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D9.2 Research report on the results of exploratory study on main ethical concerns and factors affecting risk perception

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1. Introduction.

The aim of Workpackage WP9 is to address the regulatory and ethical issues associated with the nature and outcomes of the SmartHEALTH Integrated Project. This report relates to Task 9.2, which explores stakeholder views on developing an ethical framework for subsequent clinical trials. This task has two associated deliverables:

- D9.2 Research report on the results of exploratory study on main ethical concerns and factors affecting risk perception.
- D9.3 Report on views of stakeholders in partner countries (interviews/surveys) on issues associated with possible use/implementation of bioanalytical microsystems for medical diagnostics.

This report relates to the first deliverable D9.2 which is exploratory and aims to map the main social ethical and legal issues related to SmartHEALTH in the European context. This is the necessary preliminary phase before addressing D9.3, which will engage with a number of specific issues including the development of an ethical framework for clinical trials.

This report draws upon a review of the literature surrounding the potential ethical, legal and social implications (ELSI) for SmartHEALTH technology. ELSI has become a commonly used acronym to acknowledge the importance and necessity of examining the ethical, legal and social implications of technology generally and biotechnology in particular. The late twentieth and early twenty-first centuries have been characterised by the willingness of the media and public institutions to describe and debate the claims, merits and implications of advances in technology and biotechnology. The birth of the first test-tube baby was the harbinger of a wave of converging technology and know-how that marked the advent of embryo research, and human stem-cell technology. These developments have promised much but in doing so challenged social norms, ethics and law, and created a series of challenges for policy makers. Work in genetics that resulted in the mapping of the human genome has also promised great benefit in tackling human disease but has raised concerns and fears about the potential for manipulating the human genome and exploiting genetic information. Other aspirations for biotechnology have made great promises but have been perceived as failing to deliver and this has created an atmosphere in which the hope and hype of biotechnology has become open to criticism (Martin and Nightingale, 2004; Hopkins *et al*, 2007). SmartHEALTH technology, in combining medical nano-technology, and integrated systems technology is within the spectrum of these new biotechnologies to which the ELSI approach is concerned.

The ELSI approach has number of objectives:

- Analysis of the ethical and social issues raised by specific applications of biotechnology and biomedicine in view of their being taken into account in public policy deliberations.
- Legal and regulatory aspects of new technology.
- Ethical issues including professional standards and good governance.
- Dialogue between science and society.
- Acknowledgement of the social context in which new technology is applied.

1.1. Aim, scope and objectives of the deliverable.

The SmartHEALTH project aims to integrate a new healthcare technology into existing healthcare systems and markets, across Europe and potentially globally. To understand the impact of any new healthcare technology, upon different users, the project needs to be located within the ethical, legal and social context that accompanies the introduction of any new technology into existing infrastructures. In addition, it is necessary to speculate and explore the potential for any new and specific ELSIs of SmartHEALTH applications. To an extent, the territory is already established since SmartHEALTH is operating against a background of an ageing European population and a burgeoning cancer problem. In addition, the political imperative is to seek effective screening programmes, rapid and accurate diagnosis and monitoring so as to improve the morbidity and mortality associated with malignancy. Hence this report will:

1. Scope the current territory and explore the potential ELSI challenges for SmartHEALTH Integrated Systems.
2. Provide a framework for the next phase of fieldwork by providing a rationale for selecting appropriate stakeholders to be consulted on the SmartHEALTH technology.
3. Provide a background analysis to stimulate discussion amongst SmartHEALTH partners.

1.2. Structure of the deliverable report.

The report has five main sections:

1. The introduction presents the overall aim of WP9, the aims, objectives and structure of the report; the methods employed and finally a summary of the main issues raised for SmartHEALTH and the implications for further WP9 work.
2. Background: this section locates SmartHEALTH within the context of the existing challenges of the three index cancer cases, cervical, colorectal (CRC) and breast cancer. SmartHEALTH has both a medical and technological context. Within the medical context the work of Zapka *et al* 2003 is utilised as it provides a framework based upon the process of cancer care in which a number of potential challenges for SmartHEALTH are identified. In relation to the technological context, the focus is upon Point of Care (PoC) Technologies and the inherent differences between PoC within secondary and primary care.
3. Contexts: this section offers a review of the relevant ELSIs associated with the medical context (the index cancers, screening and monitoring practices) and the technological context (PoC technologies) in regard to informational and psychosocial needs, equity and access (regulatory, legal, professional standards and practice).
4. Conclusions and Future Work outlines the implications for SmartHEALTH: this section summarises: a) the most relevant ELSI issues and b) the implications for the next stage of research for WP9.
5. Further Research Questions for WP9 Fieldwork are summarised in section 1.4.

A list of main references conclude this deliverable report.

1.3. Methods.

The following electronic databases were searched: OVID, MEDLINE, and Scopus which became the main search engine. The selected references were downloaded, or manually added to, an Endnote database and all duplicates excluded. Journal alerts were set up and content pages that contained frequently cited authors or that published specific papers concerned with the subjects of interest were reviewed manually as were relevant books and “grey” literature. The target publications were obtained, read and subjected to an initial sorting for relevance to SmartHEALTH. The literature was characterised into several groups as they related to specific issues:

- Epidemiology and mortality of the three index cancers
- Screening related research
- Ethical and legal issues
- Psycho-social issues including communication
- Technology related issues

The papers were read by the WP9 team and subjected to a thematic analysis using a number of categories which have dictated the structure of this report.

1.4. Main issues raised in this report for SmartHEALTH.

The report highlighted a number of potential ELSIs relating to both the implementation of SmartHEALTH technologies and the functionalities of these technologies. The following ELSIs need to be clarified as SmartHEALTH moves toward the next phase of the project and trial devices are developed:

Issues related to the technology:

- The exact nature of these applications, in terms of screening, therapy monitoring, disease surveillance.
- The sensitivity and specificity of the technology (biomarkers).
- quality control requirements for long term clinical use of these technologies.
- Safety and efficacy of data handling aspects of the technologies – with particular reference to data security.
- Integration with/ conflict with existing health infra-structures e.g. existing screening/ disease monitoring programmes.
- The PoC location of each application and if this PoC is new or existing within current health systems.

Issues related to the implementation of the technology:

- Personnel - who deals with the patient/participant and in what way?
- Quality of information provided – to the patient/participant user.
- Counselling provided to the patient/participant user before moving through the process.
- Quality of informed consent/ informed uptake.
- Implications of the speed of process – from testing to results.
- Managing results - quality of information and communication when disclosing results.
- PoC location of each SmartHEALTH application.

These issues raised a number of questions for further fieldwork for WP9:

- How will this new technology fit into the existing healthcare services, in terms of more accurate tests, improved access to healthcare information for health professionals?
- Will a quicker test result produce a quicker diagnosis?
- Will SmartHEALTH impact on the current lack of willingness for participants to attend cervical cancer screening programmes?
- Will improving the cancer screening stages and follow up stages impact on the other care services within the wider continuum?
- Is the location for the tests new or existing within current practice?
- How much knowledge and skill does the person using the machine require?

The above issues have implications for the design of the second deliverable (D9.3) linked to Task 9.2 (see page 4).

- Interviews will be held with different SmartHEALTH partners to discuss and clarify the functionality of the SmartHEALTH technologies..
- These in-depth interviews will provide important baseline information on how to represent SmartHEALTH technology to the different stakeholders during the two case studies, which will result in D9.6 (a report on the case study findings of main ELSIs arising from SmartHEALTH).
- This fieldwork will enable WP9 to further explore the wider ELSI issues as well as addressing the specific ethical issues to be faced in the clinical trials of SmartHEALTH technologies.

This report (D9.2) also marks the achievement of milestone M9.2 (definition of the research parameters and design of scoping study of fieldwork phase) and informs the design of D9.6 in three ways:

- Ongoing Public dialogues will be held during the development of the SmartHEALTH technologies.
- Different users, from the patient to the clinician, will be invited to discuss the SmartHEALTH technologies within suitable SmartHEALTH applications.
- There will be a specific focus on exploring how SmartHEALTH technologies could impact on the current debates around breast cancer follow-up services (see page16).

