

## Medical Law

### Topic 12[N08]: Lecture 1 (of 1)

#### Elements of Medical Research

##### Aim:

To provide a general introduction to the law and ethics of medical research.

##### Objectives

After careful study of this topic you should be able to:

1. Discuss how the need for regulating medical research arose from atrocities masquerading as medical research;
2. Discuss the law relating to research on minors, adults who are competent to volunteer for research to be performed on them and mentally incapacitated adults;
3. Discuss, in detail, the means by which ethics research committees regulate and monitor research on human subjects; and the legal control to which ethics committees are subjected.

#### Atrocities that Prompted the need for the Regulation of Medical Research

##### (i) Atrocities performed by the Nazi's in WWII

Disclosure at the Nuremberg Military Tribunals of atrocities committed by Nazi doctors during World War II, supposedly in the pursuit of medical research, was the prime catalyst leading to regulation of medical experimentation. As stated by *Mason & Laurie*<sup>1</sup>:

‘... the greatest single impulse to regulate experiments on human beings sprang from a realisation of the appalling depths which were plumbed in the genocidal era of the Second World War when, undoubtedly, much information was gathered but only at the cost of immense suffering’.

*The Nuremberg Military Tribunals* heard of *War Crimes against Humanity*. They included the following medical experiments performed *without* the subjects' consent:

**High-altitude experiments** in which prisoners of war were subjected to rapidly changing variations in air pressure in an airtight chamber so as to simulate the atmospheric effects on an aviator falling from a great height (up to 68,000 ft.) without a parachute and without oxygen. ‘Many victims died as a result of these experiments and others suffered grave injury, torture, and ill-treatment’ per *Katz*, *Experimentation With Human Beings* (1972). *Katz* noted also:

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<sup>1</sup> *Mason, K & Laurie, G* (2005). *Mason & McCall Smith's Law and Medical Ethics*, 7/e. Oxford: OUP, p648

*Freezing experiments* in which some ‘subjects were forced to remain in a tank of ice water for periods up to 3 hours’ while others ‘were kept naked outdoors for many hours at temperatures below freezing’. Many victims died as a result of these experiments: some ‘screamed with pain as parts of their bodies froze ...’ and;

*Experiments with poison* where one group of experiments involved the subjects being shot with poison bullets and experiencing torture and death.

In the opening statement of the prosecution it was said that: ‘These experiments revealed nothing which civilised medicine can use’. Indeed, at the conclusion of the hearings seven of the sixteen who were found guilty of War Crimes and Crimes against Humanity were sentenced to death by hanging.

## **(ii) The Tuskegee Syphilis study, USA**

“Arguably the most infamous biomedical research study in U.S. history” (per Katz, et al, (2006)) was that which was carried out to observe and note the succession of phases syphilis exhibited when left untreated. Initially, the research was to intended to discover whether the patients would benefit by not being treated with the then known remedies which were toxic and of questionable effectiveness.

The study was carried out in Tuskegee, Alabama, which was identified as the area having the highest prevalence of syphilis in the six southern States examined. 399 African-American men with latent syphilis and a control group (those without the disease) of 201 were enrolled on the study.

Throughout the 40 years of the study – 1932 until 1972 – the subjects were told they were being treated for “bad blood”. Some were given placebo ‘treatments’, but no-one received any anti-syphilitic treatment. Indeed, no one in the study group was treated with, or even informed of, penicillin, which had become recognised as an effective drug from the time of its availability in 1943.

The subjects were provided with warm meals on the days they were examined and, having agreed to an autopsy following their deaths, given free burials. By the time the study ended, 28 men had died of syphilis, 100 others died from syphilis-related complications, at least 40 wives had been infected and 19 children had been born with congenital syphilis.

“The longest non-therapeutic experiment on human beings in medical history” (Sharma (2005)) ended in 1972, when the press were informed by a Public Health Services venereal-disease investigator who had first expressed his concerns six years earlier.

The study was notorious for: having no experimental data from animal studies; for not providing any proper medical protection or management; and for not obtaining any of the subjects' informed consent.

In 1974, an out-of-court settlement was agreed with each survivor receiving \$37,500 in damages and heirs of the deceased received \$15,000; and in 1997, President Bill Clinton said: '... on behalf of the American people, what the United States government did was shameful and I am sorry'.

