CONTRACT

CONSENT IN A TRIAL & CARE ENVIRONMENT

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Table of Contents

Abbreviations

ATNA	Audit Trail and Node Authentication
BPPC	Basic Patient Privacy Consent
CCS	Consent Creator Service
CDA	Clinical Document Architecture
CMS	Consent Management Service
COMS	Consent Management Suite
CTD	Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
CTR	Proposal 2012/0192 for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
DICOM	Digital Imaging and Communications in Medicine
DPD	Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.
DPR	Proposal 2012/0011 for a regulation of the European Parliament and of the Council on the protection of individuals with regard to the processing of personal data and the free movement of such data, also called the General Data Protection Regulation
EHR	Electronic Health Record
EMR	Electronic Medical Record
Electronic Signatures Directive	Directive 1999/93/EC of the European Parliament and of the Council of 13 December 1999 on a Community framework for electronic signatures
HIE	Health Information Exchange
HIS	Hospital Information System
ICT	Information Communication Technology
IHE	Integrating the Healthcare Enterprise
IHE	Integrating the Healthcare Enterprise
MDM	Medical Document Messages
MPI	Master Patient Index
MSH	Message Header
N3	Notation 3

NHII	National Health Information Infrastructures
OID	Object Identifier
PDP	Policy Decision Point
PEHR	Personal Electronic Health Record
PEP	Policy Enforcement Point
PHR	Personal Health Record
PORS	Provider and Organization Registry Service
QBP	Query By Parameter
QPD	Query Parameter Definition
RBAC	Role Based Access Control
RDF	Resource Description Framework
RHIN	Regional Health Information Network
SOA	service oriented architecture
SOAP	Simple Object Access Protocol
UUID	Universally Unique Identifier
XACML	eXtensible Access Control Markup Language
XCA	Cross-Community Access
XDS	Cross-Enterprise Document Sharing
XUA	Cross-Enterprise User Assertion

1 Introduction

After having completed phase one and two of the CONTRACT work plan, this deliverable addresses stage 3 of the project: policy recommendations.

In the first phase of the project the problems and needs regarding informed consent in translational care and translational research, particularly care and research involving minors, were identified. A questionnaire was developed to gain insight in the handling of informed consent in Europe. In the second phase of the project initial good practice cases were identified and a holistic reference document on informed consent was composed.

This document aims to identify the legal, technical and clinical aspects of the handling of informed consent that could be strengthened and improved. It provides an analysis of these aspects and formulates recommendations on the future handling of informed consent for policy makers.

The document should be read together with the Final Guidelines for Informed Consent and Data Security Issues (D4.2.) which provides concrete recommendations and targeted advice on practical issues of informed consent.

- **Who is the document directed to?**

The document is in the first place directed to the European Commission. Next thereto it can also be of interest to other (European) policy makers. The document takes a future oriented approach, providing policy makers with recommendations on how the different concepts of informed consent on European normative level and in the Member States could be better coordinated in order to optimize the legal and ethical framework.

Within the consortium the document is, together with the final guidelines for informed consent and data security issues, used as a basis for the final workshop.

- **Structure of the document**

For the identification of the legal, technical and clinical aspects of the handling of informed consent that could be strengthened and improved we build on the experiences gained and the findings gathered in the first two phases of the project. In particular deliverables D2.2 Results of the questionnaire, D3.1 Initial report and guidelines on the identified good practice case, D5.1 Online helpdesk platform and D6.3 Report and proceedings from the first CONTRACT workshop.

Firstly a problem analysis is made answering a set of nine questions that were raised during the first two phases of the project. These questions mainly address legal issues. Secondly a proposal is formulated for

the way to go with informed consent. This section more precisely deals with electronic consent and harmonisations of the legal framework. The document finally concludes with a set of recommendations to the commission.

2 Problem Analysis

Introduction

"Informed consent" is a legal concept used to indicate that the wishes of a person have to be respected before acting. Unfortunately, our study showed that the concept is used by **different regulatory and legal documents** in **different ways**. Requirements to a legal informed consent differ as there is not one generally accepted definition of "informed consent". Instead the concept of "informed consent" is defined in each legal or regulatory instrument separately. Differences in the requirements often concern the form of the consent and the elements of information which have to be provided to the subject. Consequently, it has become a necessity for every practitioner compiling an informed consent form to check for each situation which type of informed consent is required, which rules apply and which exact requirements are imposed by this rule. Furthermore, it is important to notice that the right not to be treated without your consent is of high value in medical law, but it does not necessarily have the same status in other areas of law. Consent, for example, is not sought for in cases of intimate searches of suspects by police, self-defence, prevention of crime or tests on people with infectious diseases. These cases are subject to specific regulations and are therefore not included within this project.

In legal problem analysis of this deliverable we bundle the questions which we identified as most pressing to practitioners confronted with the legal obligation to obtain informed consent in their daily practice. The selection of these questions is based on our own findings as well as the valuable input from the participants to the first CONTRACT workshop organised in September 2011. When comparing the requirements to the different types of informed consent for clinical research involving vulnerable patients and analysing the responses to the questionnaire in Work Package 3, it became apparent that a few issues remain unclear under the current legal framework. Some of these issues have clear technical implications such as the question on acceptance of e-consent. Others have clear consequences for day to day clinical practice such as the question on consent for future use of data and the question on the timing of the request to consent. A third category of questions is not purely legal but also has large ethical implications such as the question how to balance the right to know versus the right not to know.

Through the analysis of these questions we aim to contribute to a future proof legal framework in which the regulations on informed consent are better coordinated and EU legislation is experienced less of a barrier to translational research in vulnerable patients.