2. Background.

The SmartHEALTH project can be represented in a number of ways, as an example of converging technologies, as a medical diagnostic device embedded within an informatics system, as the latest manifestation of an established automated screening and diagnostic technology or as an entirely new form of medical biotechnology. The diagram (Fig. 1) is one of the representations from the Description of Work document that summarises the kind of technologically integrated system which SmartHEALTH aspires to achieve. The SmartHEALTH project has a vision of innovative biomedical sensing systems combined with information technologies likely to have an immediate impact on the quality of cancer diagnosis and monitoring but with potential for much wider application. However this

vision must also be seen as existing alongside other complex social processes, public interest and political agendas for health.

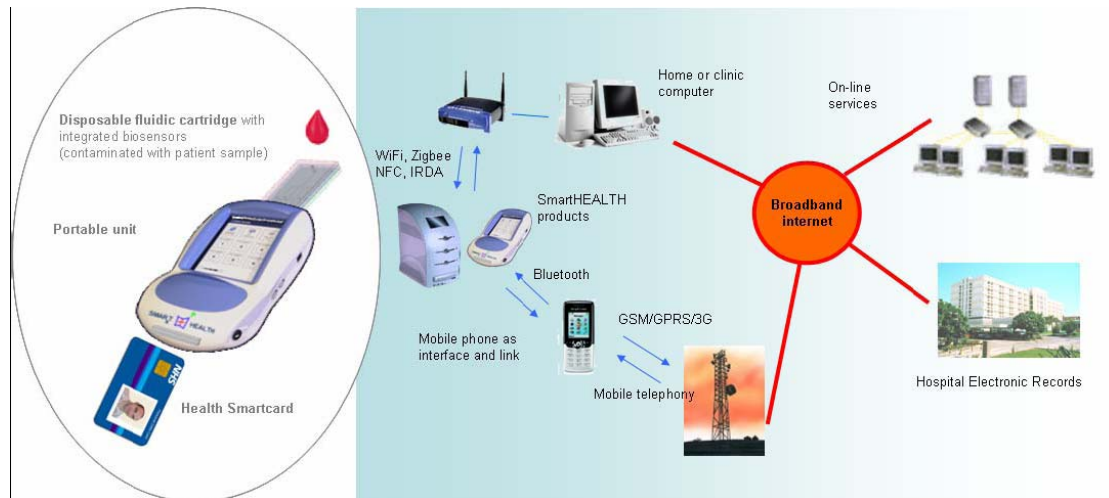


Figure 1: The SmartHEALTH system.

In order to make the ELSI aspects of SmartHEALTH more salient, it is necessary to map and explore the processes which will run parallel to the SmartHEALTH vision and to be aware of the contexts in which SmartHEALTH technologies are most likely to be embedded, such as existing public health and cancer monitoring programmes. Within these processes of cancer screening, diagnosis and monitoring, the application of SmartHEALTH technologies will impact upon different potential users from the histopathologist screening for cervical cancer in centralised clinics to a patient self-monitoring for breast cancer recurrence in their own home. A narrow definition of a “user” includes only individuals who physically handle the technology such as a technician or health professional. However, since SmartHEALTH technologies inherently produce information that will inform and aid subsequent diagnoses and treatment decisions, a user may be any individual who is part of the information process. Increasingly, within social and ethical research, it is common to view the patient as a user of medical information that impacts upon both their bodies, lives and well-being (cf. Trachenberg *et al*, 2005). As such, within WP9 and WP10 (see D10.1), the user also includes the participant or patient within all of the SmartHEALTH applications.

Patient as user of SmartHEALTH information

To explore the ELSIs of the process represented by the schema in Fig. 1, the perspective of an individual person as a “patient user” has been taken. Seen from this perspective it is possible to explore the fact that a person who engages with SmartHEALTH technology as a user may be taking the first steps in what will become their personal illness trajectory. Hence there are many factors which are relevant to the actual and perceived risks of engaging with this technology, ranging from personal experience with illness and willingness to participate in screening, whether the technology is in fact available and accessible, faith in such technologies and the trustworthiness of the wider system (Hall *et al*, 2001) in which the screening technology is embedded. Other relevant aspects include:

- Other actors within the wider process – such as personnel administering the technology
- The ethical and governance frameworks under which such technologies operate
- Public policy on cancer prevention and screening
- The type and quality of the health-care system
- Opportunity costs of implementing the technology

The relevant contexts and issues have the potential to be exponentially expanded here and therefore to provide a structure and boundary to this report the issues are grouped according to their place within the cancer care trajectory, the social and ethical aspects of the three index cancers with regard to PoC testing, and the quality of the service provision in which the technology is located.

2.1. Cancer care trajectory.

Zapka *et al* (2003) describe the process of cancer care as a means of identifying potential barriers and failures affecting the quality of cancer care. Zapka’s “continuum” model, referred to in this report as the “cancer care trajectory” is a useful way of both locating potential applications of SmartHEALTH technology and exploring some of the ELSIs. The span of care includes everything from risk assessment, primary prevention, and screening, to diagnosis, treatment, and monitoring and end-of-life care (Fig. 2).

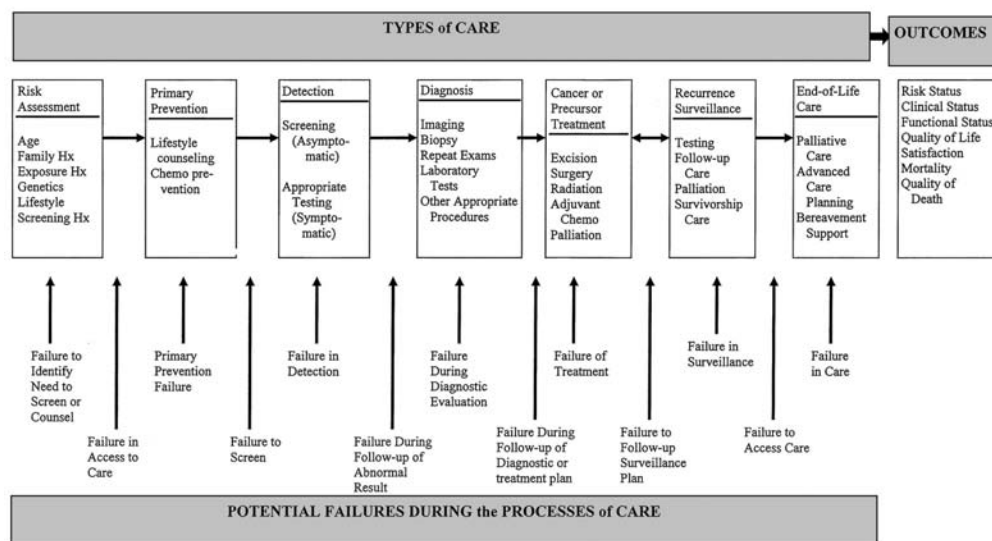


Figure 2: The continuum: from risk assessment to end of life care (Zapka *et al* 2003).

Although SmartHEALTH is being developed as a potential application for many serious diseases, the prototype is focussing on only three cancer applications, which can be located within this trajectory:

- Cervical cancer screening, which coincides with the detection box
- Colorectal Cancer (CRC) diagnosis, which coincides with the diagnosis box and recurrence/surveillance box.
- CRC and breast cancer monitoring, which coincides with the recurrence/surveillance box.

Locating SmartHEALTH within this schema indicates that the success of the applications will be as contingent upon the process in which they are embedded as it will be upon the success and efficacy of the technology itself. An efficient technology, that is, sensitive and specific, will still fail if, for example, there is a failure to screen or implement monitoring in the first instance.

2.1.1. Barriers to screening

Whilst most developed countries have long established cervical cancer screening programmes, they nevertheless all face the contentious problem of certain cohorts which are highly resistant to screening. Although the intended application of SmartHEALTH with regard to CRC has shifted from a diagnosis to a monitoring context, it is nevertheless worth noting that national screening for CRC is a relatively new phenomenon and one where issues of taboo, disgust and ignorance are strongly evident as barriers to participation (Wardle *et al* 2000, Weller *et al* 2006). At this point in the process of development, it is impossible to say whether SmartHEALTH applications will have beneficial or adverse effects upon uptake of screening or implementation of monitoring. However it is reasonable to speculate that if the technology was to be less invasive, more efficient and more easily accessible than existing technologies then this is likely to have a positive influence on willingness to participate.

