Ethical Assessment and Reflection in Research and Development of Non-Conformité Européene Marked Medical Devices

Telléus, Patrik K.; Jensen, Winnie

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Ethical assessment and reflection in research and development of non-CE marked medical devices

Patrik Kjærsdam Telléus, Ph.D. (corresponding author)

Associate Professor

Department of Health Science and Technology, Aalborg University

Email: pkt@hst.aau.dk

Phone: +45 99409968

Address:

Frederik Bajers Vej 7D

9220 Aalborg East, Denmark

Winnie Jensen, Ph.D.

Professor

Department of Health Science and Technology, Aalborg University

Email: wj@hst.aau.dk

Phone: +45 99409825

Address:

Frederik Bajers Vej 7D

9220 Aalborg East, Denmark

Short title (running head): Ethics and medical devices research

Contribute section

Patrik Kjærsdam Telléus, Ph.D.

Associate professor in Applied Ethics

Center for Health Science Education and Problem-based Learning

Department of Health Science and Technology, Aalborg University

Research areas: Clinical Ethics, Bioethics, Higher Education, Theory of Science and Methodology

Winnie Jensen, Ph.D.

Professor in Neuro-Engineering

Center for Sensory-Motor Interaction, Neural Engineering and Neurophysiology

Department of Health Science and Technology, Aalborg University

Research areas: Neural Engineering, Somatosensory modulation, Pain, Research organisations

INTRODUCTION

Today, there are multiple well-known examples of implantable medical devices on the market, including the cochlear implant, the cardiac pacemaker and the deep brain stimulator. For example, for the cochlear implant, a microprobe placed in the auditory nerve is used to transfer sound to electrical stimuli to restore hearing. The type of medical device implants that interface the body's neural tissue with recording or stimulating electrodes (also referred to as microprobes) with the purpose to regain or restore control of lost or impaired functions is relatively new. They have been considered to have particular strong ethical implications[1]. Although the aim of the technology is to restore and rehabilitate, there is a real risk of derive, i.e. new computer technologies possess the possibility to be used for enhancement purposes.

From an ethical point of view, special attention has been given on a particular sub-group of medical devices, i.e. those who are ***ICT based*** (i.e. ''devices using information and communication technologies usually based on silicon chip technology''), ***active*** (i.e. ''relying for it's functioning on an internal and independent source of electrical energy or any source of power other than directly generated by the human body or gravity procedure'') and ***online*** (i.e. ''ICT implants that rely on their operation on a connection to an external computer or which can be interrogated by an external computer'')[2].

Within the EU funded project ''EPIONE'' the objective was to develop and compare the efficiency of novel implantable or non-invasive technological solutions as a therapy for phantom limb pain. In this project, peripheral nerve electrodes were implanted in the severed nerves in the stump of the amputee to transfer electrical stimuli to restore / create natural, meaningful somatic sensations. The implantable interface system suggested by the EPIONE project for treatment of phantom limb pain falls into these three categories of being *ICT based, active* and *online*.

Novel medical devices are often driven by academia through private or public funded research and development projects over many years, before private companies take over the commercialization of the medical products. In academia, the key driving factors for the researchers are not only to find a device that can offer a cure, but also seeking new and novel inventions that often are required by funding organizations. As such, working within this field implicates that you as a researcher very often are choosing unknown paths where the techniques and technologies are in a phase where they are not yet legally approved, or perhaps not accepted by the general society. However, development of novel implanted devices is also associated with high risks-high gains for other involved stakeholders. In particular, risks are taken by the 'first-in-human' patients, i.e. when the technology must be transferred from bench-top or in-vivo animal tests to human clinical trials in order to obtain a CE-mark, but the patients may be the firsts to benefit from a possible promising treatment. Finally development of new medical devices EU and national laws has to be respected, including the EU medical device directive (the 90/385/EEC for active implantable devices) national/local ethical committees and competent authorities. These rules and regulations are primarily defined to secure that the devices are safe for the patients.

