Consent

Consent in emergency research: new regulations

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The Medicines for Human Use (Clinical Trials) Regulations 2004

Performing emergency medical research in situations where patients are unable to give their own informed consent has long been a thorny issue. For example, a common problem is whether or not a patient in the middle of having an acute myocardial infarction can really weigh up the information in a few minutes and give properly informed consent for a trial of a thrombolytic.¹ The legal basis for consent for research in the incapacitated patient changed profoundly on 1 May 2004. On this date the *Medicines for Human Use (Clinical Trials) Regulations 2004* came into force, the UK implementation of Directive 2001/20/EC of the European Parliament.

These laws may seem remote in everyday practice but they should be of interest to all emergency physicians, as even those not involved in research will be directly affected by the consequences of these changes. We can only provide effective, evidence based emergency care if evidence is available from well structured clinical trials. If new regulations do not take account of emergency research, or clinical trials in emergency medicine are inhibited or prevented by an over burdensome bureaucracy, we will not be able to advance our knowledge or provide high quality care.

From the outset it should be emphasised that the changes in the law discussed in this article only apply to consent to participation in medical research. For the latest regulations in consent for normal medical treatment, emergency physicians should be familiar with the implications of the Mental Capacity Act 2005.

THE NEW LEGAL FRAMEWORK

The detailed legislation is found in Schedules 1 and 2 of the *Medicines for Human Use (Clinical Trials) Regulations 2004*.² Key issues are contained within Part 5 "Conditions and principles which apply in relation to an incapacitated adult" (see box 1 on our website (<http://www.emjonline.com/supplemental>) for a summary).²

Under this new legislation there is a stepwise approach to consent for medical research (see box 2 on our website (<http://www.emjonline.com/supplemental>)). If the patient is competent the patient should be asked to consent to participation in the trial. In the words of the regulations: "Subject to the other provisions of this Schedule relating to consent, freely given informed consent shall be obtained from every subject prior to clinical trial participation".

There is no change to the test of capacity or competence in the emergency department. To have the capacity to consent the patient must be able to (a) comprehend and retain the information, (b) believe it, and (c) weight it up in order to make a choice. If the patient does not fulfil these criteria (derived from the landmark case of "Re C") and is therefore unable to consent for themselves (is "incapacitated" in legal terms), the new legislation includes the provision for a "legal representative" to consent on behalf of the patient. In the words of the regulations applying to an incapacitated adult the patient can participate if "the legal representative has given his informed consent to the subject taking part in the trial". This is the first time in UK law that one adult can consent on behalf of another.

For adults and minors in England, Wales, and Northern Ireland and minors in Scotland the "legal representative" can be of two types, described below (the legal provisions for incapacitated adults in Scotland are slightly different due to the provisions of the Adults with Incapacity (Scotland) Act 2000.³

1. Personal Legal Representative

The definition of a Personal Legal Representative (PeLR) is "a person who by virtue of their relationship with the patient is suitable to act as their legal representative for the purposes of the trial AND is available and willing to so act". This means that a relative or friend of the patient can give consent to participation.

2. Professional Legal Representative

A Professional Legal Representative (PrLR) can be of two types: either "the doctor primarily responsible for the treatment provided to the patient or a person nominated by the relevant health care provider". The PrLR cannot be connected with the conduct of the trial. A person connected with the trial is defined as:

- (a) the sponsor of a trial
- (b) a person who is involved in the trial management
- (c) an investigator for the trial
- (d) a healthcare professional who is a member of the trial team
- (e) a person who provides health care under the direction or control of the investigator, whether in the course of the trial or otherwise.

The first type of PrLR is by definition always a doctor. This means that if the research team is from outside the emergency department, the emergency department doctor who is "primarily responsible" for the patient's management can be their PrLR. There is no definition of grade so this could be a junior doctor. If the emergency department consultant is an investigator in the trial then the emergency department juniors could not act as PrLRs, although another emergency department consultant could, as they would not be under the "direction or control" of the investigator. However, research and development departments may take the view that the environment of close team-working in an emergency department might make it better for the PrLR for emergency department led research to come from another department.