Cervical cancer, CRC and breast cancer national screening programmes are essentially concerned with screening a healthy population. However the route to diagnostic tests is twofold, via “well-person” screening or by the self-reporting symptomatic patient. The process of moving from secondary prevention screening to diagnostic investigations is dependent upon both an effective initial screening programme and an effective gate-keeper for the worried and symptomatic patient. How this process is managed in terms of:

- Personnel (who deals with the patient and in what way)
- Quality of information provided
- Counselling provided before moving through the process
- Quality of informed consent
- Speed of process
- Managing results (quality of information and communication)

These are all significant factors in the ELSI evaluation of this technology. Participation premised upon a well-informed understanding of risks and benefits is an important part of this process. The patient/participant’s right to be given the full facts about the screening, diagnostic or monitoring programme (informed consent) has gained importance in recent years. Although within Western medicine there is a potential conflict between a patient’s right to informed consent and the public health duty to ensure that health benefits are maximised within a population. This has led to a potential conflict within the ethics of public health medicine in which secondary prevention has its place.

Within the developed world the liberal paradigm has come to dominate medical ethics, emphasising the principle of personal autonomy. This is particularly the case in the US; home of the ‘four principles approach’ to medical ethics (Beauchamp & Childress 2001), but it is also true for Europe and many other developing nations. The autonomy paradigm - underpinning the principles approach - sees the patient as an individual who takes responsibility for his/her own actions, is self-directing and is the best judge of his/her own interests. It is closely associated with the economic concept of the ‘health consumer’ and

the sociological concept of the ‘reflexive patient/consumer’ (Giddens 1991; Henwood *et al.* 2003). One implication for health providers is a strong presumption that patients must be informed and given free choice before consenting to any intervention.

However the domain of Public Health has been relatively slow to adopt the autonomy paradigm. Here the utilitarian principle of reducing collective harm has trumped the principle of individual autonomy. In turn, reducing harm has led to an emphasis on methods to ensure compliance in a cost-effective manner. Thus, the World Health Organisation’s (WHO) influential text ‘Principles and Practice of Screening for Disease’ (Wilson & Junger 1968), made no reference to respect for personal autonomy, although more recent guidance (Strong *et al* 2005) emphasises the importance of public acceptability of screening. Despite recent guidance such as the UK National Screening Committee (2006), much of the information made available in the screening context is directed towards compliance rather than self-determination (Dixon-Woods, 2001). Yet there is growing advocacy of ensuring informed choice in public health contexts. In the UK the General Medical Council (GMC 1999) now recommends informed consent for screening and advises that full information on risks and benefit should be given. The UK National Screening Committee (2006) has also signalled the need for a changed approach to information giving so that individuals are offered a choice based on appreciation of risks and benefits.

There is a strong case for the public health benefits of cancer screening, including reduced morbidity and incidence, cost-effectiveness and ensuring access for all. On the other hand, screening is not necessarily beneficial at the level of the individual as can be seen in the context of CRC and cervical cancer screening. For example, faecal occult blood testing (FOBT) for CRC has a very high sensitivity but low specificity this means that the test shows positive and so many people unnecessarily undergo colonoscopy, an invasive procedure which carries some risks. Raffle (2001) argues that cervical cancer screening also leads to unnecessary further surgical investigation and treatment. Paying more attention to informed choice may compromise the uptake of screening although there is a growing opinion that this is an acceptable price of informed and personalised healthcare. However it is emerging that the screening application of SmartHEALTH will be limited to Cervical Cancer only (see D1.2) and that both the breast cancer and CRC applications will be concerned with the detection of recurrence.

2.1.2. Breast cancer monitoring

Breast cancer monitoring is perhaps the most novel of the SmartHEALTH applications since it is not apparent that there is routine systematic monitoring for recurrence of breast cancer even though this disease is seen to be chronic in nature with a long survival following initial treatment. The use of the terms “monitoring” or “surveillance” in the SmartHEALTH objectives is ambiguous and potentially confusing. The clinical concept of “follow up” for patients during and post-treatment does not conform to a standard model in which disease surveillance is routine. “Follow up” is a process in which a patient is reviewed during a series of post-treatment clinical visits of decreasing frequency which may or may not include diseases surveillance (Beaver, *et al*, 2006). The degree to which this constitutes monitoring of disease is an open question since there is no consensus on what constitutes the “gold-standard” of follow-up or indeed what the appropriate clinical measures are beyond a verbal history and physical examination. Local

recurrence may be more easily identified both by the patient and the clinician but systemic spread, which is more difficult to identify, carries a much worse prognosis.

Breast cancer is a highly politicised and socially conspicuous disease. It is also a disease with many sources of support and information. Women are encouraged to be autonomous and self directed both through self-help “breast-health” campaigns and readiness to challenge the system to ensure the best treatment. This particular context raises a number of possibilities for SmartHEALTH applications suggesting a context in which a more personalised medicine approach including self-monitoring may be most appropriate.

2.2. Point-of-care testing.

Until the middle of the 20th century, pathology tests were carried out close to the patient, either in a hospital ward or general practitioner surgeries. As the complexity and clinical demand for tests increased during the 1960s, testing activities largely transferred to centralised pathology laboratories. Over the past decade these laboratories have focused on automation and information technology to accelerate services and reduce costs (Price, 2001). Today, healthcare delivery is under pressure due to rising costs and increased community expectations. These pressures are changing how care is provided through increasing same-day procedures and use of some community alternatives to hospital care. The use of diagnostic pathology procedures is central to medical practice and it is possible that 60-70% of diagnoses depend on laboratory tests (Royal College of Pathologists, 2004). One of the main challenges for these laboratories is the turnaround time for test results. In 2005, the Royal Society of Pathology and the Department of Health published *Modernising Pathology: Building a service responsive to patients*, that recognised the potential for the role of PoC testing and remote linking with laboratories to improve healthcare delivery (Gray *et al*, 1996). Technological advances in solid phase chemistry and miniaturising of analyses, through biosensors, have spawned a huge expansion in near patient tests. In the United States, PoC or near-patient testing comprises a fifth of all diagnostic testing with European countries following suite (The Royal College of Pathologists, 2004). European countries are following suite. Near-patient tests from blood sugar and urine analysis are routine in most British primary care centres. PoC testing is also creating new commercial markets.

Crook (2000) highlights that PoC testing has various terms such as: alternative site testing, point of care testing, physical office laboratory testing, bedside testing, limited service laboratory testing, ancillary testing, out of laboratory testing and near-patient testing (NPT). Crook uses NPT in his paper, the most common term in use within the UK, though he states that this term raises questions around: “how near is near, and what about individuals who are not patients? (such as in screening). The term PoC testing may be preferable as this would include bedside testing, in vivo testing, physician office laboratory testing and patient self testing (Handorf, 1994)”. The effectiveness of PoC testing is likely to vary according to the circumstances of its use (population, setting, operator, and clinical value of the result). SmartHEALTH is currently exploring three different applications at different points of care (see D1.4):

- | | |
|----|---|
| 1. | WP1a: breast cancer therapy monitoring.
PoC: General practitioners, clinics or in specialised laboratories (home-use may be possible). |
| 2. | WP1b: Cervical cancer screening and case findings.
PoC: General practitioners (gynaecologists), clinics or specialised laboratories. |
| 3. | WP1c: Colorectal (CRC) cancer diagnosis and therapy monitoring.
PoC: Clinics or specialised laboratories. |

Some SmartHEALTH applications are proposing new locations for testing, while others will fit into the existing healthcare systems. Current guidelines on PoC testing from the Royal College of Pathologists in the UK state that “due to (pathologists) experience and the needs of accreditation, local pathology laboratories should oversee all PoC testing” (2004:3). For PoC technologies within primary care, good communication between secondary and primary care is essential in effectively introducing and operating these types of technologies. However, historically communication between the two care services has been fraught with problems (Roland 1992, Harrison *et al* 1996).

3. Contexts: Social and Ethical Issues for the Three Index Cancers at Points-of-Care.

This subsection explores the specific ethical and social issues associated with both the three index cancers and the different Point of Care locations within the SmartHEALTH project.