2.1 Ethics of consent

Introduction

It is clear that consent – from a legal and ethical standpoint - stands at the heart of care or clinical trial situations. Since the first half of the previous century it has gradually become a widespread principle in doctor-patient relationships. Although it may not always be easy to identify what exactly constitutes consent, the principle itself may not have been questioned since[1], the conditions and variations of consent have. In the following paragraphs, a number of these issues will be subject to ethical scrutiny, in particular the ethical minimum in relation to consent, possible language and complexity issues (related to the degree of information), the need for contact between a doctor and his patient in e-consent matters.

In order to examine the aforementioned issues, the ethical principle of consent and the basic concept from which it is derived need be revisited as most of the conditions and/or variations are directly related to the understanding of consent and autonomy.

2.1.1 Consent and autonomy

As demonstrated before, the concept of **autonomy** – and, hence, consent - is one of the main concepts in medical law since Western society left the doctor-knows-best doctrine. However, several commentators have criticized the fundamental place of that principle in medical practice or, better, whether it should be the principle by which medical ethics are governed first and foremost. Herring identifies **seven 'challenges'** to its pre-eminence and draws attention to an alternative: relational autonomy.[2]

2.1.1.1 Do all autonomous decisions deserve respect?

Does a decision deserve respect simply because it was made autonomously? Herring cites John Keown who argues that the 'exercise of autonomy merits respect only when it is exercised in accordance with a framework of sound moral values'. Moral values on the other hand are obviously subject to different appreciation. What may seem justified to one, is not necessarily so to another. A Jehovah witness, refusing a blood transfusion for himself or his child, **may cause serious harm** to himself or his child. The decision not to allow a blood transfusion may be taken entirely autonomously, but may well lead to a dangerous and disastrous omission. It will be very difficult for a physician to respect that decision.

Furthermore, the autonomy touches the area of **competence** as not only religious or ideological reasons may cause disastrous outcomes. The line which forms the balance between competent and incompetent can be very thin indeed, especially as the complexity of the procedure or trial is raised.

[1] At least not in Western society where it emerged as a consequence of the liberal concept of autonomy as discussed under 2.1.1.
[2] J. Herring, *Medical Law and Ethics*, 3rd ed., Oxford, Oxford University Press, 2010, pp.193-197.

2.1.1.2 Autonomy is fundamentally Western

Within the field of moral values, it needs to be stated again that autonomy is a **Western principle** in the first place. In other societies, autonomy is often less present and more weight is given to what is good for the group rather than the individual.[3] There is a risk of imposing autonomy as a moral principle without having regard to its cultural roots. Furthermore, an individual will always be restricted in living by its moral values by the principles that are put first by the society it lives in. The tension between both shows the fragility of autonomy as an ethical principle in a global scope.

2.1.1.3 What about other values?

Another problem with the pre-eminence of autonomy is the fact that the weight which is generally attributed to it **degrades other values**. Other matters of importance include certain obligations to others, the importance of relationships in lives of others, society's set of moral values, justice.

2.1.1.4 Are health care decisions really autonomous?

To what extent is autonomy the same as self-determination? A patient or trial subject who is to consent to treatment or a procedure will be influenced by a number of factors. First of all, the question can be raised to what extent he is fully informed (and able) to take a decision that would qualify as an expression of autonomous consent. The information which the patient receives shall have an influence itself on the decision making process. Fatality rates, discomfort levels, success rates may well all be considered as external factors which will have an effect on the individual's final decision which is then said to be autonomous. In other words, **autonomy is relative** if the information provided by the physician, the nurse or investigator is taken into account as the exact scope of amount of such information may strongly effect the direction of the patient's decision.

Also, Herring points to the 'risk-relative capacity' concept according to which the degree of risk may affect the test of capacity of an individual. When the risk level is high, the test for capacity would be subject to more scrutiny than it would be in the case of a standard low-risk procedure.

2.1.1.5 Autonomy v. trust

Herring cites Onora O'Neill with the suggestion that trust in medical decision making may need to gain importance on the account of autonomy. The question is put forward whether one would prefer a deceitful doctor advising a patient who, in the end, leaves the decision of the appropriate course of action to the latter, or a trustworthy physician leaving the patient with no choice at all. It can be argued that a trusted relationship between the doctor and the patient may need emphasizing, although both **trust and autonomy are complimentary** and do not exclude one another.

[3] E. Regidor, "The use of personal data from medical records and biological materials: ethical perspectives and the basis for legal restrictions in health research", Social Science and Medicine, 2004, 1975-1984.

2.1.1.6 The capacity question

The strict line between being competent and not being competent can be troublesome from an ethical point of view. The law makes a clear distinction between both sides of that line, but in practice it is not always that clear. Instead of being a black and white difference, Herring proposes an approach which envisages also those in the grey area so that some protection can be given to those only just having capacity but who are at risk of endangering themselves, and that some respect can be given to the wishes of those who lack capacity, again only just.

Herring's point in this matter is obviously an uttering of justice and reality, but it would bring the capacity question closer to some of the above mentioned factors. Not only will the complexity of proposed care or trial procedures make the assessment of the grey zone more difficult, also the trust in the acting physician will have its role. To what extent will the answer to the capacity question be biased by the fact if a 'grey zone' patient is ready to choose for what the doctor thinks is in the patient's best interests? Studies have shown that patients were generally happy with the information that is provided to them in clinical trials, even if only half of them understood all of the information.[4]

2.1.1.7 Relational autonomy

Whereas autonomy in medical practice can be perceived as the individual patient deciding for himself what is in his best interests, it can also be argued that such perception is too narrow. We do not live our lives completely unconnected from others like some animals do, but our lives are based on the relationships that we have and maintain. We are even partly defined by those relationships and find ourselves in different networks with our relatives, friends, neighbours, co-workers… Patients will often assess their best interests in light of that **interdependency**. It is in that setting that another way of understanding autonomy can be found according to Herring.