Whereas the Tuskegee study demonstrated that the Nazi's regime didn't have a monopoly on conducting notorious "research", undoubtedly the principles that emanated from the Nuremberg Military Tribunals have provided the basis of the current ethical regulation of medical research.

## **The Formulation of Principles to Regulate Medical Research**

Ten principles emerged from the judgements. They included:

1. The voluntary consent of the human subject is absolutely essential.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.  
[And]:
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

The ten principles became known as the *Nuremberg Code*. In essence, the medical profession later endorsed these principles and formulated the *Declaration of Helsinki* (1964), revised in 1975, 1983, 1996 and again in 2000. The Declaration of Helsinki supplements the doctor's ethical commitments as expressed in the Hippocratic Oath. *The Hippocratic Oath* states that: 'I will follow that regimen which ... I consider for the benefit of my patients and abstain from whatever is deleterious and mischievous'. Provisions of the *Declaration of Helsinki* include: 'Concern for the interest of the subject must always prevail over the interest of science and society' and 'In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and discomfort it may entail. ... and that he or she is free to withdraw his or her consent to participation at any time. The physician should obtain the subject's freely-given *informed consent*, preferably in writing. ... In case of legal incompetence, *informed consent* should be obtained from the legal guardian in accordance with national legislation'.

## **Categorising medical research**

Principally, research refers to a *research intervention*. If the research involves an entrance of any sort into the subject's body this is termed an *invasive (or intrusive) research intervention* as, for example, when heart Pacemakers were introduced and operations for organ transplants and the pinning together of broken bones were first performed. The *Mental Capacity Act 2005* defines research as intrusive if it is of a kind that would be unlawful if it was carried out on or in relation to a person who had the capacity to consent to it but had not done so: *s.30(2)*.

*s.30(3) MCA 2005* provides that "A clinical trial which is subject to the provisions of clinical trials regulations is not to be treated as research for the purposes of this section".

An example of a *non-invasive* intervention is the swabbing of the subject's skin in order to obtain a sample of bacteria growing thereon.

The difficulty is in deciding at what point a medical intervention ceases to be experimentation and becomes 'ordinary' treatment. *Teff* notes that: 'On an extreme view, it could be said that all medical procedures are experimental, given the uniqueness of every subject or patient' and *Illich* has said that: 'Each treatment is one more repetition of an experiment with a statistically known probability of success'. Moreover, *Faulder* in *Whose Body Is It?* has emphasised that: '... medical advance is impossible without research and experimentation – and some of that experimentation must be done on human beings'. One way of conducting experimentation is by way of clinical trials. 'And [since] the Second World War ... the principle of randomisation [has been] introduced into clinical research. Clinical trials using the principle of randomisation are called *randomised controlled trials* [RCTs] ...'.

## **Randomised Control Trials**

*Teff* says that: 'Randomised controlled trials are widely regarded as the most effective means of comparing treatments. People with the same illness are randomly allocated to different groups and given different treatments. Thus subjects in one group will be given an experimental drug or treatment, while those in a control group will have a standard treatment or placebo. [From an ethical standpoint] *such trials cannot be justified where one treatment is demonstrably superior*'.

*Brazier* said of the last point that: 'public anxiety was highlighted by a trial involving 3000 women at risk of conceiving a spina bifida baby. Studies had shown that similar women appeared to suffer a reduced incidence of carrying a spina bifida baby if treated with special vitamin supplements. The trial involved randomising the women into four groups. One group received the full treatment under trial, another part only of the supplement, a third the other element of the supplement, and the fourth a placebo. Why should any woman at risk be denied a treatment which might help her avoid a spina bifida conception?' *Teff* concludes: '*At some stage it must become unethical, and negligent in relation to the*

*controls, to continue with the randomised trials*’. This is evident from a resume of the ethical issues noted in an older edition of *Mason & McCall Smith* where it was stated that:

‘ ... on the one hand, a relatively untried treatment which may do harm is being given to one group while, on the other, a treatment which may be of considerable benefit is being withheld from a similar group. ... the ethical problem is not so much whether a patient will be completely cured by a new treatment but, rather, would he have improved faster if he had not been restrained by the experimental protocol ... *No randomised therapeutic trial can be ethical unless the professionals genuinely do not know which treatment yields the best results.*’

### **Therapeutic & Non-Therapeutic Research**

The traditional approach in English law has been to categorise experimental medical procedures as either therapeutic or non-therapeutic research.

