

## **WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI**

### **Review of the Declaration of Helsinki: Ethical Principles for Biomedical Research Involving Human Beings**

#### **Consultation Response of the PHG Foundation**

The Foundation for Genomics & Population Health is the successor body to the Public Health Genetics Unit and the UK-funded Cambridge Genetics Knowledge Park. Its overarching purpose is to foster and enable the application of biomedical science with a view to the improvement of human health. Among its specific objectives is the promotion of a social and regulatory environment that is receptive to innovation, without imposing an undue or inequitable public burden. The Foundation has a particular interest in genetic research and its impact upon clinical and public health services.

We submit the following response to the amendments to the Declaration of Helsinki as proposed by the WMA in the draft circulated for consultation. For ease of reference, our comments follow the paragraph numbering in the amended draft.

#### **A. Introduction**

1. We note the comments of the WMA.

Whilst the scope of biomedical research should properly include research using anonymised human material or data, some of the ethical obligations imposed by the amended declaration are not compatible with epidemiological research using anonymised tissues and data. It needs to be clarified when obligations in the declaration do not apply to research using anonymised material as well as identifying special conditions that apply to epidemiological research (paragraph 22A). In some situations it may be ethically justifiable to retain existing distinctions between research using identifiable and unidentifiable human material.

In the UK differing protections are accorded to data and tissue depending upon whether they are identifiable or not. To an extent this is dependent upon a consequentialist view that the misuse of identifiable data confers greater harms than misuse of unidentifiable data. For example, in England the Human Tissue Act 2004 provides that appropriate consent is required for research using identifiable material, but use of anonymised tissue can be retained, stored or used without consent subject to conditions (such as approval from a research ethics committee).

Similarly the Data Protection Act applies only to identifiable personal data (section 2). This Act is based upon the Data Processing Directive which applies throughout Europe.

2. In practice the boundaries between clinical care, audit and research are sometimes difficult to gauge. Arguably the duty to promote and safeguard health should extend to participants in experimental treatment and clinical audit.

4. Such populations have historically been neglected because the potential harms of proceeding with research may be greater in severity or different in type than those predicted by available evidence (from animal studies for example). However justice issues such as provision of equitable access should be balanced by reasoned consideration of the distinctive harms and benefits which might accrue to these populations through proceeding with this research. This requirement could benefit from qualification.

We suggest that the words:

*'having taken account of the harms and benefits of proceeding with research in these groups'* are inserted at the end of this section.

5. The UK Mental Capacity Act 2005 states at clause 33(3) 'the interests of the person must be assumed to outweigh those of science and society'. In this context the interests of the sponsor are assumed to be part of those latter classes of interest.

6. Agreed.

## **B. Basic Principles for Biomedical Research**

10. There are some classes of research such as epidemiological research involving secondary use of tissue or data where it is considered that the public interest in proceeding with research outweighs any harm caused to individuals by proceeding with research without explicit consent, or in some circumstances knowledge. Some would argue that proceeding with research of this type is itself a breach of confidentiality. We would disagree since researchers engaged in secondary research are still mindful of their duty to treat data in a confidential manner and are required to have appropriate encryption/security policies.

For this reason we would prefer to see the words *'right to self-determination'* deleted from this draft. In our view the imposition of a universal duty to respect self-determination would prevent some types of epidemiological research from proceeding.

13. We would not wish the amendment (and rationale) to exclude research where no such committee exists (such as in some developing countries). In these cases the use of a specially appointed ethical review committee may be justified.

Providing for compensation for injury incurred during research is a complicated area since harms may result due to negligent and non-negligent actions and different provisions may need to be in place for each type. Research ethics committees may have limited authority to insist that there are provisions made for non-negligent harms. This requirement may therefore require qualification.

14. It may not always be appropriate for post trial access to take place. Indeed in some types of trial there is debate concerning the extent to which research subjects should be contacted directly – such as where genetic analysis in a research setting reveals clinically relevant information.

We would suggest inserting *'any'* after *'identify'*.