The assessment of patient's decisions should be made while taking into account his relationships, which include and/or even create concerns for others, feelings of responsibility, obligations. Hilde Lindemann states (partly citing Jodi Halpern) that, especially in families, autonomy is 'an **interpersonal process** in which other people's recognition of a person's agency, or the lack thereof, is highly influential'.[5] As an example, Herring portrays the woman with breast cancer who sees the decision on treatment as a joint decision with her partner.

Lindemann identifies two systems of ethics.[6] The first would be the orthodoxies of health care ethics, which firstly focuses on the patient, his or her autonomy and free informed consent. The other are the orthodoxies of family ethics, where patients are viewed within their family network, their autonomy is therefore **relational**, which often makes trust more important than consent.

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[4] A. Grubb, J. Laing, J. McHale, 'Principles of Medical Law', Oxford, Oxford University Press, 2010, 13.39.

[5] H. Lindemann, 'Protection of Persons not able to Consent: a Feminist View', in A. den Exter (ed.), *Human Rights and Biomedicine*, Antwerpen/Apeldoorn/Portland, Maklu, 2010, p.211-212.

[6] *Ibid.*, p.210.

It is clear that relationships do have an influence on the patient's decision making. However, how and by whom are the effects thereof to be assessed? Some have argued that relational autonomy includes a real danger of overriding a patient's wishes too easily by taking into account the wishes or needs of others. Herring cites Christman who points at the danger of such assessment, as such approach denies the impact of time and change in such relationships, but also the variability in self-conception and multiplicities of identity which are characteristic of modern populations. The example of the woman deciding on breast cancer treatment is also applicable as a counter-example: Should women be influenced by their partners in their decision on what treatment they want to receive?

Obviously, relational autonomy is a valuable concept. At least in theory, as relationships (and their influences) are by definition personal and subjective and may vary over time. They are not only so for the patient, but also for whomever were to assess them and their impact.

2.1.2 Ethical minimum

Given the questions raised regarding autonomy and consent, one may wonder to what extent a patient or trial subject actually gives his informed consent while using his right to autonomy to the fullest. In practice, the process of giving consent often encounters difficulties when it comes to autonomy. Lack of medical knowledge, a degree of trust in the staff and possibly panic makes patients more inclined to follow the doctor's advice, rather than doubting it. Consent is often nothing more than a ritual, a formality, required from and by the physician for solely legal reasons, despite medical professionalism and effort surrounding it. Is that situation in practice sufficient, or is there a need for a certain ethical minimum with regard to autonomy in consent decisions?

According to Herring, a clear and strict conception of autonomy will allow it to triumph over beneficence, whereas a rich understanding of the concept is that of 'a fully informed and genuine choice, free from improper pressure'.[7] The paradox with that definition is that the requirements for consent will have to be strict, so that the number of people covered by it will be fewer and, hence, the more will be regarded as incompetent which will raise the cases of beneficence. The condition of being **fully informed is paramount** for patients **to fully understand** what the proposed treatment means. However, not only does the full informing of a patient seem nearly impossible, it may well not be the best course of action in the sense that a not medically trained individual may encounter more difficulty in forming his judgment and make a fully considered decision. Then again, informing a patient too little completely undermines the purpose of informed consent. Can an ethical minimum be identified given the wide range of treatments or trials with each having their own level of complexity, not to mention the even wider range of patients?

The same author cites Onora O'Neill to whom the question is not whether informed consent protects the patient's autonomy, but rather whether it offers protection against coercion or deception.[8] In that

[7] J. Herring, *Medical Law and Ethics*, 3rd ed., Oxford, Oxford University Press, 2010, p.198.
[8] *Ibid*, p.199

context, it may already be easier to identify an ethical minimum. That approach could possibly solve the issue of the patient not willing to be informed at all. Whereas in current theory that patient would not have consented, consent would be valid under O'Neill's approach as the patient has not been deceived or coerced.

A counter-example would however be that, even if the patient does not want to hear all the aspects the treating physician wants or needs to inform him about, it may well be that after the treatment or procedure, hence in hindsight, the patient realizes that he would have made a different choice if he had been aware of a certain aspect. In such case, the patient will feel as being treated in the old paternalistic way of 'doctor knows best' and O'Neill's approach may prove to be too limiting regarding the scope of what informed consent is.

Avoiding coercion and deception could however be a good starting point, if a few of the above mentioned parameters are included (cf. under section 3), especially as it does not take into account the reality of the relationships a patient may be part of at the time of decision and which are bound to influence him to a certain degree.

Also, with regard to clinical trials, one could argue that the research subjects' right under Article 27 of the Convention on Human Rights and Biomedicine on Biomedical Research to 'know any information collected on their health' is a victory for the pre-eminence of autonomy. In practice however, this may lead to difficulties regarding the subject's right *not* to know.[9] In case of studies which are undertaken over a very long period of time and which are related to the subject's genetic susceptibility to certain diseases, one can imagine that a participant, once confronted with the information, may not have wanted the information and his right not to know may have been infringed. How and about what the participant is informed needs further attention. It is clear that in case results have immediate clinical relevance to the subject's condition, the participant needs to be informed directly. In other cases, it may be advisable to verify the results first in order to avoid any risk of error.[10]

2.1.3 Language & complexity issues

Another problem that is encountered in medical practice, is explaining complex medical problems and possible treatments to the not medically trained patient. Medical staff may take the necessary time and put all reasonable effort in trying to clarify what they are proposing as treatment exactly, chances are that quite a number of their patients understand only very little and may not even recall all that much at a later stage. An individual may well have, legally speaking, given informed consent, it can leave the treating physician ethically frustrated with the situation. In order to respond to such concern, an adapted conception of informed consent may be in order.

[9] A. Grubb, J. Laing, J. McHale, 'Principles of Medical Law', Oxford, Oxford University Press, 2010, 13.101-13.103; see also the above section on the right (not) to know.
[10] *Ibid.*, 13-103.