The second type of PrLR need not be a doctor, as they are simply "a person nominated by the relevant healthcare provider", so a nurse, paramedic manager, or priest could act in this role. The "healthcare provider" is the NHS Trust through the research and development department. Arrangements are likely to vary between NHS Trusts depending on availability. As an example, the "duty senior nurse" for the hospital is always on site and carries a pager, so might be a good person to act as the PrLR for all research within the hospital.

DISCUSSION

When the EU Clinical Trials Directive was first discussed there were many fears that research would be inhibited. There is certainly an additional layer of bureaucracy and regulation. However, for the first time the rules around consent in incapacitated patients are defined in law—replacing the previous system which was heavily dependent on the vagaries of the opinion of local

research ethics committees. There is now a structure that we can use with confidence.

Different countries have approached this question in different ways. The American system of a “waiver of consent” means that the researcher can enter the patient into the trial provided that the incapacitated patient fulfils the trial entry criteria. The safeguard to the patient is in the ethics committee’s review of the study protocol before it starts. The new European system takes a slightly different approach. It still emphasises the role of the research ethics committee, but provides the additional safeguard of a legal representative for the patient. It is certain that the ethics committee will closely scrutinise any research proposal that involves the inclusion of incapacitated patients. Particular attention will be paid to the risk/benefit balance for the trial, the potential for harm, and the strength of the supporting evidence. The ethics committee will no doubt also need to be satisfied that there is no alternative way of answering the research question in other patient groups who are able to consent for themselves.

Each country within the EU has incorporated the EU Directive into national law in a slightly different way, so that regulatory approval has to be obtained for each country participating in an international study. However, even if the details differ, a common framework for research consent and research governance across Europe might enhance international research collaboration.

The basis on which the PrLR would make a judgement about consent (the patient’s “presumed will”) is not entirely clear. It is not the role of the legal representative to judge the quality of the research project; this has already been done by the research ethics committee. It is difficult to see what grounds there might be for refusing to consent to patient participation (see box 3 on our website (<http://www.emjonline.com/supplemental>) for a quote from the draft Department of Health (DoH) guidelines⁴), unless some specific information is available that might act as a guide to the patient’s thoughts. Such information is unlikely to be available and so the UK system, in practice, may not be different from a “waiver of consent”.

None of this discussion applies to routine clinical patient care. This area is addressed in the Mental Capacity Act 2005.⁵ The legal framework provided by this Act will also need to be considered when the full DoH guidelines for consent in medical research are produced.

CURRENT QUESTIONS

As with any new system there are many areas around the practical application of these regulations that have yet to be defined. Unfortunately, DoH advice to researchers has not kept pace with the changes in the law. A draft revision of the 2001 document *Research Governance Framework for Health and Social Care Second Edition* was published for consultation in Autumn 2003, but only contains a footnote which says: “Under the Medicines for Human Use (Clinical Trials) Regulations 2003, specified conditions and principles will apply to informed consent, and to the recruitment of minors and incapacitated adults.” The Medicines and Healthcare Products Regulatory Authority (MHRA) has produced a Draft Guidance⁴ for researchers, which is clear and helpful, but seems to be remaining in draft form pending incorporation of the Mental Incapacity Act 2005. The COREC (Central Office for Research Ethics Committees) has recently given some guidance for ethics applications.⁶ However, full guidance to researchers within the NHS is not yet in place for changes in the law that happened over a year ago, creating confusion and inhibiting emergency research.

