it is recognised that this process is overly bureaucratic and will be improved in future CSP developments”. (ref 2). This type of statement inevitably has an adverse effect on sponsors when they are considering where to place their trials.

Recommendations

- A review of the UK legislation to consider how NHS Trusts can be drawn into it to provide statutory timelines. There is no doubt that this has had a beneficial effect on ethics review
- Central political will to make the UK a great place to do clinical research once again.
- Every NHS Trust to have a Board member responsible for R&D oversight and championing.
- Exemplars to be widely publicised and the NIHR Director to have powers to ensure good practice is introduced rapidly in all Trusts.
- Review of the Health and Social Care Act to ensure that research governance is treated as a national standard that local Trusts have to follow and not locally interpret.
- Incentivisation of NHS Trust CEOs to improve year on year on their R&D activity.
- NIHR Director to be an executive member of the newly proposed NHS Board.
- Better coordination between all four UK nations on R&D. Global companies do not understand devolution and its implications.
- Payment by Results (PbR) to be reviewed. This has had a negative effect on patients being referred as potential research participants from one Trust to another as the referring Trust is likely to lose income under the PbR system.
- There should be a lead NHS Trust for multi-centre trials to avoid repetition of review.

Other Comments

- In the call for evidence letter, it states that the regulatory framework for medical research has become over burdensome. This is not true, the MHRA as the Competent Authority works well within its statutory timelines for CTAs and the introduction of risk-based inspection should reduce the burden around site inspection. Research Ethics Committees are working well within the NRES system and the introduction of IRAS has been beneficial. As outlined above, the real issue is around NHS Research Governance and its interpretation at local level.
- The FPM fully supports a risk-based proportionate system e.g. the use of a technology within its indication in a trial should require much less regulation and governance than a new innovative technology in early phase trials.
- The ABPI and NHS R&D Directorate have produced a suite of Model Clinical Trial Agreements (MCTAs) and these should be used as far as possible without modification thus reducing the need for bureaucracy at a local level.
- Earlier this year the European Commission held a consultation on the review of the Clinical Trials Directive. The FPM's response is appended to this response as it contains a number of recommendations that Sir Michael might like to consider for the UK.
- The UK is unique with its NHS and the potential of using the electronic patient record for research purposes ought to make the UK one of the leading places in the world for

research and particularly in the field of pharmaco-epidemiology. Due to current financial constraints, a universal electronic patient record remains some way off. Nevertheless, the UK has a number of important databases in existence e.g. GPRD, MEMO and real efforts should be made to federate these for research purposes including performing feasibility studies for clinical trials.

- Finally, the FPM believes that research training should begin early in a doctor's career. Some companies and Contract Research Organisations are now providing four month secondments for F2 doctors in their research departments and this could be expanded. All doctors should be able to critically appraise research papers and this skill needs to be part of the medical curriculum. A research culture needs to be engendered in all new doctors so that the desire for all patients to have access to appropriate research can become a reality.

References

1. MHRA CTA data –
<http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/UKclinicaltrialauthorisationassessmentperformance> last viewed 27/05/10
2. NIHR Coordinated System for gaining NHS Permission (NIHR CSP) Operating Guidelines Version 4.1, Effective 30/10/09
http://www.ukcrn.org.uk/index/clinical/csp/resources/mainColumnParagraphs/0118/document/csp_operating_guideline last viewed 27/05/10 and is still latest version on website