As researchers we may therefore be ''caught'' between a wish to develop new devices with a real capability of helping people with disabilities, a need to respect the law, the patient's hope of an available and effective treatment in the near – and a general fascination of the technology and its potentials often driven by the public press. As such, the challenge that we faced within the EPIONE project was that the required ethical assessment, to tackle, e.g., problems such as the Collingridge dilemma[3] or the burden of responsibility[4,5] in this particular setting, needed to incorporate both ethical consultation as an advisory role, as well as a regulatory role, into a moral commitment within the researchers[6].

Studies in the field of biomedicine show that it is important that ethical awareness and reflection are extended beyond the decision on a particular cause of action to allow the decision makers to express and evaluate the moral reasoning that enables, warrants and affirms the decision they are faced with[7,8]. Further, studies also indicate that the quality and competence of such reasoning is enhanced when the participants can combine their ordinary or popular moral views and attitudes with concepts and positions from ethical theories or normative ethics[9,10].

Therefore, we hypothesized that selected activities could be the instrument needed to promote the researcher's engagement and facilitate a framework for ethical reflection on their own research from regulatory, legal and scientific perspectives.

In this article we, representing both a researcher and an ethicist, look closer at the EU funded EPIONE project as an actual research case. An Independent Ethical Advisor (IEA) with a regulatory and advisory role was assigned to the project. We utilized the IEA as a means to facilitate and support the participating EPIONE researchers in the process navigating within the ethical field of medical devices. We suggest a novel framework based on action research where we draw in elements and theory related to the interdisciplinary learning environment for building ethical assessment and reflection, and the theoretical reasons warranting them.

1. METHODS

Introduction to the case – the EPIONE research project

The research project in the present case was the 'Natural sensory feedback for phantom limb modulation and therapy' referred to by the acronym EPIONE (project N° 602547, FP7-Health-2013-Innovation programme). This project was coordinated from Aalborg University, Denmark and included 12 partners (Denmark, Sweden, France, Germany, Spain, Italy and USA). The objective of the project was to develop and compare the efficiency of novel, dedicated technological solutions to actively create natural, meaningful sensations as a therapy for phantom limb pain. Phantom limb pain (PLP) is a frequent consequence of amputation, spinal cord injury or peripheral nerve damage. PLP is notoriously difficult to treat, likely because the understanding of the underlying pathophysiological mechanisms responsible for PLP is poor. In 50-80% of amputees, neuropathic pain develops in the lost limb, which is also referred to as phantom limb pain (PLP)[11]. Recent evidence suggests, that PLP may be related to plastic changes of the neurons in the brain. In EPIONE we aimed to build novel and innovative technological pre-industrial systems for delivering invasive/non-invasive sensory feedback to compare an invasive and a non-invasive route for delivering sensory feedback to offer more long-term or permanent therapies for amputees suffering from phantom limb pain[12].

- Route 1: Direct peripheral nerve sensory feedback. Multiple transverse, intrafascicular electrodes (TIME-4H) were implanted in the median and/or ulnar nerves of volunteer amputee subjects. Electrical stimulation was delivered through the active sites by the multi-channel, miniaturized electrical stimulator placed outside of the body. The TIME-4H electrodes were surgically removed after completion of the study. To deliver the electrical stimulation sequences and to obtain quantitative and qualitative measures on the effect of the microstimulation, a semi-automatic and computerized platform was used[13].

- Route 2: Non-invasive sensory feedback. Either mechanical sensory feedback (i.e., air pressure) through silicone pads, or electrical stimulation was applied through off-the-shelf electrodes. We used a computerized psychophysical testing platform to deliver stimuli and obtain the patient's response, and we statistically analysed the results[14].

One volunteer participated in receiving 'direct' peripheral sensory feedback[15], and 8 volunteer subjects participated in the non-invasive trials.