Therapeutic research is research consisting of an activity which has a therapeutic intention as well as a research intention towards the subjects of the research whereas non-therapeutic research is a research activity which doesn’t have a therapeutic intention. Thus, *therapeutic research is characterised by its dual intentions.*

*The Institute of Medical Ethics* in a 1986 Working Party Report stated that:

One reason why it is necessary to establish whether such a project is therapeutic or non-therapeutic is a legal one. The removal of blood samples from [an] infant would be [a battery] unless consent had been given. Although there is no specific statement of the law in such circumstances, it is likely that the courts would always regard unconsented invasive non-therapeutic research as unlawful. They might take a somewhat more lenient view of unconsented *therapeutic* research, though not necessarily.

#### **(A) Therapeutic Research**

*Kennedy & Grubb* state that: ‘There are at least three situations in which therapeutic research may be carried out:

- (1) a doctor tests the efficacy of a new treatment where none had previously been available and the patient would receive ordinary nursing care, symptomatic relief but nothing else;
- (2) a doctor test the efficacy of a new treatment as against other established forms of treatment;
- (3) a doctor tests treatments A, B and C (all of which are established) because it has not been established which is the most efficacious.

All these types of research can be generically described as clinical trials’.

However, there is no difference in the general law and ethics relating to the doctor-patient relationship in clinical trials, i.e. a doctor still has a duty to act in the best interests of his

patient (beneficence) and not to harm him (non-maleficence). Furthermore, where a patient has the capacity to make a decision for himself, the doctor must respect that patient's right to self-determination (respect for the principle of autonomy).

Respect for the principle of autonomy is the ethical principle at the basis of the law relating to consent. When analysing the legal aspects of consent it is convenient to categorise patients as competent or incompetent.

## **(1) Competent Patients**

The common law rebuttable presumption of an adult having capacity is now enshrined in statute: *s.1(2) MCA 2005*.

Also under statute, *s.8(1) FLRA 1969* provides that a minor who has attained the age of 16 can: '... consent ... to any surgical, medical or dental treatment which, in the absence of consent, would constitute a trespass to his person ...'

As to whether an over 16 year old minor could consent to therapeutic research will depend, *inter alia*, on whether therapeutic research equates with 'treatment' within the act so that a minor over 16 is *prima facie* competent. As therapeutic research has two intentions – noted by *Kennedy & Grubb* as (i) to treat and (ii) to do research – then this may exceed the meaning of 'treatment' within the Act and so 'the power to consent would remain with the proxy until the minor reaches majority, i.e., 18, unless found to be competent as explained in the *Gillick* decision'. However, *Teff* asserts that: 'There seems no reason in principle why [the *Gillick* decision] should not ... be the case for both therapeutic and non-therapeutic research'.

### **(i) Voluntariness**

That the subject's consent must freely be volunteered there is no doubt: that it has been in particular circumstances is not so certain. So, for example, in the case of a prisoner it was said in *Freeman v Home Office* (1984): 'that where, in a prison setting, a doctor has the power to influence a prisoner's situation and prospects a court must be alive to the risk that what may appear, on the face of it, to be a real consent is not in fact so'. The issue becomes a matter of fact, not law.

### **(ii) Information**

The general rule in *Chatterton v Gerson* (1981) is that as long as a person 'is informed in broad terms of the nature of the procedure which is intended and gives (his/her) consent, that consent is real'. Because of the dual intention in therapeutic research it again becomes necessary to analyse whether lack of adequate information would lead to a battery or negligence.

## **Battery**

**Kennedy & Grubb** assert that '[as] there is a dual intention on the part of the doctor, i.e. to treat and to conduct research, any failure to inform the patient concerning *both* of these intentions and their possible consequences would amount ... to battery. This is because in the absence of such knowledge the patient will have assented to a procedure which is materially different in its nature from that which the doctor intends to carry out'. To avoid such liability 'the doctor must make explicit his intention to carry out research'.