O'Neill's basic idea of consent protecting patients from deception and coercion may be too limiting as a final understanding of the concept, it can serve as a starting point. The fact that a patient is not subject to coercion, that he is not forced into treatment he does not want, is after all the basis of every understanding of the concept. In addition to that, the question should not be to what extent a patient or trial subject needs to be informed but, rather, **how is the patient informed**? Relational autonomy, capacity, trust and cultural issues may be resolved if O'Neill's approach is taken as a basis, and if the patient is furthermore sufficiently informed about the aspects of the treatment that matter the most to him, placed in his network of relationships. This does however also imply that the informing staff will need to have sufficient background knowledge of the patient, which can only be achieved if the process of informing includes the questioning of the patient. The result would be a process that consists of conversation rather than a one way explanation with some questions coming from the patient. Conversation and the showing of interest in the patient's situation, fears, values and beliefs would also benefit the patient-physician relationship of trust. In essence, such an approach would result in an individualized process of informing whereby the basic protection of the patient is guaranteed and during which the patient obtains the amount of (individualized) information that is necessary for him to make an informed decision. The process also takes into consideration the aforementioned capacity question, possible cultural differences and (partly) rules out the interference of external factors that may adversely influence or confuse the patient. Rather than focussing on the amount of information that is or needs to be provided, such approach would aim at adequately informing the patient while taking all individual aspects in account.

2.1.4 E-consent: face to face contact necessary?

In light of the established above, a specific question can be raised if the consent process is introduced in the area of modern (communication) technologies: does an e-consent process require face-to-face contact between the doctor and the patient/subject?

Arguments for such contact could definitely be found in what has been stated above on the relationship of trust between a physician and his patient. One of the criticisms of the current consent procedure is that the pre-eminence of autonomy puts other valued aspects of the entire process in the shade. In the context of e-consent, it could be argued that contact with the treating staff is even lessened. But in the individualized approach established above, **trust** is a key factor. Therefore, face to face contact at some point appears to be paramount, also to guarantee to some extent that the patient will be free from deception. The exact timing of such contact is of lesser importance as long as the goals of the proposed approach are fully met.

On the other hand, e-consent may be an ideal tool for treatments or trials with low complexity and risk. Imposing real life contact between the protagonists could be counterproductive in that aspect. Nevertheless, the question needs then to be raised who will assess whether the levels of complexity and risk allow an e-consent procedure without actual contact between the patient and the doctor? The physician may be well placed to assess the risks involved, but given the variation in complexity of the purpose of the consent and the fact that every person/patient is different, he may only be able to do so

after having spoken with the patient. Furthermore, in the setting of a clinical trial, the Clinical Trials Directive (Article 3, 2b) still imposes the obligation that a patient needs to have had the opportunity of interviewing the investigator. Practice will have to show what the exact minimal requirements will be, taking into account all further innovations in communication technology. Such evolutions may leave room for leniency in case of treatments or trials with low complexity and risk, as long as the patient's right to an adequate approach are not violated.

2.2 Consent for the re-use of data and consent for the future use of data

Recent technical developments both in medicine, as in computer science now allow collection of vast amount of patient data. This information is collected within primary care setting, as well as within the clinical trial setting. However, despite technical availability of information, the usage of data collections is often problematic, as **the data collected for one purpose can only with difficulty be used for another**.[11]

The reason for this are the current regulations in data protection; specifically those concerned with the purpose of processing, and those concerned with informed consent for processing of data. It is argued that "research involving personal data has been damaged by the complexity, inconsistency and length of time involved in the assessment of research proposals"[12] and those are caused by the complex legal framework. Furthermore, the obligations this legal framework imposes for valid consent for data processing are seen as "considerable, and sometimes prohibitive, cost to research."[13]

However, consent in a right framework is also considered to be part of the solution for these hurdles. This chapter will be concerned with prospective research and the influence consent can have on it. It will be analysed – whether it is possible to use broad consent to secure the possibility of retaining data in the future and for different scope that it was originally collected.

Both interests which are at stake here –patient's privacy and the social benefit of knowledge have to be considered.

2.2.1 The setting

Each time a patient receives health care, or takes part in a clinical trial a record of his/ her visit and all the examinations done to him/ her is being made. Medical and surgical interventions, diagnosis and treatment outcomes, as well as any specific examination such as x-rays, CTGs, laboratory tests, etc. create a patient's data file– a so-called medical record. These data sets are created for each patient and in the big picture create a vast collection of medical information.

The medical data collected does not mean much unless it can be **quantified, analysed and used** – and it is used within the specific purpose for which it was collected – a medical record of patient is used in providing care to him/ her and clinical trial records are used to test the trial hypothesis. This is however where the primary purpose of collection is reached and where the use of the data should be put to stop.

[11] Julian Peto, Olivia Fletcher, and Clare Gilham, "Data Protection, Informed Consent, and Research," *BMJ : British Medical Journal* 328, no. 7447 (May 1, 2004): 1029–1030.
[12] Academy of Medical Sciences (Great Britain), *Personal data for public good : using health information in medical research* (London: Academy of Medical Sciences, 2006), 4.
[13] Ibid., 58.

However, data which was collected with such an effort could be further used. This re-use is usually seen as a **secondary purpose**, where data already collected for one cause is re-used for another purpose, specifically to pertain different types of research (but not only: clinical and financial audits; health service planning; resource management; teaching and training; national statistics; public health surveillance and drug safety monitoring[14]).

Medical research is a driving source of medical development and so can benefit society. In fact the European Union for a longer period of time is supporting the "**bench to bedside approach**" where two-way data flow from the researchers to the physician and patient and the other way round should support treatment and research.