The IEA

All funded EU projects within the HEALTH programme under the 7th framework program that included human volunteer subject in clinical trials was legally required to appoint an Independent Ethical Advisor (IEA). The overall obligation for the IEA was to ensure that the work within the project was conducted in accordance with relevant guidelines and legislation (i.e. a regulatory function), and that during the project ethical awareness and reflection was carried out as a committed and integrated part of the project (i.e. an advisory function)[16]. That meant that the IEA supervised: 1) that the research followed the ethical EU-guidelines on medical research, as well as the general principals of bio-ethics, and 2) that there was substantial ethical consideration within the project consortium, including application of a precautionary principle and informed consent, and significant ethical analysis and reflections.

Action research approach

In the field of methodology there is a branch broadly called action research. From its early departure in the work and writing of Kurt Lewin, the methodology as well as the methods it carries has evolved in numerus fashions. However, there is a strong emphasis on action research investigating, and perhaps more importantly, initiating and supporting the reflective development of practice[17]. Some

more philosophically oriented thinkers in the field, like Olav Eikeland, has drawn distinctive parallels and comprehensions between actions research and the concept of *phronesis* (ethical reasoning) in Aristotle[18], supporting the idea of action research being both an investigator and a developer of an ethical rationality in practice. Adding to this is the action research approach of Greenwood and Levin[19] that emphasises the participatory and collaborative approach to both the goals and the means of action research initiatives.

As we implemented the approach of action research we focused on a variety of initiatives and actions, and made sure to give them the consecutive structure that should provide an adequate time for elaborative development of awareness and attitude, as well as the saturation of qualitative justification of actions and processes of change. These are: 1) the use of informed consent; 2) a survey amongst the research partners; 3) a workshop session; 4) observation of consortium meetings; and 5) an interview with a participating patient.

The initiatives were within the action research framework, a way for us to express and facilitate "multilevels of ethics". By multilevels of ethics we mean that ethics have several layers or levels ranging from awareness to reflection, including related but also diverse elements such as regulation, assessment and deliberation, as well as elements ranging from more concrete to more abstract levels. From this perspective ethics is viewed as an integrated part of moral life[20,21], rather than as an argumentative or discursive practice. It is also allowing ethics to have a developmental character in a way related to similar level- or stages- learning theories like the SOLO taxonomy[22]. This opened for an interpretation of the action research framework that included a perspective of learning and learning theories.

The useful link between the action research approach to ethics in EPIONE and the idea of a learning development we found was in the construction of an interdisciplinary learning environment. From the literature on interdisciplinarity, we draw out three important characteristics. First, it is a synthesis or merger of different disciplines; second, it is embedded in and integrated with a non-academic reality; and third, it is problem-oriented[23–25]. To grasp the ethical perspective as an interdisciplinary activity punctuates that it is a way of thinking that on the one hand requires capabilities like those of disciplines, such as analysis, theories and objectivism, but on the other hand is not a discipline in itself but should be merged with the scientific discipline of one's own.

To motivate such an approach, we need the other two characteristics. To acknowledge the embeddedness of a scientific project is to understand and adhere to motifs, intensions, interests and demands from others, which forces us to comprehend the scientific project on a larger scale, as an integrated part of the world, and not as something isolated and contained. Frodeman summarizes all these elements into one concept, that of audience, making a distinction between the scientific activities that is preforming for themselves, i.e., purely academic pursuits and evaluations, and the scientific activities that are more applied and are preforming for an audience outside of academia[25].

Here is where the problem orientation becomes relevant. The claim is that the problems of the world are not equivalent to fitting neatly into the disciplinary categories of the departments and faculties of science; being problem-oriented means to not just see a disciplinary defined object of study. This way, although ethics is external to the disciplinary point of view, ethics is incorporated into the motivation and execution of the scientific project as a natural aspect of a problem orientation.[26]

The approach also allows us to be focused on creating spaces for active involvement, using group dynamics to generate a collaborative deliberation that forces the moral considerations to move in between the familiar (the practical and theoretical reality of the scientific project) and the unfamiliar

(the ethical perspective of others and the normative theories of moral philosophy) and to emerge as solid reasoning instead of merely personal or commonly held opinions.[27,28]

2. RESULTS

Informed Consent

EPIONE is a research project that included human volunteer subjects. Therefore, EPIONE is required to enrol patients as participants for their research experiments, trials and observations. Recruiting human subjects for such use can only be admissible if the acceptance of enrolment is undertaken by the procedure of informed consent. In short, this means that the project partners in EPIONE all must inform the patients of the project and ensure their consent, before using them for research purposes. The IEA collected documentation of informed consent that the different partners had drawn up and had received approval by their local authorities. The documentation concerned the research trials carried out in Sweden, Denmark, United States of America, Italy and Switzerland.