The new legislation only applies to trials involving “medicines”, so there is still uncertainty around other forms of medical research. However, it would not seem sensible to have two different systems for consent, so we would predict that the DoH will apply the same rules to all medical research in the future (this would be the safest assumption for emergency medicine researchers planning projects). A trial that does not involve a medicine does not need a MHRA Clinical Trials Authorisation, but “... must still comply with the NHS Research Governance Framework, a Sponsor must be identified and approval obtained from an Ethics Committee and relevant NHS R&D Departments”.⁷

There is no specific guidance about how close a relationship a potential PeLR should have to the patient. The phrase that they are suitable “by virtue of their relationship with the patient” can be interpreted in different ways. However, this form of words is probably the best that can be used, as each individual patient will have different personal circumstances. Any more precise definition (such as a first degree relative) will not be applicable to all patients. It seems that the underlying principle is that a PeLR should be someone who knows the patient well enough to be able to make an educated guess about what their wishes might be. This system is very close to the old system of gaining “assent” from a

relative, and means that the person taking the consent will continue to make a decision about whether a particular relative or friend is suitable to act as a PeLR.

There seems to be the need for an information leaflet about the role and responsibility of being a PeLR. This should be combined with a verbal explanation so that the relative/friend fully understands the situation when they are asked if they are willing to be the patient’s legal representative. It is likely that, in time, the NHS will have a standard explanation leaflet.

There is little advice about what should be the appropriate level of training for a PrLR. The legislation only states that they should have “an interview with the investigator, or another member of the investigating team, in which he has been given the opportunity to understand the objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted”. They should probably also understand the principles of good clinical practice in medical research, the role that they are being asked to fulfil, the relevant legislation, and the indemnity/support arrangements that are in place within their employing organisation.

The way in which these regulations might be applied to prehospital care research is unclear. It may be that the medical director of the ambulance service is the “doctor with primary responsibility” for patient care and can therefore give a consent for all patients to be entered; however, this does not really follow the underlying principle which makes individual decisions for each patient. As an alternative the ambulance service could nominate (and train) all of its paramedics as PrLRs. There would be an initial training burden at the beginning of each project as all staff would have to be briefed on the project and their role, but paramedics could then enter their patients into the trial.

It is also unclear how research could be carried out in situations where there may not be time to contact a PrLR, or to have discussions with the PeLR. For example research into the treatment of cardiac arrest may not be possible under the current law. In recognition of this problem, consultation on a government amendment to the 2004 Regulations was proposed in January 2005.⁸

SOURCES OF FURTHER INFORMATION

This article carries a warning, as the process of defining the interpretation of the new regulations is still in progress. The article contains our best guesses about the way the new rules should be

applied, but researchers should look for more up to date information on the following websites, as this is likely to be a rapidly changing area. There is a DoH/MRC toolkit,⁷ which is a good source of advice for the trial management side of the new rules which also gives advice about what you should do if you are running an existing trial, as there will be a transitional stage for projects already in progress. The NHS Research and Development Forum has a webpage with a series of useful links⁹ to most of the available resources on this topic. The MHRA is the government agency with responsibility for the regulations.¹⁰ Important additional reading is the International Committee on Harmonisation Good Clinical Practice Guidelines (ICH GCP) for research produced by the European Agency for the Evaluation of Medicinal products¹¹ and the Medical Research Council guidance for researchers.¹² Further advice on how to conduct emergency medicine research can be found in the Research section of the Faculty of Accident and Emergency Medicine website.¹³

SUMMARY

The new regulations around consent that came into force in May 2004 give a much clearer framework for consent in emergency medicine research, particularly in situations where the patients cannot consent for themselves. This gives a clear way forward for anyone designing a research project and is likely to resolve a number of long term difficulties that have inhibited research in our speciality. However, there are a number of areas that are still unclear and advice to researchers has lagged behind changes in the law.

KEY POINTS

- All emergency physicians are affected by changes in the law surrounding clinical trials.
- A legal framework now exists to define the rules around research on patients who are unable to consent for themselves.
- A Personal Legal Representative (PeLR) or Professional Legal Representative (PrLR) can now consent on behalf of the incapacitated patient.
- The PrLR can be the doctor in charge of the patient's treatment, providing that they are independent of the trial.
- The PrLR can be a person appointed by the NHS Trust (through the R&D department).
- NHS advice is lagging behind the legislation giving rise to confusion, and inhibiting emergency medicine research.

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The legislation has been summarised by the author on our website.

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