For a plethora of reasons re-using is interesting and beneficial for the society. First of all the medical records are sources of valuable information for researchers and could support creation of knowledge. As Singleton mentions[15] there are already a number of discoveries, which are an outcome of secondary use of data, and more can be reasonably expected if researchers of different specialities would be allowed to make use of different kind of information collected.

Of course, one could argue, that this information could be collected for this particular, new, different purpose, notwithstanding that the original collection exists. However – from the economical perspective data are extremely costly to obtain and creation of such records needs time, also their maintenance is costly – therefore it is sound to maximise and optimise the use made of it.

Furthermore, the creation of those records is based on the examinations done to the patients – often painful and time-consuming they furthermore impose stress, and whenever possible - also for the patient's wellbeing - examinations should be reduced to a practical minimum.

Finally, in cases of rare diseases finding sufficient amount of patients is particularly hard, if not to say impossible – therefore practically forbidding re-use of information may render any research impossible.

For those reasons the already collected health records can be seen as highly valuable and, to a certain extent, an irreplaceable source of knowledge. Therefore, balancing interests of individuals on the one hand and of the society on the other is particularly important in this case.

Re-using personal data is only a singular issue out of many questions surrounding re-use of data[16], however this chapter is concerned only with the aforementioned questions of re-using patient/ clinical

[14] Ibid., 11.

[15] Peter Singleton and Michael Wadsworth, "Consent for the Use of Personal Medical Data in Research," *BMJ : British Medical Journal* 333, no. 7561 (July 29, 2006): 255.

[16] Compare: a study approaching the questions of sharing data in general (as in not only personal data) RO Sinnott et al., "Large-scale Data Sharing in the Life Sciences: Data Standards, Incentives, Barriers and Funding Models (The Joint Data Standards Study)," The Biotechnology and Biological Sciences Research Council, The Department of Trade and Industry, The Joint

subjects health records in a legally compliant and ethical way and focuses only on the data processing and consent for thee (leaving out the questions of eventual property rights, intellectual property etc.)

2.2.2 Legal (data protection) problems around prospective use of data

It is in the general interest of society, medical institutions, single patients and government to increase patients healing rate, improving availability of treatment and reduce treatment costs – a road of achieving those goals often leads via research, which is fed with information that is contained in medical records.

From the data protection point of view this medical files are understood as personal data, and classified as a special category of data – data concerning health (Article 8 of the Data Protection Directive (DPD)). The use of any personal data and so also those records is **bound to the purpose they were originally collected for** (Article 6(b)). Therefore the medical data which were collected and are maintained within the hospital archives principally cannot be used for any other aim. The Data Protection Directive states that processing of personal data is only permissible if a **legal ground** for that processing exists. Furthermore, it says that if processing occurs it has to be limited to its original purpose and each processing done for a different purpose will require a different and separate legal ground.

That principle is explained in Article 6(b), which states that data shall be "collected for specified, explicit and legitimate purposes and not further processed in a way incompatible with those purposes". That article requires not only that the collection has been created for a specific purpose but also that this purpose has to be legitimate[17] – and the same has to be the case also for any new purpose introduced at a later stage.

If such a new legitimate ground cannot be provided the data protection regulations would require the data controller (the person/ entity who collected the information) to delete it when it is no longer needed (for the purpose for which it was originally collected).

If data should be used for another reason a new legal ground has to be found. Medical records are, according to Article 8 of the Data Protection Directive, classified as special categories of data, the ground for processing has to be found within the ones specified in Article 8.

2.2.3 Solution

However, using a broader model of consent could facilitate making use of the various data collected. In such a model whenever a collection of data for a any medical purpose would be about to start the

Information Systems Committee for Support for Research, The Medical Research Council, The Natural Environment Research Council and The Wellcome Tru (2005).

[17] Leonard F. M. Besselink and Sacha Prechal, *The Eclipse of the Legality Principle in the European Union* (Kluwer Law International, 2011), 278.

patient/ research subject has to be asked for signing **informed consent for future use** of the data collected.

Such a **broad consent** would be obtained notwithstanding the original purpose of collection and its only aim would be to secure a legal ground for future research.

2.2.3.1 A broad consent as a ground of processing

2.2.3.1.1 The critics

If securing a legal ground for the new processing at the later stage faces difficulties it seems the easiest and reasonable solution to, from the beginning of data collection secure that the secondary purpose has a legal ground – the legal ground most suiting for that aim is, as explained already before in various parts of the project, the consent for data processing (considering all the criteria for legitimisation of data processing from Article 8 of the Directive). When collection of the data is about to start an informed consent of the data subject (patient, or the trial subject) should be therefore obtained for the aim of future research. That consent has to be sought despite the way the primary collecting is legalised – in case of medical care the processing is legal due to Article 8(3) (processing for the purpose of preventive medicine, medical diagnosis, the provision of care or treatment or the management of health-care services) and for the aim of clinical trial informed consent as advised in Article 8(2)a.

At the outset of processing the informed consent for data processing has to be wide enough to accommodate possible future uses of data. That however is seen as problematic, as when asking for consent the researchers **cannot yet explain** to the individual the scope of consent he or she is giving as often the research which should be done is not yet defined. Therefore, the major critic against broad consent focuses on the fact that due to its scope it **cannot be informed** and as a consequence looses the quality of being a real choice.

As underlined the term consent is being attached to the adjective "informed" to reinforce the importance of information for the process of taking decision. Therefore, the consent for future research raises questions of validity: can consent be given to something which is at the moment of consenting not yet defined? Does not that negate the sole idea of consent itself, which is based on the possibility of taking a conscious choice based on the information given?