## **Negligence**

Here the issue to be resolved 'is whether the *Sidaway* test of judging what information a doctor must volunteer by reference to current medical practice will be adopted in the context of research' per **Brazier**. 'No' is the answer offered by **Kennedy & Grubb**. They assert that liability for negligence can be avoided only by:

- a. the doctor making explicit 'his intention to carry out research' and by disclosing
- b. 'the information which appries the patient of the *material risks* associated with the research; and
- c. 'the information must also be disclosed, in addition to any risks, which is material to allow the patient to make an informed decision.' [i.e. alternative procedures would have to be disclosed].

As to the meaning of 'material' risks, in *Halushka v University of Saskatchewan* (1965) **Hall JA** said: 'There can be no exceptions to the ordinary requirements of disclosure in the case of research as there may well be in ordinary medical practice. ... [i.e. that risks might sometimes legitimately be concealed from patients could] ... 'have no application in the field of research'.

**The strong inference from the above is that the doctrine of "informed consent" / something greater than "real consent" is applicable to cases of therapeutic research.** However, a cautionary note is made by **Teff** who points out that 'in ... [*Gold v Haringey Health Authority* (1987)] the Court of Appeal held that there is no legal distinction between medical advice given to patients in a therapeutic and non-therapeutic context. The accepted professional practice, or *Bolam* test was said to apply in both situations'. Of course, this should now be read in the light of judicial dicta in **Bolitho**, **Pearce** and, perhaps, **Chester v Afshar**.

### **(iii) Limits of Research**

It must be the objective of every researcher to minimise the inherent risks in all experimentation. Effectively, principles 4 & 5 of the Basic Principles of the **Declaration of Helsinki** state that:

- (4) the risk must be proportional to the importance of the objective;

- (5) the risks must be assessed before the experiments begin and, so far as is possible, eliminated by previous animal experiments and by a carefully considered experimental protocol.

Risks have to be assessed with reference to the experimental subjects which may be, e.g., individual patients or a group of patients who are suffering from one particular condition [patients who have no association with the disease or process under review but who are readily available – e.g. medical students / the unemployed / members of the armed forces / prisoners; and healthy volunteers]. *Mason & McCall Smith* stated that: ‘... the risk taken in the case of the individual patient may be considerable in certain circumstances. It being axiomatic that ‘experiments’ with subjects involve patient care, they are effectively confined to the use of new drugs or treatment when established methods have failed; a foreseen risk is clearly acceptable if the patient is otherwise dying or the disease process is rapidly progressive’.

## **(B) Non-Therapeutic Research**

Non-therapeutic research has a research intention only: it is an activity which does not have a therapeutic intention.

Experimental subjects include healthy individuals and groups of subjects readily available – e.g. medical students; the unemployed; prisoners; members of the armed forces.

### **The Competent Volunteer**

*s.8(1) FLRA 1969* does not apply to non-therapeutic research i.e. there is no statutory provision that permits an over 16 year old to consent to non-therapeutic research. As *Kennedy & Grubb* note: ‘The capacity of a child under 18 to consent to non-therapeutic research is, therefore, governed by common law’. There is agreement amongst the principal commentators – *Brazier; Kennedy & Grubb* and *Teff* – that *Gillick* is applicable here. The only qualification appears to be that: ‘The greater the risks or the more serious the consequences for the child, the more likely it is that a court would decide that a child lacked the capacity to give a valid consent in law’ per *Kennedy & Grubb*.

#### **(i) Voluntariness**

As for therapeutic research: (see) *Freeman & Home Office* (1984).

#### **(ii) Information**

As for therapeutic research (see supra)) but with the proviso, perhaps, that a subjective consideration of ‘materiality’ in relation to risks replaces the conventional objective approach in negligence. This latter point is made both by *Kennedy & Grubb* and *Teff* despite dicta to the contrary in *Halushka v University of Saskatchewan* (1965). Without this safeguard the volunteer would not only have no potential cause of action in battery (he’s consented to a research procedure) but neither would he have a cause of action in

negligence if a defence akin to 'therapeutic privilege' was claimed. Despite dicta to the contrary in *Sidaway* the defence was permitted in *Blyth v Bloomsbury Health Authority* (1987). It was based on the *Bolam* test.