The IEA analysis of all the informed consent documents showed that they all adhered to a general set of requirements for ethical assessment[29] as follows:

- The information about the research project and participation in the research was presented in a clear and objective manner, avoiding persuasive and manipulative language
- The information about the research project and participation in the research was presented in such a way that a non-health care professional could, without any special knowledge or specific ability, comprehend the text and interpret the consequences and conditions for participation.
- The information about the research project and participation in the research included the following:
    - Details about the process
    - An assessment of the potential risks
    - Explicit explanations of benefits and financial compensations

- Procedures for confidentiality
- Description of the possibility for termination of participation on the research subject's own initiative.

- It was made perfectly clear that participation in the research project was voluntary and that withdrawal of participation had no negative effects on current treatment or access to future treatment opportunities.

The analysis also showed that the informed consent documents differed in length and structure between partners and countries. Some were more formal (strict and bureaucratic language), whereas others were more informal (inviting or personal language). Some included quite detailed scientific information about the research, while others had less emphasis on the science behind the research project. The documents from Sweden differed from the other ones on one important point. The Swedish researchers collected an informed consent for each individual procedure or separate trial, while the other institutions used only one informed consent form, where the different elements of the research, trials, interviews and observations were made clear as part of the information package.

These differences indicated diversity in customs and traditions between countries, and we can call them cultural, but as such they are also moral, and therefore merit an ethical reflection. It was clear that some informed consent forms were constructed in a more paternalistic setting, with the researchers in a clear authoritarian position. Others approached patients in, what we today might refer to, a nudging fashion, and asked the potential participant to engage having the positive outcomes in mind. Some took this a step further, and were examples of the commodification of health care with an almost seller-buyer communication strategy.

These differences definitely showed a shift in the researcher – patient relationship, and also in the value structure between participants, products and means of this kind of project. These cultural differences were also revealed through the working process of the EPIONE consortium; and were an

indication of international collaborations need for understanding that general principals and abstract concepts cannot escape a more culturally flavoured comprehension. To avoid misunderstandings and potential harmful or unfruitful situations these differences called for further deliberative articulation of moral values and assumptions amongst participations across the inter-cultural landscape, even when there seemed to be consensus on the core principals and ethical regulations.

One other thing that raised concern regarding the information package presented to the volunteer subjects were that they all directly emphasized the benefits of the research, both for the participating individual and the overall outcome, The benefits were presented in a such a way that made them appear to be quite reachable, which may have indirectly persuaded patients despartely seeking for a treatment while being susceptible to ignore the risk assessments.

In general, the practice of applying the informed consent in EPIONE followed the established norms and regulations. The documentation showed that moral themes like autonomy, precautionary principle, and humanity were appreciated, as well as the four guiding principles from principlism. The researchers appeared to be thoughtful, open and respectful in their approach to and relationship with the participating research subjects. However, the heavy emphasis on benefits may be viewed as rhetorical persuasion, and the culturally bound differences ought to be an area of further discussion and concern.

Survey

A survey was conducted among the research partners in EPIONE. The purpose of the survey was to establish a common ground for the ethical aspects regarding the research and research process within the project and the researchers' initial reflections and attitudes towards these perspectives. The survey consisted of eight questions in total, to which the respondent answered by ranking a list of possible answers or by choosing one answer amongst others. Each question also included the possibility to

comment or to elaborate. The survey also asked for some biographical information. The survey was distributed by a link. The data from the survey were stored and analysed in accordance with the codes of conduct and legislation for confidentiality, agreed upon between Aalborg University and Datatilsynet (Danish governmental agency overseeing the treatment of research data).