3.1. The three index cancers.

An important ethical consideration in the evaluation of health technologies is the extent to which these technologies confer a benefit (beneficence) or prevent and avoid harm (nonmaleficence) (Beauchamp and Childress 2001). Cancer morbidity and mortality are serious causes of human harm and it is in the prevention and amelioration of these harms that SmartHEALTH is likely to have the greatest impact.

3.1.1. Cervical cancer

Cervical cancer is the third most common cancer world wide (Koliopoulous *et al*, 2003). Eighty percent of cases occur in developing countries where some 200,000 women die as a result of cervical cancer each year. This number accounts for 10% of all female cancers making it the second leading cause of cancer death in women (Parkin, 2001). Rates of cancer differ between countries and also ethnic populations in the same countries (Parkin 1999).

European countries have a relatively low incidence of cervical cancer. However there were 2,799 cases of invasive cervical cancer in the UK, accounting for 2% of all female cancers diagnosed, and approximately 1,250 women die of cervical cancer each year in the UK (Cancer Research UK 2003).

The cervical cancer screening debate

Some commentators, e.g. Raffles, *et al* (2001), have argued that the presumed benefit of national cervical cancer screening programmes is open to question since the implementation of screening was never scientifically evaluated. However Peto *et al* (2004) using UK epidemiological data have argued that effective screening has prevented a potential cervical cancer epidemic. This claim has itself been challenged as being too selective in the data used in the analysis of Peto *et al*. Bonneux (2004) observed that opportunistic screening over screened women at low risk, but missed women at high risk with the associated harms of increase in the number of worried well, over-treatment of some women, and failure to treat women with potentially curable lesions. Raffle (2004) argued that there is also an important opportunity cost with serious ethical implications associated with cervical cancer screening programmes within publicly funded healthcare. Raffle (2004) has observed that increasing the frequency and extending the range of cervical screening is an expensive strategy per life saved when compared with the same resources used in alternative public health programmes such as smoking cessation. These commentators do not dispute that cervical cancer screening has achieved an important human *good*, they argue that the costs and benefits be properly evaluated with full weight given to the ethical issues that screening raises.

These observations present both an opportunity and a challenge to the SmartHEALTH programme. The challenge will be to show that SmartHEALTH applications within the context of cervical cancer screening at least maintain if not improve the preventive role which cervical cancer screening plays in developed countries. Also, by applying the technology in ways deemed accepted to potential users then SmartHEALTH may also present a technology that is applied more ethically through a process of informed uptake. These are important issue to be explored in the later stages of the project.

A greater potential to confer benefit exists in the prevention of cervical cancer within developing countries where it is estimated that only 5% of women are screened (Koroltchouk 1999). However, whether the SmartHEALTH technology will have a significant impact in developing nations will be contingent upon the cost, the infrastructure required, and the specific social contexts, which vary widely in the varied religious and cultural contexts (Forbes *et al*, 2002).

3.1.2. Colorectal cancer (CRC)

Colorectal cancer is a common form of malignancy in developed countries but is less common in the developing world. Occurrence is age related, with 80% of cases arising in people who are over 60 years old. Rates are similar between the sexes up to the age of 50 but after this age the disease is predominant in men. In 2002 there were an estimated 275,579 new cases of colorectal cancer in the European Union (IARC 2002). Although CRC is potentially curable by surgical intervention this is only possible when the cancer is diagnosed at an early stage. Only 10% of patients are diagnosed according to the international classification as Dukes stage 0 or stage I. Other diagnostic stages are distributed between Dukes stages II - IV. It is likely that the average General Practitioner (GP) will see only one new case of colorectal cancer every year and therefore diagnosis may not occur until the cancer is advanced (Hobbs 2000). Prompt referral to a specialist centre for all patients with suspected colorectal cancer is recommended in order to maximise survival.

In the early phase of the SmartHEALTH project the potential for a secondary prevention application via PoC testing for CRC screening (see milestone M1.10 in the DoW) was proposed. A successful application in this context may have the potential to convey most benefit since it is likely that CRC could be diagnosed quickly and at an earlier stage. However the benefit would only be realised if screening was not opportunistic in nature but became routine and with a high degree of compliance. Subsection 1.1 discussed some of the social and ethical issues associated with CRC screening and these would also pertain if a PoC screening application were adopted. However, technical challenges in the development of SmartHEALTH applications has meant that the focus for CRC has changed from PoC screening to disease monitoring and diagnosis of recurrence, a process to be managed by specialist doctors within the clinic (see WP1: D1.2 & D1.4). The social and ethical aspects of this application may echo those related to the breast cancer applications and therefore the issues related to recurrence monitoring will be discussed together.

3.1.3. Breast cancer

Worldwide breast cancer is the most common cancer in women. North America has the highest incidence whilst the lowest risk of breast cancer is in Asia and Africa (Parkin *et al*, 2001). Breast cancer is also the most common cancer in women in Europe. In 2000, there were 350,000 new breast cancer cases, while the number of deaths was estimated at about 130,000. Breast cancer is responsible for 26.5 % of all new cancer cases among women in Europe, and 17.5% of cancer deaths (Tczyński *et al*, 2002).

Survival rates for women with breast cancer have continued to improve over the last two decades but 5 year disease-free survival does not equate to “cure”. As with most other cancers, survival rates for breast cancer continue to fall beyond five years after diagnosis. Post-treatment recurrence of breast cancer several years after treatment remains a significant problem. Breast cancer is therefore an important cause of morbidity and mortality. It is therefore a reasonable intuition to presume that a process of post-treatment follow-up involving clinical monitoring with a view to early detection of disease recurrence is likely to convey benefits on a number of fronts; the equitable and fair use of public resources, health and psycho-social benefits to individual patients. It is an intuition of this kind which seems to be implicit within the SmartHEALTH application for post-treatment monitoring of both breast cancer and CRC.

Post-treatment monitoring: some ethical issues.

SmartHEALTH is proposing to develop an integrated biosensor with the potential application of monitoring disease recurrence for CRC and breast cancer. The context of this application can be recognised with reference to the concept of the cancer care trajectory as illustrated in Fig.2. Locating the application of this technology within this trajectory provides a means of highlighting the potential social and ethical implications, of which there are two broad categories; public benefits and *personal* benefits. Public benefits are concerned with the justified use of public resources such as the resources of a publicly funded health service understood in terms of use of physical resources, time of personnel, and use of consumables but also in more nebulous terms of the public good that comes from the use of public resources for a “good” purpose. Although individual patients will also share in the public benefits they also stand to gain personal benefits

which may mean longer survival but also by having addressed the psycho-social sequelae of cancer which detract from an individual's quality of life.

Post-treatment-monitoring or "follow-up" is an historical approach to the management of cancer and is regarded as having a number of benefits. Beaver *et al* (2006) list these possible benefits as including; early detection of recurrence, local and metastatic, monitoring of treatment outcomes and rehabilitation, and providing psychological support. However many authors have begun to doubt the achievement of such benefits rendering the very concept of routine surveillance as controversial (Rojas *et al* 2000, Montgomery *et al* 2007). Evidence has emerged from empirical studies which throws into question whether routine follow-up achieves either the public or personal benefits claimed (Rojas *et al* 2000, Beaver and Luker 2005, Beaver *et al* 2006). This body of evidence is something which must be taken into consideration by the SmartHEALTH applications to CRC and breast cancer. One of the ways in which WP9 proposes to address this issue is through stakeholder consultation with specialist doctors and cancer patients.

The breast cancer follow-up debate

Rojas *et al* (2000), in a systematic review of follow-up strategies for women with breast cancer, concluded that there was no difference in overall survival and disease-free survival between women who received intensive follow-up including laboratory tests, and those who had an annual check-up. Beaver and Luker (2005) argue that:

The costly system of follow-up currently in operation is historically rather than evidence based, and subject to increasing demands and limited resources. Alternative approaches are needed that address the diversity of patients' needs rather than searching for recurrent disease. (2005:94)

The cost and service implications for routine hospital follow-up of breast cancer was raised as problematic as long ago as 1995 by Grunfeld *et al*. Montgomery *et al* (2007) have observed that multiple diagnostic surveillance aimed at detecting recurrent disease is no longer recommended. This is echoed in the National Institute for Health and Clinical Excellence (NICE 2002) guidelines for England and Wales, which recommend against intensive surveillance and favour of regular mammograms and self examination.