16. We advocate this in the UK (although not all sponsors adhere to it).

22. Adding the words ‘*any other relevant details of the study*’ to this sentence seems to weaken the obligations imposed by this paragraph. A more helpful formulation might be as follows:

*‘...entail. The potential participant should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. Wherever possible the type, content and delivery of information provided should be tailored to the needs of the individual potential participants. Potential research participants...’*

In the UK there is no legal requirement for non-written consent to research to be witnessed (i.e. signed by a third party). Good practice guidance encourages written consent.

The description - ‘*observational epidemiological research*’ may not adequately capture all those instances of research ‘*where informed consent is impossible, difficult or unethical to obtain or poses a threat to the validity of research*’. We favour the term ‘*epidemiological or secondary research*’ which is a broader definition.

Our view is that the justification for this type of research to proceed without consent is that it would be highly impractical to seek individual consent and that the benefits of the research are such that the interference with privacy is proportionate to the protection of health.

By way of background, the distinctive elements of this research are a combination of:

- *the size of the database*: In the UK regulations allow research to proceed where informed consent is ‘*impracticable*’ to obtain, rather than ‘*difficult*’. This is the basis for the class exemptions to the obligations for confidentiality imposed by the Health and Social Care Act 2001, the Health Service Act 2006 and the Health and Social Care Bill 2007.
- *the nature of the data collected*: i.e. that epidemiological data are inherently less sensitive than other data. Frequently this data has been collected for clinical purposes, and its use for research is a secondary use. As a result this type of research is often entitled ‘*secondary research*’.
- *unethical to obtain*: this is the case where data is collected to compile registers of all those affected by a particular disease or condition. In such cases, relying upon consent would bias the register and result in substantial undercounting.
- *threat to the validity of research*: this might include errors such as double counting.

24. The Mental Capacity Act 2005 provides for similar justifications of research in those lacking capacity to consent, but also provides that research of equal value should not be capable of being carried out using de-identified material.

25. Obtaining an assent from non-competent children involved in research is good practice.

26. Delaying research is only relevant if there is a reasonable prospect of the delay resulting in the research subject regaining competence. The Mental Capacity Act 2005 addresses this problem by providing explicitly for research in such circumstances subject to certain safeguards.

26A. This wording exceeds the requirements of existing UK law.

The Human Tissue Act 2004 provides that appropriate consent and/or ethical approval is not required for existing holdings of human material (held before 1 September 2006). However the Human Tissue Act Consent code of practice suggests that it may be good practice to consider whether any additional consent should be sought in such circumstances. This

requirement could impact upon research using existing holdings of tissue if the terms of the original consent were framed with an explicit project in mind (as was the custom in the UK a decade or more ago). For this reason it might be inequitable to apply this condition retrospectively to existing samples held for future research.

The declaration should be amended to emphasise the care that needs to be taken in framing the scope of the initial consent. If it is drafted too narrowly, any subsequent reuse will necessitate an additional consent or application for ethical review. The Human Tissue Act 2004 Consent Code advises that a general consent should be used where applicable (e.g. research approved by a research ethics committee).

26B. The use of patient clinical trial registers are encouraged in the UK but not mandatory.

### **C. Additional Principles for Biomedical Research Combined with Medical Care**

28. The nature of research is that there should be clinical equipoise concerning the proposed intervention: risks are unknown. To require that the physician is '*convinced*' is not legally coherent in this context.

29. We note that the meaning of '*best current*' has not been further defined and could refer to the best in existence, or the best available in a local context. We suggest that the latter definition be adopted, and the provision amended to reflect that due to resource constraints the '*best current*' may not be universally available.

The more divisive issue in paragraph 29, as to the circumstances in which the use of placebos may be acceptable, similarly remains unresolved, although we agree with the suggested amendments. The proposal retains the prohibition on the use of placebos if a proven treatment exists, but collapses together into one what was previously two exceptions to this rule. It now reads that where a proven treatment exists, a placebo control cannot be used unless there are both compelling scientific reasons for it *and* the patient is subject to no additional risk of serious or irreversible harm. (This leaves open the question as to what might constitute a compelling reason for the use of a placebo where there *is* a risk of serious harm to patients, but given the inclusive nature of the criteria it is unnecessary to answer it).

We would encourage further work through the individual assessment of the risks and benefits of placebos on a case-by-case basis in order to establish evidence-based guidelines for a wide variety of conditions in order to determine those circumstances in which the use of placebos may be acceptable.