The survey was distributed to 25 participants, with 14 responding in full and 2 giving a partial response, resulting in a total of 64% response. Nine institutions were represented. There was an even distribution in terms of age groups, and there was an 86% male 14% female ratio. The demographic information also showed that 86% had attended an academic seminar, course or workshop in bioethics and that 2 of the people who answered the survey had written or presented papers with an emphasis on ethical content.

In the questions, the responders were confronted with evaluating principles, motivations, oversight and moral practices regarding their work and participation in EPIONE. They were also asked to rank the importance of different forms of moral phenomena to establish their basic approach to initiate moral reflection and ethical awareness.

The questions were directly or indirectly connected to both principlism- and character-based ethics, but none went into any explicit ethical theory or demanded knowledge of normative ethics. All four themes from the initial considerations were represented in the questions.

The main outcomes of the survey were;

- Autonomy was regarded as the most important principle, and justice was the least important one.
- The patient perspective appeared to be a key source of motivation among researchers.
- Declarations of rights and religious parables were regarded as better examples of moral excellence than real life cases or fictional stories.

- Cost benefit analysis was considered an important part of ethical reflection regarding EPIONE.
- There was a slight difference in how the responders ranked ideas on ordinary morality and the way they ranked the same ideas regarding EPIONE. The latter set of ranking values viewed practical accountability higher than the former set.
- The oversight and ethical assessment of EPIONE was satisfactory, but there were also frustrations and doubts about parts of the processes (especially the work of certain committees).
- Everyone believed that EPIONE has 'major' or 'minor, but important' ethical implications. The comments also suggested that some do take an active interest in ethical issues.

The cohort of the survey was too small to make any reliable statistical analysis, and therefore it cannot provide any valid claims. However, the answers can still offer dependable information on the small scale of the EPIONE case. As such, it could serve its purpose of facilitating the basis for further ethical deliberation amongst the participants.

Workshop

The IEA facilitated a workshop on ethics for the partners in EPIONE. The participants in the workshop were the same people and represented partners as had attended the lecture on ethics the day before. The workshop lasted for 90 minutes.

The workshop was initiated and managed by the IEA and executed as a round table discussion between all of the participants. Everyone was active, and approximately half of the participants, representing eight different partners, spoke on more than one occasion. In the beginning of the session, the IEA spoke some but became quieter as the session went on. This silence was performed on purpose to stage the session as a peer-learning activity.

To set the stage, the IEA provided the participants with a brief brush up on some normative positions and the bioethical principals, both the American and the European ones, and some principals for scientific research. The IEA also illustrated the set of question frameworks discussed earlier and applied it to the practice of informed consent. The participants were asked to reflect and elaborate on the themes of autonomy, commercialization, precaution and humanity by using the set of questions and a problem-oriented approach.

Several issues were discussed in the workshop. Very few led to open debate; one of these was on the issue of using healthy subjects for research experiments. The general impression was that each issue was addressed by offering the participants a) principal statements on the issue; b) experiences of the issue or similar kinds; and/or c) deliberations on the issue that included the use of normative theories and justifications and reasons for values and principals.

Some of the main points from the workshop session were:

- Benefits are important! We do what we do to help patients and reduce suffering. First are the medical benefits, but benefits for society or humanity at large are also part of the equation.
- Patients are vulnerable and have needs we try to meet. The patents are also brave and most generous as they volunteer for the needs for research purposes.
- Principals are good but also theoretical and abstract. The task of conceptualizing them into actions and attitudes is difficult and comes with experience. For example, applying a principle of justice means being impartial and being aware of inclusion and accessibility for patients, and applying a precautionary principle means always looking for alternatives that lower the risks and negative side effects.
- Transhumanism is mostly science fiction, but it is important for the public to understand that normality is a flexible and changeable concept. What we do might push the boundaries of

normality, but that in itself is not unnatural, but on the contrary most natural for societies to do.