In terms of personal benefit to patients several studies (Beaver *et al* 2006, Montgomery *et al* 2007) have shown that far from meeting patients' needs for psycho-social support and reassurance; frequent hospital visits exacerbate anxiety and do not address patients' concerns. Collins *et al* 2004 remarked upon the lack of evidence for the effectiveness of routine follow-up for breast cancer. More recently there is a growing body of evidence that alternatives to hospital follow-up such as follow-up by GP, Specialist Nurse and telephone support are more effective at meeting the psycho-social needs of patients (Koinberg *et al* 2002, Koinberg *et al* 2006, Beaver *et al* 2006, Jiwa *et al* 2004).

On a more controversial note, Allen (2002) has asked:

are we as health professionals, and therefore people who patients believe to be in the know, responsible for triggering anxiety in woman by asking them

to attend follow-up clinics regularly, by implication to detect the sign of disease recurring?

However, alternative forms of follow-up specifically do not involve testing or monitoring for disease recurrence. In addition, while secondary care welcome the shift of PoC from secondary to primary care to reduce their increasing workloads, many consultants express concerns over GPs' and nurses' lack of oncology training and knowledge. As such, while the NICE guidelines state that follow-up care should move to primary care within three years, many consultants do not refer their patients for up to five years (Donnelly *et al*, 2007)

3.2. Point-of-care technologies.

The final point of use for SmartHEALTH applications has not been fully determined at this stage in the development process although the three most probable contexts are:

- Specialist/hospital clinic
- General Practitioner /family physician surgery
- Patient's own home

As outlined earlier, there are a number of possible agents who may be the prime users of the technology including:

- Junior/senior/specialist doctors (e.g. gynaecologist)
- General/specialist nurses/technicians
- Family doctors/ practice nurse/ community nurse
- Patient self-testing

Adding to these potential permutations of contexts and personnel; the frequency of testing; speed of results; nature and detail of results, then it is apparent that this is a complex arena in which the SmartHEALTH technology may offer some significant advantages but also faces a number of the challenges already identified by commentators (Handorf 1994, Crook 2000).

In the context of cervical cancer, the SmartHEALTH technology is likely to be applied in ways that parallel current cervical screening utilising tissues obtained via the Papanicolaou cervical scrape (Gontijo *et al* 2007) (see deliverables D1.4, D1.6). It is also likely that the usual personnel will be involved in the procedure which currently includes GPs, practice and family planning nurses, and gynaecologists. Although the involvement of the GP in cervical cancer screening is well established across Europe (Coleman *et al* 1993, Hermens *et al* 1998), SmartHEALTH applications will potentially introduce some key differences. The main differences will be in terms of the timing and nature of the results which may be available within minutes or hours of testing and are likely to report not only on abnormal (dysplastic) cells but also on the screening participant's HPV status. A number of factors make this an ethically challenging clinical application; the immediacy of results, potential diagnosis of a cancer or pre-cancerous condition, and in addition the diagnosis of a sexually transmitted disease all to take place within the primary care setting of a family

practice/GP setting. For SmartHEALTH technology to be applied within a point of care context for cervical screening these factors will have to be efficiently and ethically managed. The Royal College of Pathologists (2004) in the UK have recommended that any PoC testing such as screening carried out by GPs must be embedded within a total quality assurance plan which ensures the quality of both the process and of the technology.

The deficiencies in the quality of the informed consent to uptake of screening have already been noted in this report (Raffle 2001, Jepson *et al* 2005). The success of a public health programme of cervical screening has historically been presumed to require a high degree of compliance but this is often at the expense of *informed* uptake and overlooks women who do not engage with screening (Raffle *et al* 1995, Austoker 1999). There are many factors which influence participation in cervical screening not least the fact that women eligible for screening come from diverse populations with diverse social and cultural attitudes to cervical screening. Austoker (1998), Jepson (2000) and others have described other specific factors in failure to accept screening including anxiety, fear of cancer, and embarrassment. French *et al* (2004) have shown that anxious women who receive an inadequate or ambiguous result from their test are less likely to return for a repeat test within the recommended period. Maissi *et al* (2005) and Gray *et al* (2006) have shown some evidence that information and support which addresses specific concerns goes some way to alleviating the anxiety of these women.

Women who are fully informed regarding cervical screening, which also involves testing of HPV status, may also be discouraged from participating because of the connotation of sexual promiscuity associated with HPV infection (Jepson 2007). McCaffrey *et al* (2003) have shown how these concerns run across different ethnic groups and have a particularly negative impact on women in long term monogamous relationships. However, the alternative of not fully informing women but merely encouraging participation on the basis that screening is an uncomplicated health benefit does not conform to legal standards or ethical norms (General Medical Council 1999). It is likely that with the advent of easy and effective means of testing that HPV becomes a routine aspect of national screening programmes (Sasieni and Cuzick 2002, McCaffrey *et al* 2003) However, there is little evidence of how this may be achieved in a way which also manages the social ethical and legal implications of screening. Recent research claims that the nature of HPV and cervical cancer screening is not well understood by the general public, and there is an increasing call for more public awareness programmes for both women and men (Jepson *et al* 2007.). In addition if the SmartHEALTH technology will permit routine HPV screening by GPs then there will be a need for the training of personnel to provide quality information, counselling and support to women undergoing screening with a process for the audit and evaluation of these services.

In the context of breast cancer and CRC disease monitoring then a likely application of SmartHEALTH technology will be in the specialist follow-up clinic. "Follow-up", as a concept and as a process of disease monitoring, has already been described in this report as problematic (Rojas *et al* 2000). As reported, some commentators have argued that follow-up should be regarded as a means of responding to the ongoing psycho-social needs of patients rather than appearing to offer disease surveillance; mainly because most

cases of recurrence are self-reported by patients (Beaver *et al* 2006, Wattchow *et al* 2006).

The use of alternative means to hospital clinic consultations is being advocated as a more effective method of providing long-term support of patients following treatment (Beaver and Luker 2005). However should SmartHEALTH provide a simple and accurate test capable of monitoring both disease response during treatment, and disease recurrence following treatment, then this would radically change the context. The early detection of disease recurrence may have a major impact on long-term survival with breast cancer and CRC although this will be contingent upon the availability of further options for treatment. The most serious implications are likely to be upon the provision and service adjustments required to accommodate this new technology. The availability of, and access to, the technology for these patient populations will be significant since there is the serious possibility that a “techno-divide” within and between nations could exacerbate health inequalities and thus prove divisive in terms of equitable access to health resources (Bain and Campbell 2000).

Introducing technology with new capabilities will also have an impact on the service in which the technology is utilised. The diagnosis of recurrent disease is another important transition point on the cancer care trajectory (Zapka *et al* 2003). For some patients, this will mark the transition from having a curable or, in their perception, “cured” cancer to having active progressive disease or even a terminal illness. Therefore the training of personnel, the provision of appropriate information and the time and skill required to convey significant news to patients in an effective and supportive manner will all be important aspects of the implementation of SmartHEALTH technology in this context.

PoC within primary care or secondary care

There is a further implication for the monitoring of breast cancer by SmartHEALTH technology since it is speculated that monitoring may also take place via the GP or through self-monitoring by the individual patient in their own home. Some of the implications of GP screening for cervical cancer, previously reported, will also be relevant here particularly if results of positive tests are to be made immediately available. Allgar and Neal (2004) have reported that little is known about the GP’s role in the cancer care trajectory although Campbell *et al* (2003) have called for an increased role for GPs in the management of all cancers. However if there is to be an increased role for PoC testing by GPs then the 1999 review of the literature by Delaney *et al* is significant. In a review of 101 papers Delaney *et al* (1999) concluded that the performance of most PoC tests have not been subject to adequate evaluation in GP settings, and little attention paid to the impact of such devices in terms of improving patient outcomes or cost-effectiveness.