### **(iii) Limits of Research**

*Kennedy & Grubb* agree with *Nicholson* that any research on a healthy volunteer which on the basis of existing knowledge properly analysed poses a risk which is more than a 'minor increase over minimal' would in law amount to a battery and even, possibly, the crime of maim in appropriate circumstances. *Nicholson* had defined 'minimal risk' as:

... the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

### **Does the offer of payment to healthy participants volunteering for a research project constitute an 'undue inducement' and, hence, a limit to research?**

In essence, before a new drug is marketed, the research programme on human beings that follows successful trials on animals, is divided into three phases each phase involving an increasing number of people. Phase 1 involves only a small number of healthy volunteers and the aim is to establish the safety of the drug and to determine what the most effective dosage of the drug might be.

TG1412 was a biological agent, a 'monoclonal antibody' targeted as treating diseases such as rheumatoid arthritis. In laboratory tests, TeGenero, the German developer of the drug, said it had performed as they had hoped.

Because Phase 1 trials confer no benefits on those who take part in them, payment was offered at about £150 per day or just over £2,000 for a commitment of a couple of weeks. Half-a-dozen healthy volunteers and a control group of two injected with a placebo, participated in the trial at Northwick Park Hospital, London, in March 2006.

All six who were injected with TGN1412 became very ill very quickly and all suffered some degree of multiple organ failure and required admission to intensive care. One volunteer was so badly affected that he had to have some fingers and toes amputated. This followed the heart, liver and kidney failure and pneumonia and septicaemia he had already suffered.

The trials that were due to start in Germany were abandoned.

Later, a report published by the *MHRA (Medicines and Healthcare Products Regulatory Agency)* concluded that the harm suffered by the volunteers was due to an 'unpredicted

biological action' in human beings. The conclusion was reached after finding no evidence of crime or a technical error.

However, the report of the *Expert Scientific Group on Phase One Clinical Trials* that followed made 22 recommendations and accused the MHRA of being too lax in its decision to approve the TGN1412 trial.

Perhaps the most controversial element of being offered inducements for taking part in Phase 1 trials, however, is that it is a offering a financial 'reward' to healthy participants for accepting unknown risks – albeit that proper testing on animals should alert the developers to any possible risks / side effects.

Yet, whereas the ethics of offering financial inducements to those who are not financially independent and are willing to accept risks may be questionable, the risks remain the same if they are accepted by those acting altruistically – though, perhaps, the market for such do-gooders is appreciatively smaller.

The law relating to the clinical trials of medicines is discussed *infra*. Here, it will suffice to note that: **regulation 32** of **SI 2004/1031** (The 'Clinical Trials Regulations') requires an investigator to report 'any serious adverse event which occurs in a subject at a trial site at which he is responsible for the conduct of a clinical trial immediately to the sponsor'; and that **reg.15** requires provision to be made for the insurance or indemnity of the investigator (researcher) or sponsor.

## **(2) Incompetent Patients**

### **(i) Adults**

Both the *Declaration of Helsinki* and the *Mental Capacity Act 2005* contain provisions relating to research on incompetent patients. Moreover, the common law has now explained how research – or, at least, experimentation - may be performed in the best interests of an incompetent patient, viz;

### **Declaration of Helsinki, paragraphs 24 and 25**

24 For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25 When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

## At common law

### **Simms v Simms [2003] Fam 83**

In two separate cases the patients, an 18-year-old male (JS) and a 16-year-old female (JA), were suffering from probable variant Creutzfeldt-Jakob disease (“vCJD”). Whereas no recognised effective treatment or cure had yet been found, overseas medical research had identified a treatment which seemed successful in mice. The parents of the incompetent teenage patients sought declaratory relief that it was lawful for them, as being in their best interests, to have the treatment which, of course, had not been tested on humans.

**Held:** The declarations were granted in each case. There was a responsible body of relevant medical opinion which supported the innovative treatment proposed; and that the concept of “benefit” to a patient suffering from vCJD encompassed an improvement from the present state of illness, a continuation of the existing state of illness without deterioration and the prolongation of life. Thus, it was decided that there were possible benefits to the patients from such pioneering treatment where there was no alternative treatment available. Accordingly, it was in the best interests of each patient that the proposed treatment be carried out.

Three points worthy of consideration in relation to this case are: First, at paragraph 48 of her judgment, **Dame Elizabeth Butler Sloss P** said:

To the question: “Is there a responsible body of medical opinion which would support the ... treatment within the United Kingdom?”, the answer in one sense is unclear. This is untried treatment and there is so far no validation of the experimental work done in Japan. The *Bolam* test ought not to be allowed to inhibit medical progress. And it is clear that if one waited for the *Bolam* test to be complied with to its fullest extent, no innovative work such as the use of penicillin or performing heart transplant surgery would ever be attempted: see **Lord Diplock** in *Sidaway v Board of Governors of the Bethlem Royal Hospital and the Maudsley Hospital* [1985] AC 871, 893. I do, however, have evidence from responsible medical opinion which does not reject the research.