From the three pillars of consent – competence, voluntarism and understanding of the decision taken, on the first view the consent for future research seems to lack the third. When consent is in question it "involves providing specific information about the nature of the research, who will be conducting it and what the specific anticipated outputs are".[18] However, consent for future research should be possibly broad, as any narrowing down of the consent may later on hinder researchers from conducting particular studies. If data is being collected none of those three is being known – a person should

[18] Mark Sheehan, "Can Broad Consent Be Informed Consent?," *Public Health Ethics* 4, no. 3 (November 1, 2011): 226.

informingly consent for a study that "has not been designed – or if designed, may not occur for months, years, or decades."[19] Arnason argues that understanding broad consent as informed is false: "the more general the consent is, the less informed it becomes. It is misleading to use the notion of informed consent for participation in research that is unforeseen and has not been specified in a research protocol."[20]

However, broad consent is widely supported in community. The line of mainstream arguments used for defending broad consent focuses on **the importance of research done in the future**. Furthermore, it is argued that premises securing **safety** of information (the safe handling of information in question; right to withdraw consent at any time; and finally the ethic boards of ethics commission supervision over the research questions that will be posed in the future) are secure to a degree which would justify collecting information. An additional argument is based on the ethical base of consent – autonomy, which is supposedly reinforced whenever individuals can consent broadly. Those arguments will be analysed below.

According to Hansson[21] the importance and potential of future research which can be conducted based on information stored in biobanks[22] (and accordingly in other medical files) shall be a justification for the broad consent and that many findings based on the secondary use of information shall be a sufficient reason for accepting such consent. However, this argument does not really touch the core of the question whether broad consent can be valid – if it is so it is because of fulfilment of the set of requirements posed before it and cannot be because having such consent would be beneficial. If future research is vital to society then specific legal means should be adapted rather than arguing that the ones existing shall be used accordingly to the needs, but possibly against their nature.

The same is true with another argument proposed by Hansson[23] – namely that if research is allowed without consent on the base of ethics-review boards mandate, as done in Sweden and UK, or done on anonymous data, as allowed in Norway, Netherlands, Germany and the US, it would be consistent to allow it with consent, if only with a broad one. This argument is sound as much as it reinforces the individual's right to make decision and indeed broad consent could be seen as more valuable then no consent at all. However, sound in this respect the argument does not address the nature and validity of consent.

[19] Timothy Caulfield, Russell Brown, and Eric M Meslin, "Challenging a Well Established Consent Norm?: One Time Consent for Biobank Research," *Journal of International Biotechnology Law* 4, no. 2 (March 20, 2007): 69.

[20] Vilhjalmur Arnason, "Coding and Consent: Moral Challenges of the Database Project in Iceland," *Bioethics* 18, no. 1 (2004): 28. Similarly also: M McQuillan, et al., "Consent for genetic research in a general population: The NHANES experience" Genetics in Medicine no. 35 (2003): 40.

[21] Mats G Hansson et al., "Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?," *The Lancet Oncology* 7, no. 3 (March 2006): 267.

[22] Which are also discussed in: B Hofmann, "Broadening Consent--and Diluting Ethics?," *Journal of Medical Ethics* 35, no. 2 (February 2009): 127.

[23] Hansson et al., "Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?," 267.

The argument, which on the contrary, is based on the nature of consent claims that giving broad consent is **supporting individual's autonomy**[24] and as such should be an acceptable way of consenting. In ethics autonomy is seen a primary justification for the informed consent[25] and consent is "intended to promote the autonomy of potential participants, enabling them to make choices about research participation that align with their values and interests".[26] As Sheehan argues the ideas of autonomy and self-governance as justifying reasons for consent do not specify the scope of choices the individual is entitled of making, neither the way in which their choices govern their life.[27] What the individual is agreeing on, when consenting for future research is permitting some other entity to decide how this data will be used in the future[28] - broad consent is therefore consent for governance.

The argument over governing power has to be considered from two dimensions – the first is the ethical one, where the question has to be posed whether giving up the control over future decisions is possible and the second is whether such understood consent could be accepted under the law governing it, which is the Data Protection Directive.

What should be noted is that the consideration given to the question of consent is often focussing on the ethical side of the notion. Also the arguments above did restrain from analysing the wording of the Data Protection Directive and questions whether they in any way describes how much information has to be given to the data subject in order for the consent to be considered valid.

Article 2(h) brings a general definition of consent for the scope of Data Protection Directive; additionally Article 8 requires consent for the processing of sensitive data to be explicit. The Data Protection Directive is not putting any requirements on what exactly information has to be given, especially if compared to the much more elaborated description of consent for clinical trial participation given by the Clinical Trials Directive. However, it does explain that consent has to be specific.

The Art. 29 Working Party clarified that a broad, or blanket clause in consent is inacceptable[29] and further stated: "To be specific, consent must be intelligible: it should refer clearly and precisely to the scope and the consequences of the data processing. It cannot apply to an open-ended set of processing activities. This means in other words that the context in which consent applies is limited."[30]

That elaboration is clearly against the idea of consent for future research, which by itself most importantly aims at keeping (and processing) personal data without a time limitation (while it is imaginable that a time limitation for that reason could be introduced into the possible consent forms).

[24] Sheehan, "Can Broad Consent Be Informed Consent?," 230; Hansson et al., "Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?," 267.
[25] Ruth R. Faden and Tom L. Beauchamp, The History and Theory of Informed Consent (New York; Oxford University Press, 1986).
[26] Ezekiel J. Emanuel, The Oxford Textbook of Clinical Research Ethics (Oxford; New York: Oxford University Press, 2008), 591.
[27] Sheehan, "Can Broad Consent Be Informed Consent?," 228.
[28] Ibid., 227.
[29] Opinion 15/2011 Consent, p.17
[30] Ibid.

However, a broad consent could address the scope and consequences of processing to certain extent – it can elucidate on the goals of the research, the values governing it, or the general direction the research can be conducted. Furthermore, it can narrow down what the data will not be used for and what institutions will not be allowed to use the data.