Fitzmaurice (2004) predicted that PoC screening within primary care will be used more for testing than for diagnostic use. Fitzmaurice stated that tests have an important value in reducing the uncertainty in which doctor’s practice, referring to a Dutch study with GPs which found that the results confirmed the GPs’ original diagnosis in 82% of cases and was ‘reassuring for both doctor and patients’ (Bjerrum & Munck, 2004:p776). Fitzmaurice highlights that patients return visits may be avoided, if patients wait for the results of the test, though he refers to a study of desktop analysers in a London that found

that, even though the analyser was used, 15% of patients were asked to return. (Rink *et al.*, 1993) Fitzmaurice believes that GPs prefer to use laboratory tests rather than NPT to provide a delay in which they can resolve diagnostic problems, while ensuring the patients are satisfied that their symptoms are taken seriously. In contrast, there are concerns within secondary care that PoC in primary care will lead to inappropriate testing (Crook, 2002).

PoC within the home

The concept of self-monitoring or self-surveillance is a more radical innovation. As Crook (2000) observed self-monitoring has become almost routine in the management of some chronic conditions such as diabetes or coagulation disorders. In addition there are now a plethora of off-the-shelf test kits and monitoring devices from pregnancy and ovulation kits to cholesterol tests and blood-pressure monitoring, with an increasing number of cancer specific kits available (The Observer Dec. 2006). It is possible that this is indicative of a trend, consistent with the concept of consumer-autonomy that *some* people are now more willing to be proactive in health matters but this is by no means conclusive for all patients in all contexts. Crook (2000) identified a number of possible advantages of self-monitoring which included the fact that most devices are less invasive, patients become more involved with their own treatment, availability to patients in remote areas, shorter test result turn-around, and possible cost savings on personnel and transport to laboratories. Crook (2000) also noted the potential disadvantages which may also include *increased* costs because of the need for multiple readers, and problems in the maintenance and quality control of the technology.

Patient self-monitoring for breast cancer recurrence is likely to constitute the most intensive form of surveillance. The possibility of intensive surveillance may have a strong appeal to certain cohorts of women, for example, those with BRCA I and BRCA II positive cancer. However, Warner (2004) reports a lack of research evidence on which to estimate the clinical or the psycho-social impact of intensive surveillance. As Warner (2004) observes, the psycho-social impact of intensive surveillance may be positive or negative or both and therefore the implication for SmartHEALTH applications in this context is that they must be accompanied by rigorous evaluation of their impact. There are of course a number of possible strategies for implementing SmartHEALTH technologies and the integrated nature of these has the potential to convey a number of benefits, such as improved access for housebound patients, such as older groups of people. The capability of SmartHEALTH technology to send data from local readers to distant sites such as GPs' surgeries or specialist centres could allow self-surveillance to be utilised as an adjunct to more conventional forms of follow-up. This would mean that whilst the patient is responsible for performing the test he or she would not have access to immediate results which would be mediated by the GP or Oncologist. [For the GP or specialist, the information from the test itself is rarely sufficient to form a diagnosis and a number of individuals are involved in the final decision.] It remains clear however that whatever strategy is adopted for patient self-monitoring this would need to be implemented alongside a careful evaluation of the clinical and psycho-social impact of the technology, which raises a number of ethical concerns.

3.2.1. Social and psychological issues

In recent decades there has been a volte face in the attitude of health professionals with regard to the open discussion of cancer with the patient and their family. The position has shifted from one in which open discussion was avoided and believed harmful to one in which open discussion is the presumed starting point in patient communication (Okin 1961, Novack *et al* 1979). The period of time in which this change has taken place coincides with the coming to prominence of respect for patient autonomy as a cornerstone of medical ethics. Respect for autonomy at the very least requires that patients are adequately informed and allowed to make their own healthcare decisions (Faulder 1985, Beauchamp and Childress 2001). This principle has also been recognised in most civil and common law jurisdictions through the legal concept of consent, which recognises the individual's right to self-determination. Alongside consent is the recognition that a failure to adequately inform patients constitutes negligent behaviour. As discussed in Section 1, there are many instances of public health screening that are yet to fully implement the concept of informed consent or informed uptake to the same extent as this has become an accepted norm in the treatment context (Raffle 2001, Irwig *et al* 2006).

The past few decades have also seen a growing body of empirical research which has explored the social and psychological impact of a cancer diagnosis (Fallowfield *et al* 1990, Greer 1984, Fallowfield and Jenkins 1999), the informational needs of cancer patients (Faulkner 1994, Cox *et al* 2006), as well as the effectiveness of communication by health professionals (Sutherland *et al* 1989, Faulkner *et al* 1994). It is well established that the possibility, as well as the actual diagnosis, of cancer has a traumatic impact on patients and their families. The impact of this trauma can be ameliorated by effective communication, appropriate information, and specific support from health professionals (Shilling *et al* 2003). It has also been established that health professionals need specific training to be effective communicators and that time is also a factor if these skills are to be applied (Maguire *et al* 1996). These are some of the quite specific challenges relevant to the deployment of SmartHEALTH; challenges that will be more or less complicated depending upon the point of use and the specific application of the technology.

3.3. Legal and regulatory issues.

SmartHEALTH technologies will potentially challenge some of the established norms and practices in the clinical setting as well as in the relationship between health professional and patient. These challenges are likely to have significant implications for both policy and practice. Although technologies such as those proposed within SmartHEALTH may only differ in degree from some existing technology, the integration of these devices with communication systems is of a magnitude difference from the range of portable diagnostic and screening technologies currently available. Therefore legal and ethical issues that are already inherent in current screening and testing processes are likely to be of equal or even greater significance in the SmartHEALTH context.

Whilst there is optimism for the potential of Ubiquitous Computing (Weiser 1993) regulatory and advisory bodies are much less sanguine. Advances in the development of genetic testing, and the increasing reliance upon genetic epidemiology through ever larger bio-banks have revealed the need for caution and careful governance (Tutton and Corrigan 2004). Many of the legal and ethical issues acknowledged within the genomics field may also be relevant to the context of SmartHEALTH. Genetic factors associated

with breast and CRC are already recognized as raising particular concerns requiring policy and practice responses (Human Genetics Commission, 2000, 2002, Nuffield Council on Bioethics 2003). The potential for the use and misuse of genetic information, or indeed any health information is now well recognized. The wider social implications for the individual patient and their family members extend beyond the predictive potential of genetic information to matters of employability, and insurance and issues of autonomy and privacy. Drawing on the parallel to genomics suggests that similar precautions may be required in the clinical use of SmartHEALTH technologies (Sidarous and Lamothe 1995, Knoppers and Chadwick 2005).

In addressing these concerns, one must view the legal frameworks, and relevant case law currently in place relevant to screening and monitoring in order to subsequently identify potential legal and policy challenge areas for SmartHEALTH technologies. However there are also important issues relating to commercialisation and intellectual property which may affect the deployment of SmartHEALTH technology and these are addressed briefly here.

Commercialisation and intellectual property: Equity and access

Subsection 2.2 introduced the concept of a techno-divide between those countries, regions, and individuals who may and those who may not have access to new health technologies. SmartHEALTH technologies will be focused upon three of the major causes of cancer related morbidity and mortality and there is therefore a strong public interest in ensuring that access to such technologies is equitable and fair. There are a number of factors which may influence equity of access not the least are the opportunity costs within publicly funded health care systems which may simply not be able to afford such innovations.

There are a number of potential obstacles in the commercialisation of micro/nano-based health technologies including issues of intellectual property, problems of knowledge transfer from research to engineering and production, challenges of marketing new paradigm products, challenges of regulatory and insurance control, challenges of educating doctors and consumers on the advantages and uses of new healthcare products.

Perhaps the most complex barrier is that between patent law and healthcare policy. There is already a significant precedent in the form of Myriad Genetics position regarding the genetic tests for BRCA I and BRCA II. Myriad Genetics has U.S. and Canadian patent on the test kits for these genes and has attempted to enforce patent rights against publicly funded laboratories performing these tests. Although the European Patent Office has ignored Myriad's claims the case is indicative that public access to novel technologies is not guaranteed (Tilstone 2004). Moreover medical devices employing innovative micro/nanotechnologies combined with communication systems could be subject to multiple patents which may prove a barrier not only to clinical application but to future research. Commercialisation, intellectual property and patent law are complex and specialist areas and detailed discussion of their implications lies outside of the remit of this report.