Secondly, the distinction between ‘research’ and ‘experimental treatment’ (if one exists) is debatable. Generally, research is subject to a pre-determined protocol, including a control group, and ethical approval; and research on the effect of drugs human participants generally follows extensive testing on animals. By contrast, experimental treatment may be the ‘last resort’: the only possible course deemed available in the absence of any proven therapeutic procedure. Even so, experimentation must be carried out in the best interests of the patient. As noted in *Simms v Simms*, the performance of experimental treatment is likely to be subject to the granting of a declaration of lawfulness from the courts. Of course, the reference to ‘experimentation’ in paragraph 4 of the Declaration of Helsinki and ‘medical research’ in paragraph 5 clouds any perceived distinction between experimentation and medical research. Moreover, it is just as debatable as to when research on (say) organ transplants evolves into what is akin to ‘routine’ *treatment*.

Thirdly, not only is there is no statutory definition of what constitutes research, there is no primary legislation exclusively devoted to regulating the conduct of research on human subjects. (The limited provisions of the Mental Capacity Act 2005 are discussed below). By contrast, the Animals (Scientific Procedures) Act 1986 regulates research on non-human vertebrates.

By contrast with *Simms v Simms*, in *An NHS Trust v J*, the patient's family opposed the administration of innovative treatment.

### **An NHS Trust v J [2006] EWHC 3128 (Fam)**

An application was made by the NHS trust to withdraw all life sustaining treatment to a 53-year-old woman who had been in a persistent vegetative state for more than three years. The proceedings had the support of J's family – J's husband, two daughters and J's mother - who were devoted to her. However, just before the hearing, an article was published suggesting that patients in the PVS might be revived to a level of wakefulness that would enable them to communicate in a meaningful manner upon the administration of Zolpidem, a drug normally used for the treatment of insomnia. On the basis of expert testimony that if the drug was administered and there was no response within three days there would be no response at all, the Official Solicitor opposed the declaration. Following administration of Zolpidem on three consecutive days, noting there was no increased mental awareness and hearing then that there were no clinical reasons why artificial nutrition and hydration should not be removed, Sir Mark Potter P granted the declaration sought by the trust.

(N.B.: Now that the Mental Capacity Act 2005 is in force, invocation of certain of its provisions could ensure that a different outcome would be perfectly possible. See ss.1-5 and 24 for some principles and advance decisions to refuse treatment, respectively).

## **Elements of the Mental Capacity Act 2005 relating to the participation of adults lacking capacity to consent to research: ss.30-34**

### **30 Research**

(1) Intrusive research carried out on, or in relation to, a person who lacks capacity to consent to it is unlawful unless it is carried out—

(a) as part of a research project which is for the time being approved by the appropriate body for the purposes of this Act in accordance with section 31, and

(b) in accordance with sections 32 and 33.

(2) Research is intrusive if it is of a kind that would be unlawful if it was carried out—

(a) on or in relation to a person who had capacity to consent to it, but

(b) without his consent.

(4) “Appropriate body”, in relation to a research project, means the person, committee or other body specified in regulations made by the appropriate authority as the appropriate body in relation to a project of the kind in question.

...

### **31 Requirements for approval**

(1) The appropriate body may not approve a research project for the purposes of this Act unless satisfied that the following requirements will be met in relation to research carried out as part of the project on, or in relation to, a person who lacks capacity to consent to taking part in the project (“P”).

(2) The research must be connected with—

(a) an impairing condition affecting P, or

(b) its treatment.

(3) “Impairing condition” means a condition which is (or may be) attributable to, or which causes or contributes to (or may cause or contribute to), the impairment of, or disturbance in the functioning of, the mind or brain.

(4) There must be reasonable grounds for believing that research of comparable effectiveness cannot be carried out if the project has to be confined to, or relate only to, persons who have capacity to consent to taking part in it.