- When speaking with the media, we would like to have arguments. We get caught or trapped in the ethics and it would be very nice to have the ability to reply with a well-structured bottom line claim.
- Ethical committees are here to stay and should ensure that both the public perspective and the patient's perspective are represented and respected.
- Our kind of research is embedded in the medical technical industry. It is a part of that industry, that is just the way it is, and if it was not, we probably could not do what we do.
- Technical trails that do not lead to finished products are difficult to handle when recruiting and evaluating patient participation. Here, most thought that to be explicit about it and allow for voluntary participation is the way to go. However, others were not convinced.

The IEA and the EPIONE management evaluated the workshop as successful. Many relevant issues were addressed, and most participants demonstrated well-informed and skilled reasoning on the matters. Some participants were less interested, and some comments were slightly hostile and dismissive of the ethical perspective. However, that is also part of the collective and shared deliberation that the workshop represents and facilitates. It was clear that many took the opportunity to talk about ethical issues, not to debate or solve them, but mostly to formulate and ventilate ideas and experiences. In this sense, the session worked as a form of peer-learning exchange.

The ethical perspective remains, by most, to be in the form of an add-on and not a naturally integrated part. The comments were often clearly divided between a theoretical, academic formulation and a regular practical comment. The former being regarded as correct medical ethics, and the latter as just natural, not truly having anything to do with medical ethics, partially because the interdisciplinary perspective and the 'in-between' are difficult to articulate and comprehend. Bridging the formal

ethical articulation of principals, regulations and patient perspectives, and the informal practices and subjective or common moral opinions is probably too ambitious of a task for a 90-minute session. However, it was also clear that some participants began to ponder the idea of this approach to the ethical perspective.

Observation

As part of the regulatory role, the IEA observed the sessions on Exploitation and Dissemination during the EPIONE partner meeting in Montpellier on the 29th-30th of November 2016. In the sessions, the medical tech company Novosense and all partners participated. The purpose of the observation was for the IEA to investigate how moral issues appear and how they are dealt with when they are not explicitly addressed as ethical issues. This could be issues of unintended consequences, following procedures, communication failures or misunderstandings, cooperation and coordination of joint ventures, and respecting patients (also when they are not present).

The observation revealed that the partners were aware of and addressed the following interesting issues:

1. Reporting all results, and not withholding results from one another.
2. Agreeing on publication strategies.
3. Coordinating and acknowledging the use of each other's data.
4. Respecting deadlines.
5. All partners committing to the project.
6. Harmonizing data collection.
7. The use of data according to the agreed upon method, and the improper collection of data.
8. Seeking ethical approval when changes to surveys are made.
9. Sharing knowledge on laws and regulations for medical devices.

10. Overcoming practical problems, such as accidentally deleted files in Dropbox.

All these issues include ethical considerations that constitute the guiding principles and values of the research project. These include a) respecting collaborative decisions; b) following and knowing the laws and regulations that apply; c) taking responsibility; d) trusting each other; e) acting for the benefit of all; and e) open and honest participation. The observation showed that these issues were actual issues in EPIONE and that the partners were addressing them and dealing with them to the best of their abilities.

The observation also revealed that language is an unresolved and unattended obstacle for projects such as EPIONE. Everyone is not equally comfortable in speaking English. It is commonly assumed that scientists are competent English speakers, but that is not necessarily the case. We should recognize this fact, not ignore it, and be open about our linguistic abilities, and not pretend as if everyone fully understands and can expresses themselves in English. Even if one can, one can be uncomfortable or just out of practice in doing so. This is a problem of communication, but it certainly has moral consequences (misunderstandings, inequities, distrust, etc.) for interpersonal relationships such as in research collaborations.

Interview

To include the patient perspective, the IEA conducted an interview with one of the participating patients in EPIONE. The interview was set up with a volunteer subject at Aalborg University. The patient, when asked, voluntarily accepted the interview. The patient was in the final phase of his participation. All other information about the patient will not be revealed, since it does not have any impact on the purpose of the interview. The patient shall remain anonymous.

The interview was prepared as a semi-structured interview, ensuring that the IEA was able to get around to the issues of interest but at the same time allowing the patient to speak freely. The interview

lasted approximately 30 minutes, and present during the interview were the IEA (interviewer), the patient (interviewee), and associate professor Lontis and a research assistant (both silent during the interview).