Legal Issues: Consent and confidentiality

Consent

The common law principle of consent, a principle shared by most jurisdictions, is that for any lawful touching of a person to occur then the consent of the person is required. In the healthcare context, the consent of the patient is required before any lawful treatment can take place. A failure to obtain consent, in all but exceptional circumstances such as the necessity to act to save life, may result in the Tort of Battery – a civil wrong in which liability requires the payment of damages (Mason and Laurie 2006). In extreme cases the criminal law may also be engaged. Although there are few cases in which a patient has *successfully* sued a doctor for battery, the tort is still important. It represents a statement by the law as to the importance of the patient's right to self-determination. Further proof of this is the fact that the plaintiff need not have suffered harm so as to recover damages. Disputes in law have often revolved around the quality of the information provided by health professionals. Failure to counsel patients on the risks, side-effects and alternative therapies available is regarded by the courts as actionable in negligence (c.f. the English Law position in the following cases: *Chatterton v Gerson* [1981] 1 All ER 257 *Sidaway v Royal Bethlem Hospital* [1985] 1 All ER 643 (HL)). For a successful negligence action there must be foreseeable damage resulting from the negligent behaviour of the health professional. Whilst there is no agreed standard as to the level of disclosure required in the health context the US and Canadian jurisdictions have for example moved towards a high standard of disclosure and a concept of *informed* consent based upon the expectations of the "reasonable patient." The English Courts have only recently begun to move beyond the standard set by a reasonable body of *professional* opinion (*Bolam v Friern Hospital Management Committee* [1957] 2 All ER 118). It should be noted that many commentators have come to regard the legal requirement as a bare minimum and that professional practice should adhere to the higher ethical standard entailed by the principle of respect for autonomy which requires the most complete disclosure of information. This standard has been most actively incorporated into practice in the context of genetic testing in which counselling is regarded as a necessary part of the consent process (Sharpe 1997). Consent must also be voluntary and within the capacity of the consenting individual, nor must the patient be subject to inducement or undue pressure. Capacity issues are particularly relevant for example when engaging adults with mental health problems and learning difficulties in screening programmes (Biswas *et al* 2005, Werneke *et al* 2006). The principles contained in new European guidance on mental capacity such as that contained within EU Directive 2001/20/EC (Clinical Trials Directive), and specific legislation such as the Mental Capacity Act 2005 (England and Wales) must therefore be taken into account if screening programmes are to be inclusive.

The particularly challenging context of genetic testing is unlikely to be an appropriate model for all forms of health screening and monitoring since positive genetic test results are rarely accompanied by the prospect of either treatment or cure. However it is now well recognised that the standard of informed consent to participation in cancer screening often falls below either legal or ethical standards (Raffle 2000, Irwig *et al* 2006). Public health screening is widely regarded as anachronistically paternalistic and new guidance has begun to endorse a more autonomy sensitive approach (Strong *et al* 2005, UK National Screening Committee 2006). However questionable practice still persists such as in Australia and the UK where health professionals are given financial incentives to achieve screening targets and where many women may well be pressured into complying with cervical cancer screening (Irwig *et al* 2006).

Implications for the application of SmartHEALTH technologies are therefore clear. Not only must clinicians be able to explain the nature of the technology but they must also be required to explain the benefits and risks of the screening programme in which the technology is embedded. This has been a particular challenge in the context of cervical cancer screening where the nature of the result and its implications for health has proved difficult to explain. The legal challenge in *Penney, Palmer and Cannon v East Kent Health Authority*. (QBD (Canterbury): Judge Peppit QC, Feb. 15 1999 has led to serious concerns that screening may become unworkable (Smith 2000, Raffle 2000). The introduction of HPV testing may be no less controversial as described in section 2.2 where a higher level of pre-test counselling must be required in what is effectively testing for a sexually transmitted disease. Translation of SmartHEALTH technology from laboratory to clinic must therefore be cognisant of the legal and ethical context of these applications. Time and effort must go into an adequate consent process and it will therefore be essential to evaluate the impact of SmartHEALTH technologies on the clinical services where they are deployed. An important question will address whether doctors and other health professionals will be prepared to take on the pre and post-test counselling themselves particularly if rapid results are available.

Confidentiality

There is a general common law duty for a doctor and any health professional to respect the confidences of his patients which is part of a general recognition that personal information is open to abuse, can lead to personal harm and is open to commercial and other forms of exploitation. In the UK this has been established in quite specific case law such (*Stephens vs. Avery* [1988] Ch 449) but also in non-medical contexts such as the famous “Spy-Catcher” case which concerned the publication of the memoirs of a former secret agent (Court of Appeal in *A-G vs. Guardian Newspapers Ltd (No 2)* [1990] AC 109) which affirmed that there was a public interest in a legally enforceable protection of confidences. Many regard the application of the law in the medical context as a legal affirmation of the ancient recognition present in the Hippocratic Oath and reaffirmed in the Declaration of Geneva. Respect for confidentiality is also regarded as an inherent part of the right to respect for family and private life advocated within the European Convention for the Protection of Human Rights (1950) now incorporated into English law under the Human Rights Act 1998 (Article 8), in addition many other European jurisdictions have specific privacy laws which are also applicable here. Although respect for confidentiality and privacy are regarded as legally and morally important rights, they are nowhere regarded as absolute rights. There are several specific contexts in which there are legal requirements to disclose confidential information and some of these relate to the safety and interests of third parties. Genetic tests that have implications for other family members are one context in which the issue of disclosure to others has been raised. There is therefore the potential within SmartHEALTH applications that some of the cancer markers may in effect by proxy genetic tests and carry some of the implications that genetic testing has for family members. Whilst we regard this as a peripheral issue at the current stage of the project, it should nevertheless be noted and reconsidered as the project continues.

With the burgeoning of informatics and ever more efficient means of collating and handling data there is recognition of a new dimension to confidentiality namely that data protection and the European Directive 95/46/EC (*Protection of Individual with Regard to Processing Personal Data*) has been influential on the development of legislation within

individual member states. SmartHEALTH technologies will therefore engage with the issues of confidentiality and data protection at a number of levels, generic medical confidentiality in relation to personal medical information, information of specific import such as genetic information, processing and transfer of data, data collation and storage. As issues of data processing, transfer and storage fall within the remit of WP7, these issues will not be discussed further here. It is not anticipated that the clinical application of SmartHEALTH technologies to the three index cancers will raise any new issues of confidentiality. However this is not to say that issues of confidentiality and privacy should not be part of any further evaluation of the application of the technology. Adherence to guidance and regulation has proven lax in many instances within health contexts and therefore ensuring that the highest standards are maintained must be regarded as an essential ethical prerequisite of SmartHEALTH.

4. Conclusions and Future Work.

SmartHEALTH is a programme of work entering a field that is already sensitised to the ELSIs of biotechnology, both the potential benefits and the potential costs and risks. There is no doubt that SmartHEALTH has great potential to do good and to contribute to the amelioration of cancer and other serious diseases. It would be a mistake however to regard SmartHEALTH technology as operating within a technological vacuum. Therefore the recognition of the various contexts in which SmartHEALTH technologies will be applied, the processes and systems in which it will be located, and the variety of “users” from technicians and health professionals to patients and screening participants are all considered important aspects.

This report has located SmartHEALTH within the cancer care trajectory in order to explore some of the specific ELSIs with which SmartHEALTH is likely to engage. The cancer screening and diagnostic applications of SmartHEALTH will operate against an already established background of knowledge of the most salient social ethical and legal issues and the report has speculated where these are likely to be significant for SmartHEALTH. It will be apparent therefore that the most important ELSIs will be related to the implementation of SmartHEALTH technologies rather than the functionalities of these technologies themselves; although this too raises issues.