Broad consent is ethically problematic, as it is less informed then the one for already well-defined research questions. However, due to importance of the prospective use of data for the society ways of ethically addressing the issue need to be found. It seems that the current Data Protection Directive, especially interpreted by the Art. 29 WP, does not give a sufficient answer on how this issue should be addressed.

2.3 Timing of informed consent and the law?

2.3.1 Introduction

An obvious requirement for valid informed consent is that the consent is requested from the patient before action is taken:

- Before commencement of the treatment
- Before enrolment in the clinical trial
- Before collecting (or in any other way processing) personal data

This requirement is inherent to the goal of consent, this is to allow the subject to express his wishes. Less obvious is however the connected requirement to inform the subject. When exactly does the subject need to be provided with (all) the information necessary to make a mature decision?

As pointed out by Forgó: "Informed consent procedures consist of several steps. The first task is to ask […] for participation and provide information; the last is to receive the signed consent form"[31]. Informed consent is thus an **ongoing process** rather than a one-time thing. Barnett says "It is a shared decision-making process in which the professional communicates sufficient information to the other individual so that she or he may make an informed decision about participation in the professional relationship", "Professionals have knowledge, skills, and expertise that others seek out for assistance. But, as all professional services bring with them some risk of adverse impact, however small it may be, prospective participants need adequate information at the outset to help them weigh the potential benefits and risks of both participation and lack of participation"[32]. Often, the weighing of the potential benefits and risks is however a complicated process. Not only may the information which the subject is being given be difficult to understand and overwhelming, the request for informed consent in healthcare often comes at unpleasant times: after having been given bad news. Therefore many researchers plead for a staged informed consent.

In this chapter we will firstly look into the theoretical legal requirements for each of the three informed consents. This will be followed by a discussion of proposal for staged informed consent and a brief study of consent in emergency situations.

2.3.2 Timing of informed consent for treatment

The right to informed consent for treatment has been implemented in EU Member States in various ways, but one seems to agree that the informed consent needs to be obtained before treatment is

[31] N. Forgó et al., Ethical and Legal Requirements for Transnational Genetic Research, Verlag CH Beck oHG, 2010, 141.
[32] J. Barnett and A. Maryland, "Informed consent, too much of a good thing?", Professional Psychology: research and practice, 2007, Vol 38, 2, 179-186.

started and information needs to be provided to the patient in advance and on time to take a well considered decision[33].

One seems to furthermore agree that the period of consideration regarded necessary depends on the gravity of the disorder on the one hand and the degree of urgency on the other hand. The more severe the disorder is, the more time the patient should get to reflect in all conscience on the proposed intervention. If the intervention has however, to be performed extremely urgent, the reasonable period of consideration can be limited considerably[34].

However, a professional consensus on when exactly the informed consent needs to be obtained, seems hard to find. Since it is intrinsic to the concept of informed consent that the decision is made without any coercion, the patient should possess of full awareness and adequate reflection capacities. Case law suggests that the situations such as when the patient is already drowsy due to drugs[35], when he is on the operation table[36] or when he has been administered an aesthetic[37] can therefore not be accepted as a timely informed consent. But apart thereof, literature often raises that not only the informed consent in itself is a process rather than a one-time thing, treatments are a process and too often run over a longer period of time. Should consent then be obtained prior to the first intervention or action of the physician and re-obtained for each following action? Or should this rather depend on the patient and his or her knowledge? Because the answers to these questions seem to primarily depend on the specific circumstances of each individual case, a **flexible approach** viewing the informed consent as a continuous process throughout the course of the therapeutic relationship was already suggested in the '80s by Appelbaum, Lidz and Meisel[38].

2.3.3 Timing of informed consent for data protection

The Data Protection Directive does (currently) define neither when the informed consent needs to be given, nor when the information needs to be provided to the data subject.

To give an '*informed*' consent entails the consent is given only after being provided with the necessary information to counterbalance the advantages and risks arising from the agreement to process personal (medical) data. In other words, the data subject has to be able to fully appreciate and understand the

[33] H. Nys and T. Goffin, "Mapping National Practices and Strategies on Patients' rights", in M. VISMAR, et al. (eds.), *Cross-border healthcare: mapping and analyzing health systems diversity*, Brussels, European Observatory on Health Systems and Policies, 2008, Chapter 4; J. Dumortier and G. Verhenneman, "Legal Regulation of Electronic Health Records: A Comparative Analysis of Europe and the US" in Carlisle George, Diane Whitehouse and Penny Duquenoy, eHealth: Legal, Ethical and Governance Challenges, 2012, Springer-Verlag, 398.

[34] R. D'Haese, "Medische contracten in het licht van het recht op eerbied voor de fysieke integriteit", TBBR, 2010, 430-457; J.-L. fagnart, "Information du patient et responsabilité du médecin", 2006, (51) 81; B. Sluijters, M.C.I.H. Biesaart, G.R.J. De Groot en L.E. Kalkman-Bogerd, Gezondheidsrecht: tekst en commentaar, Deventer, Kluwer, 2008, 462.

[35] Ontario High Court of Justice 1983, *Ferguson vs Hamilton Civic Hospitals*, 122 BLR (3d) 214.

[36] Gent 11 maart 1992, *T.Gez./Rev.dr.Santé* 1995-1996, 54.

[37] Antwerpen 13 september 2005, *T.Gez./Rev.dr.Santé* 2006-2007, 117.

[38] P. Appelbaum, C. Lidz and A. Meisel, "Informed consent: Legal theory and clinical practice. New York: Oxford university press.

facts and implications of an action[39]. Moreover, the data subject also has to be aware of the consequences of not consenting. Therefore, transparent and accurate information has to be provided in a clear and understandable manner. Vague or general phrasing is thus not sufficient, as it will not enable the data subject to make such an analysis[40]. Consequently, the information will have to be provided at the latest before the data processing starts.