During the interview, five different themes were covered. These were a) reasons for participation; b) the conduct and conditions during trials; c) the benefits of participation; d) medical priorities; and e) transhumanism. These themes were meant to cover both the personal story and the more general issues, as well as to evaluate the recruiting process.

The patient had the following comments, concerns and reasons:

1. He wanted to participate, as soon as he heard about it an he felt that he needed to participate.
2. He had knowledge of previous similar research and knew some of the researchers beforehand
3. His main motivation for participation was to obtain a better life.
4. He believed that he received all relevant information and he received the necessary help to understand them.
5. He stated that he was very well taken care of.
6. He trusted the researchers and experienced "good chemistry" with them.
7. He was happy with the outcomes of the research project
8. He experienced less pain and no major side effects.
9. He felt that he had, during the process, come to learn and understand his pain better, which also helped him deal with his daily life.
10. He supported this kind of research and development of novel medical treatmenst, since he believed that ''we cannot afford not to do it''.

11. He believed that if Aalborg University did not do the research, someone else would have carried it out and the he would lose out.
12. For the price of this treatment, many other patients with other deceases or difficulties could have benefitted. But he did not approve of that argument, since the resources are not taken from one medical pursuit and given to another. He claimed that it is not the same resources.
13. He did not think of himself as a transhuman or something comparable to that.
14. He believed that ''technology is simply a tool that we use to achieve good things''.
15. In this case the researcher just imitates what the natural body already does. In that sense, although it is technology, it is simply natural.

It is fascinating that the issue of transhumanism versus natural humanity was not a concern at all. With that in mind, and adding the same thoughts on the issue that the researchers addressed, it seemed that this issue of transhumanism was more a theoretical or popular media concern than it was an actual part of comprehension of the research and the possible treatment.

The effect of ''getting to know one's pain'' and ''better handling it'' indicates that the EPIONE project managed to go beyond just about making a product that functions and also touched upon something that interacted with the patient's life. It is important for researchers to respect and acknowledge these facts, both when it has positive consequences but also in cases where the consequences are negative.

Obviously, this patient was very pleased with the process. Taking the success of the device and the medical benefits aside, other things also mattered in building and maintain a good relationship is an apparent factor in success. The trust and good chemistry arose from 1) taking the time with the patient, showing respect and acknowledgement, 2) understanding that the work was *with* the patient, not *on* the patient, 3) recognizing that the researchers and the patient both used each other, but not letting that use become the dominating feature of the collaboration. In this case,

In relation to financical issues, medical priorities and research possibilities, the patient was less convincing. Obviously, he was happy about the opportunity to be part of the project and enjoyed the benefits, but it is hardly a qualified utilitarian argument. There is certainly something right about the resources not being comparable. It is not one bag of money. However, from a public or more neutral point of view, the research and possible treatment was not motivated by immediate benefits, but, apart from the epistemic motivations, from a hope of a possible treatment becoming available in the future. However, like among the researchers themselves, there is a slight reluctance for discussing or questioning this issue of resources, of a finical cost-benefit analysis if you will. The costs is accepted as the way it is, and that is that.

3. DISCUSSION

Methodological considerations

It was clear that the task of ethics in EPIONE had several different aspects to consider. There were some regulations that needed to be followed and some assessment that needed to be evaluated. There were also demands for awareness and a more deliberative approach, as well as perhaps an internal need for reflection. The IEA – the ethicist – had parts to play in this, but in many ways EPIONE – the researchers – were the important and active participants. The choice of an action research framework for the ethical activities enabled us to engage on these fronts and with these players, as a mean to create an environment for the ethics similar to an interdisciplinary learning progression.

We did see the ethics of EPIONE being integrated into the science of EPIONE, through collective activities as well as through a thicker and thicker involvement, mirroring both a progression along a line from awareness to reflection, as well as a deliberative interplay between the abstract / theoretical and the more hands-on practises and experiences. The activities were creating a unity and a linier development to some extent, drawing on the learning process and outcome from each other, but this could have been better emphasized and also more fruitfully explored.