4.1 Issues related to the technology.

As SmartHEALTH moves toward the next phase of the project in which trial devices are developed, a number of issues will need to be clarified in order to evaluate the ELSI impact:

- The exact nature of these applications, in terms of screening, therapy monitoring, disease surveillance (re. WP 1 & 6)
- The sensitivity and specificity of the technology (biomarkers) (re. WP1)
- Quality control requirements for long term clinical use of these technologies
- Safety and efficacy of data handling aspects of the technologies – with particular reference to data security (re. WP7)
- Cost implications (re. WP8)
- Integration with/ conflict with existing health infra-structures e.g. existing screening/ disease monitoring programmes
- The PoC location of each application and if this PoC is new or existing within current health systems

4.2 Issues related to the implementation of the technology.

SmartHEALTH applications will both echo some of the established processes for screening and monitoring as well as introduce some novel aspects. This report has attempted to address the ELSI implications of both aspects by drawing on established knowledge and research to identify the known risks and concerns and to identify potential new ones. All of the issues fall more or less under the general rubric of information and communication with different implications for the various “users” within the processes of applying SmartHEALTH technologies. The following bullet points summarise the main categories:

- Personnel - who deals with the patient/participant and in what way?
- Quality of information provided – to the patient/participant user
- Counselling provided to the patient/participant user before moving through the process
- Quality of informed consent/ informed uptake
- Implications of the speed of process – from testing to results
- Managing results - quality of information and communication when disclosing results
- PoC location of each SmartHEALTH application

There are also a number of specific points relevant to the three index cancers as described below.

4.2.1 Cervical cancer screening

The application of SmartHEALTH to the context of cervical cancer screening should be on the basis of informed uptake by the participant. Factors to consider in this context include:

1. Timing and nature of the results which may be available within minutes or hours of testing
2. Disclosure of the participant’s HPV status

The complications of a potential diagnosis of a cancer or pre-cancerous condition, and in addition the diagnosis of a sexually transmitted disease may be exacerbated by the social context in which this takes place.

- The application of SmartHEALTH technologies must therefore take into account the feasibility of this being conducted effectively within the primary care setting of a family practice/GP
- Regardless of setting, the routine screening for HPV status will require the careful training of personnel to provide quality information, counselling and support to women undergoing screening
- A process for the audit and evaluation of these services should also be in place
- The wider public health context in terms of public engagement/education and organisation of screening programmes must also be considered (see WP14)

4.2.2 Breast and colorectal cancer monitoring

The most likely application of SmartHEALTH to breast cancer and CRC is in the context of post-treatment-monitoring or “follow-up”. The historical approach to this has taken the form of regular visits to a specialist doctor and included a variety of forms of “surveillance” with a wide range of efficacy at detecting disease recurrence. However, this method has been subject to serious evidence-based criticism with many authors doubting its efficacy. These findings throw into question whether routine follow-up achieves either the public or personal benefits claimed for the patient. This body of evidence is something which must be taken into consideration by the SmartHEALTH applications to CRC and breast cancer.

Nevertheless, should SmartHEALTH provide a simple and accurate test capable of monitoring both disease response during treatment, and disease recurrence following treatment, then this may radically change the context. The flexibility and portability of SmartHEALTH technology gives a potential for use in contexts other than specialist settings although the evidence suggests that wherever the technology is deployed then this must be in conjunction with adequate attention to the information and psycho-social needs of patients. Therefore performance of all aspects of PoC testing must be subject to adequate evaluation in the settings in which they are used. In summary:

- Introducing technology with new capabilities will have an impact on the service in which the technology is utilised. For example, tests with improved sensitivity and specificity may reduce invasive diagnostic surgery, such as a colonoscopy
- The diagnosis of recurrent disease is an important transition point on the cancer care trajectory as the patient may move from a curable to an incurable cancer
- The training of personnel, the provision of appropriate information and the time and skill required to convey significant news to patients in an effective and supportive manner will be important aspects

4.2.3 Patient self-monitoring

The possibility of patient self-monitoring for breast cancer recurrence is the most innovative application of SmartHEALTH technology and is likely to constitute the most intensive form of surveillance. The possibility may have a strong appeal to certain cohorts of women but this is something which should be adequately explored in advance. This is likely to form part of future work within WP9, as there is a lack of research evidence on which to estimate the clinical or the psycho-social impact of intensive surveillance.

Finally, the early detection of disease recurrence may have a major impact on long-term survival with breast cancer and CRC although this will be contingent upon the availability of further options for treatment. The most serious implications are likely to be upon the provision and service adjustments required to accommodate this new technology. The availability of, and access to, the technology for these patient populations will be significant since there is the serious possibility that a “techno-divide” within and between nations could exacerbate health inequalities and thus prove divisive in terms of equitable access to health resources.

5. Further Research Questions for WP9 Fieldwork.

This report has addressed the first phase of Task 9.2 and in doing so has raised a number of further research questions to be addressed in the fieldwork.

5.1 *Some potential research questions under three themes.*

These are presented under the following three themes in relation to the SmartHEALTH applications (both medical and technological contexts).

5.1.1 **Current European cancer screening programmes and breast and CRC follow up services**

Currently, SmartHEALTH is focusing on the secondary prevention (screening) of cervical cancer and the monitoring and follow up of breast and CRC cancer. SmartHEALTH is introducing new biomarkers for screening and follow-up that aim to be more accurate and produce quicker results. The technology also aims to improve access by health professionals to patient health records to support the diagnostic process.

Possible WP9 research questions:

- How will this new technology fit into the existing healthcare services, in terms of more accurate tests, improved access to healthcare information for health professionals?
- Will a quicker test result produce a quicker diagnosis?
- Will SmartHEALTH impact on the current lack of willingness for participants to attend cervical cancer screening programmes?

5.1.2 **Cancer trajectory services: current types and stages of cancer care services**

Currently SmartHEALTH aims to fit into the screening phase, diagnostic phase and the follow-up phase.

Possible WP9 research questions:

- Will improving the cancer screening stages and follow up stages impact on the other care services within the wider continuum?

5.1.3 **Point of care technology**

Each SmartHEALTH application has different points of care location and some PoC locations will be new to the current healthcare service.

Possible WP9 research questions:

- Is the location for the tests new or existing within current practice?
- How much knowledge and skill does the person using the machine require?

5.2 Implications for further fieldwork design/ protocol

SmartHEALTH impacts on a number of individuals from the patient/participant to the clinicians within the cervical cancer screening and breast cancer follow-up processes. In order to understand the ELSIs within the different context, there is a need to explore different users' perceptions of SmartHEALTH. However, SmartHEALTH is a complex set of converging technologies and there is a prior need to discuss these technologies further with each partner to ascertain what basic infrastructure SmartHEALTH requires in terms of time and resources. This information is particularly important for medical staff who may wish to compare this new technology within current practices and existing technologies.

Next steps for WP9

D9.3: A report on views of stakeholders in partner countries (interviews/surveys) on issues associated with possible use/implementation of bioanalytical microsystems for medical diagnostics.

- Interviews will be held with different SmartHEALTH partners to discuss and clarify the functionality of the SmartHEALTH technologies. Partners are experts in their fields and therefore important stakeholders within this project.
- These in-depth interviews will provide important baseline information on how to represent SmartHEALTH technology to the different stakeholders during the two case studies (see D9.6 below).
- This fieldwork will enable WP9 to further explore the wider ELSI issues as well as addressing the specific ethical issues to be faced in the clinical trials of SmartHEALTH technologies.

D9.6: Report on case study findings of main ELSIs arising from SmartHEALTH

Two case studies will be carried out in two European countries (one in the UK and the second in another European country, possibly Norway or the Netherlands). Based on the information gathered during interviews with partners (D9.3), different key users of the SmartHEALTH technologies will be invited to discuss their perceptions of the SmartHEALTH technologies and predict how these technologies will impact upon their current work practices or/and their everyday lives. These case studies will include the following three components:

- Ongoing public dialogues during the development of the SmartHEALTH technologies
- Different users, from the patient to the clinician, will be invited to discuss the SmartHEALTH technologies within suitable SmartHEALTH applications
- A specific focus on exploring how SmartHEALTH technologies could impact on the current debates around breast cancer follow-up services.

Note: it is expected that the different users will re-interpret the potential benefits and challenges of SmartHEALTH technology, as outlined in this report or presented by SmartHEALTH partners (D9.3), in line with their own work practices and lives. These different interpretations and meanings of SmartHEALTH technologies will be an important part of the WP9 research findings.

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