(5) The research must—

(a) have the potential to benefit P without imposing on P a burden that is disproportionate to the potential benefit to P, or

(b) be intended to provide knowledge of the causes or treatment of, or of the care of persons affected by, the same or a similar condition.

(7) There must be reasonable arrangements in place for ensuring that the requirements of sections 32 and 33 will be met.

### **32 Consulting carers etc.**

(1) This section applies if a person (“R”)—

(a) is conducting an approved research project, and

(b) wishes to carry out research, as part of the project, on or in relation to a person (“P”) who lacks capacity to consent to taking part in the project.

(2) R must take reasonable steps to identify a person who—

(a) otherwise than in a professional capacity or for remuneration, is engaged in caring for P or is interested in P’s welfare, and

(b) is prepared to be consulted by R under this section.

(3) If R is unable to identify such a person he must, in accordance with guidance issued by the appropriate authority, nominate a person who—

(a) is prepared to be consulted by R under this section, but

(b) has no connection with the project.

(4) R must provide the person identified under subsection (2), or nominated under subsection (3), with information about the project and ask him—

(a) for advice as to whether P should take part in the project, and

(b) what, in his opinion, P’s wishes and feelings about taking part in the

project would be likely to be if P had capacity in relation to the matter.

(5) If, at any time, the person consulted advises R that in his opinion P's wishes and feelings would be likely to lead him to decline to take part in the project (or to wish to withdraw from it) if he had capacity in relation to the matter, R must ensure—

(a) if P is not already taking part in the project, that he does not take part in it;

(b) if P is taking part in the project, that he is withdrawn from it.

...

### **33 Additional safeguards**

(1) This section applies in relation to a person who is taking part in an approved research project even though he lacks capacity to consent to taking part.

(2) Nothing may be done to, or in relation to, him in the course of the research—

(a) to which he appears to object (whether by showing signs of resistance or otherwise) except where what is being done is intended to protect him from harm or to reduce or prevent pain or discomfort, or

(b) which would be contrary to—

(i) an advance decision of his which has effect, or

(ii) any other form of statement made by him and not subsequently withdrawn,  
of which R is aware.

(3) The interests of the person must be assumed to outweigh those of science and society.

(4) If he indicates (in any way) that he wishes to be withdrawn from the project he must be withdrawn without delay.

### **34 Loss of capacity during research project**

(1) This section applies where a person ("P")—

(a) has consented to take part in a research project begun before the commencement of section 30, but

(b) before the conclusion of the project, loses capacity to consent to continue to take part in it.

(2) The appropriate authority may by regulations provide that, despite P's loss of capacity, research of a prescribed kind may be carried out on, or in relation to, P if—

(a) the project satisfies prescribed requirements,

(b) any information or material relating to P which is used in the research is of a prescribed description and was obtained before P's loss of capacity, and

(c) the person conducting the project takes in relation to P such steps as may be prescribed for the purpose of protecting him.

...

**N.B:** The requirement for ethical approval and the potential for the research to benefit the patient should be noted. Together with the ‘additional safeguards’, the provisions of ss.30-34 aim to protect the patient from harm and promote treatment that would be beneficial to him. Note that the provisions apply to adults, only: s.2(5) provides that the Act does not apply to minors under the age of 16.

## **(ii) Minors**

Here the proxy (the authority with power to act on behalf of the child) must act in the child’s best interests. This, of course, assumes that the child does not satisfy the test of *Gillick* competence.

## **Research Ethics Committees**

The Department of Health first recommended the establishment of local research ethics committees in 1975. The committees would aim to ensure that researchers achieved acceptable minimum standards in the protocols underpinning their studies and that they managed risk acceptably. It was another 16 years, however, before more formal guidance was given to the then local health authorities who were each required to establish at least one local research ethics committee (LREC). Given that such committees were unsuitable for appraising the proposals for research carried out at simultaneously at one site, the Governance Arrangements for Research Ethics Committees (GAFRECs) led to the establishment in 1997 of multi-centre research ethics committees (MRECs) and the continuation of LRECs. MRECs would complete the ethical review and then disseminate the protocol to LRECs for consideration of local issues. In 2000 came another development with the establishment of COREC – the Central Office for NHS Research Ethics Committees – having the functions of, inter alia, issuing guidance to RECs and appointing MRECs whilst Strategic Health Authorities became the appointing authorities for LRECs. Further change took place in 2005 with the National Patient Safety Agency (NPSA) (see Ch.1) assuming the responsibility for COREC. The evolution has continued and a new body, the National Ethics Research Service (NRES), which is a part of the National Patient Safety Agency (NPSA), took over from COREC and NHS RECs on 1<sup>st</sup> June 2007. Under NRES, research ethics advisers at both national and local level will, hopefully, be able to speed-up decisions via a more effective triage system that has been implemented to permit quicker decision-making in respect of research which doesn’t have any contentious ethical content. Moreover, ethical approval is, henceforth, likely to be given by specialist advisors rather than a local committee.