The IEA dual role as both regulatory and advisory became increasingly apparent during the course of the project. These two roles are not always compatible, but to be aware of them and the difference between them are important if the ethicist should have an integrated part to play in scientific research. The regulatory role is important because it enables 'the other', those not represented in the research or by the research, to have a voice and a say in the development, the means and the ends, of the research. This in turn is important to connect scientific activities and values with them of the society and to acknowledge the joint venture that progress and welfare captures. This is even more important

in the case of EPIONE, were the society is not represented by a single nation or a homogenetic culture, but by an international community and a heterogenetic culture. In such cases the expressed and evaluated regulation is important both as rules to follow and respect, and as rules allowing for some leniency and range of interpretation.

The advisory role is important because this is where the integration takes place between the ethical and the scientific research. Whether it is in the form of a provider of theories and interpreter of concepts, or as a partner in a dialectic exchange, or as guidance in an explorative pursuit, the advisory role is one which both makes the ethics familiar and that empowers the more abstract needs and unfamiliar considerations. In this way the advisory role really becomes the tool of the interdisciplinary approach, in practise often as the problem initiator.

Ethical reflections on the conducted research

A research project like EPIONE is obviously almost constantly under some form of ethical scrutiny and assessment. These forms of evaluations and considerations target the interface between politics, society and science, and try to ensure the development of a sustainable future in which science and technology contribute with desirable consequences in a responsible fashion[30]. This is one way of comprehending the ethical perspective in and on EPIONE. However – the researcher – also enlighten us on another perspective, that of the researcher him/herself. Our action research framework, with the interdisciplinary learning qualification, also tried to address this issue; i.e. the issue of facilitating an ethical progress within and amongst the EPIONE itself, to somehow integrate moral philosophy / ethics into the scientific project of EPIONE.

Moral philosophy is the philosophical, reflective study of certain values that concern human beings"[31], claims Bernard Williams in an introduction to ethics. He continues: "A sense of ethical

values informs people's lives, directly in deciding what to do, and in their comments and judgements on people and actions, including their own. People try, in varying degrees, to shape their lives by reference to such values"[31]. Scientific researchers are also engaged by such value reflections, and they are recognizable in articulated norms and acclaimed practices, such as the famous CUDOS standard[32]. As science is increasingly regarded in light of its capacity to interact with society, the deliberation on research values is even further articulated:

"The establishment of high standards, to judge our work by, and the duty constantly to raise these standards by hard work, are both indispensable. At the same time, we must constantly remind ourselves (especially in connection with the application of science) of the finitude and fallibility of our knowledge and the infinity of our ignorance."[33]

By now the researchers' reflective study of certain values is an inevitable part of scientific research, allowing, as seen, the establishment of a connection between the values of research and the values of society. In this the scientist – the researcher – is in some way asked to do moral philosophy. It is a daunting task, but our case of EPIONE did see these reflections turn up and express themselves in different recognisable themes, such as patient perspectives, use of resources, the fear and hope of transhumanism and so on. The idea of an ethical progress, from awareness to reflection, was also present in terms of the activities provide, from the simple survey to the peer-learning and dialectic exchange of the workshop. Although it is difficult to actually document and evaluate such a reflection, especially if it is – as intended – carried from the activities into the normal practise, it is fair to say that the awareness was unavoidable and the articulation of ethics in EPIONE as least manifested itself as an conception of responsibility.

"Perhaps when all the world is happy, calm and rational all questions can be perused, if there would then be no danger of their answers being misunderstood or misused. Until that day, a scientist, like

any other human being, cannot escape his moral responsibility, especially his responsibility to bring about a happy, calm and rational world."[34]

4. CONCLUSION

It is our opinion that, even though there are good reasons for further theoretical exploration of values and methods, and for further deliberation on interesting issues, overall the case of the EPIONE project has clearly demonstrated a comprehensible framework and strategy of an adequate ethical approach, including assessment as well as reflection, to and within research and development of non-CE marked medical devices.

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