Note, also, that in all cases NHS researchers require Research and Development Management approval and the research must not start until this approval is obtained. This will not be granted unless NHS indemnity arrangements are in place.

The coming into force of the *Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1031* established the UK Ethics Committee Authority (UKECA) as part of the NPSA. Reg.5 provides that the UKECA recognises and monitors the subordinate bodies that are permitted to review the protocols for clinical trials in investigational medicinal products (CTIMP).

## **Medicines for Human Use (Clinical Trials) Regulations 2004**

The 2004 Regulations, SI 2004/1031 (as now amended), were enacted to give the force of law to Directive 2001/20/EC and to ensure compliance with the principles of Good Clinical Practice.

### **Interpretation**

1. – (1) In these Regulations -

‘the Directive’ means Directive 2001/20/EC of the European Parliament and of the Council on the approximation of laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use;

**N.B.:** It is important to note that four other Directives are referred to in the interpretation provisions and that, of those, Directive 2005/28/EC is, for the purposes of this section, the most important as it is the good clinical practice Directive.

Some noteworthy provisions of Directive 2001/20/EC are:

- The statutory establishment of ethics committees;
- The additional safeguards for protection of vulnerable groups (minors and incapacitated adults); and
- The requirement that all clinical trials be conducted in accordance with good clinical practice.

Reg.28 and Sch.1 contain the principles of good clinical practice

### **Good clinical practice and protection of clinical trial subjects**

28. – (1) No person shall –

- (a) Conduct a clinical trial; or

(b) perform the functions of the sponsor of a clinical trial .. otherwise than in accordance with the conditions and principles of good clinical practice.

## SCHEDULE 1

Regulation 2(1)

### CONDITIONS AND PRINCIPLES OF GOOD CLINICAL PRACTICE AND FOR THE PROTECTION OF CLINICAL TRIAL SUBJECTS

#### PART 1

##### APPLICATION AND INTERPRETATION

1. - (3) If any subject of a clinical trial is a minor, the conditions and principles specified in Part 4 apply in relation to that subject.

(5) If any person –

(a) is an adult unable by virtue of physical or mental incapacity to give informed consent, and

(b) has, prior to the onset of incapacity, refused to give informed consent to taking part in the clinical trial,

that person cannot be included as a subject in the clinical trial.

3. - (1) For the purposes of this Schedule, a person give informed consent to take part, or that a subject is to take part, in a clinical trial only if his decision –

(a) is given freely after that person is informed of the nature, significance, implications and risks of the trial; and

(b) either –

(i) is evidenced in writing ... so as to indicate his consent, or

(ii) if the person is unable to sign or mark a document so as to indicate his consent, is given orally in the presence of at least one witness and recorded in writing.

## References

- Brazier, M and Cave, E.** *Medicine, Patients and the Law*, 4/e. London: Penguin, 2007, Ch.16;
- Herring, J.** *Medical Law and Ethics*, 2/e. Oxford: OUP, 2008, Ch.11;
- Mason, K and Laurie, G.** *Mason & McCall Smith's Law and Medical Ethics*, 7/e, 2005, Chs. 18 & 19;
- Stauch, M, Wheat K and Tingle J.** *Text, Cases & Materials on Medical Law*, 3/e Abingdon: Routledge-Cavendish, 2006, Ch.10;
- Teff,** 'The law and ethics of medical experimentation', Professional Negligence, November/December 1987, pp182-186.

## Questions

1. RCTs are unethical. Discuss.
2. Critically assess what you would expect to be the appropriate quantum of information to be disclosed to a competent patient who has volunteered to undergo therapeutic research.
3. To what extent, if at all, is it accurate to assert that ethical guidance and English law provide adequate safeguards for human participants in medical research programmes?