The same conclusion was drawn by the UK Data Protection Tribunal in 1984, as described by Kosta[41]. The UK ICO repeated that position under the 1998 UK Data Protection Act: "it should be presumed that for the fair processing information must be provided to the data subject at the time that the data are obtained"[42].

2.3.4 Timing of informed consent for the participation in a clinical trial

Due to the little time available for the enrolment in clinical trials, the timing of the informed consent for participation in a clinical trial is probably the most debated of the three types of informed consent.

The current Clinical Trials Directive states in its Article 3, 2 under (d) that a clinical trial may only be undertaken if "the trial subject or, when the person is not able to give informed consent, his legal representative has given his written consent *after being informed of the nature, significance, implications and risks of the clinical trial*". That means not only that informed consent must be given **prior to the start of a clinical trial** by the trial subject but also that certain time needs to be taken into consideration during which the trial subject (or his legal representative) is being informed. Moreover, the same article, under (b) states that a trial subject "has had the opportunity, in a prior interview with the investigator or a member of the investigating team, to understand the objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted and has also been informed of his right to withdraw from the trial at any time". In practice, the actual informing of the trial subject will consist of the information he or she is given on the (well) established informed consent form and of the further oral explanations given to him or her by the investigator during the interview. The Directive does not impose a specific timeframe as that may well vary and depend on the nature of each clinical trial. The good clinical practice requirements as adopted by the ICH also indicate that before consent can be obtained, "**ample time and opportunity**" needs to be provided to the trial subject or his representative to inquire about the details of the trial and also to decide on the subject's participation or the refusal thereof, but fails to mention any specific timeframe.

Taking into account the degree in which a trial subject needs to be informed, the complexity of the trial and nature and severity of the possible underlying subject's condition, the process of informing a

[39] D. De Bot, "Verwerking van persoonsgegevens", Kluwer Antwerpen, 2001, 403.
[40] T. LEONARD and Y. POULLET, "La protection des données à caractère personnel en pleine (r)evolution. La loi du 11 décembre 1998 transposant la directive 95/46/CE du 24 octobre 1995 », *J.T.* 1999, 380.
[41] Kosta, E., Unravelling consent in European data protection legislation - a prospective study on consent in electronic communications, Leuven, 2011 (unpublished doctoral dissertation, KU Leuven).
[42] As referred to by Kosta: UK Information commissioner's Office, 'Data Protection Act 1998 – Legal Guidance, Version1' 3.1.7.7.

subject will take more time in one trial than in the next. When children or minors are involved, one can imagine that the process of informing the parents or legal representative may take more time as they may request or need more detailed information. After all, they take full responsibility for the child which makes it a different decision process than if they were to decide for themselves.

From this discussion it is clear that a clinical trial can under the current Directive only start if on the one hand consent is formally obtained and the trail participant on the other hand understands the consequences thereof. By many researchers it has however appropriately been questioned what this means in practice.

Patel gives the striking example of research into intrapartum complications because in intrapartum complications there is little time to provide detailed information about the trial, a women is anxious and distressed from labour pains at the moment she needs to make the decision and may moreover fear to being treated poorly or risking the life of the baby. In his study Patel notices four main approaches: a) all women were approached antenatally and consent procedures were completed at that time even though a small percentage of them will end up eligible for inclusion; b) information was distributed to all women antenatally but the informed consent was only sought once the complication developed; c) consent was sought at the time of the complication without prior information or d) consent was obtained post-event, meaning no consent was taken at time of the recruitment[43]. In the US and the UK, were his study was conducted, the current main stream instructions recommend a trial-by-trial approach. When there is a high risk of occurrence (10-100%) full informed consent should be obtained from all potentially eligible women antenatally and confirmation should be sought at the time of the complication. When the risk is lower (1-10%) it is recommended to distribute information to all women antenatally with signed consent only once the complication develops. And for very rare complications (<1%) it would be better to only inform and seek consent when the complication actually develops in order not to cause anxiety and completely medicalise normal pregnancies[44].

From the questionnaire conducted in the CONTRACT project as well as the workshops organised by the project it became apparent that also in paediatrics there is a need for a trial-by-trial and case-by-case approach allowing the consent to be **staged**. As striking as the example described by Patel, is the situation of children being confronted with cancer. Currently most children with cancer are treated in clinical research trials and the high participation rates are often linked to significant improvements in treatment. Nevertheless, participation in a trial should remain a voluntary decision to be made by the parents in – depending on their age – consultation with the child[45]. The problem is however again that little time is available to start treatment (within or outside of the trial) but parents need more time to make a decision. Eder found from his study how to improve informed consent from parents of children

[43] D. Patel et al., "Historical trends in the timing of informed consent for research into intrapartum complications", BJOG 2012; 119:361-356.

[44] Association for Improvements in the Maternity Services, The National Childbirth Trust, "A Charter for Ethical Research in Maternity Care", London: AIMS/NCT, 1997; Royal College of Obstetricians and Gynaecologists, "Obtaining valid consent to participate in research while in labour", Clinical Governance Advice 6. London: RCOG, 2010.

[45] Insert reference to D4.2.

with leukaemia that the most frequently expressed wish of the parents is to have more time to make a decision: "Parents […] pointed to needing an opportunity to consult with others and cope with their emotions before making the decision. *They* wondered why a decision had to be made so far in advance of the randomization portion of the treatment".[46] As suggested by his parent advisory group on informed consent Eder pushes a staged consent model which regularly checks for understanding and choice. A test with such a staged informed consent model was conducted by Angiolillo[47]. He found that a staged consent process where initial consent was sought for induction to the treatment and a consolidating consent was sought before randomization improved parents' trust in and understanding of the trial and can thus help "to obtain a more truly informed consent".

2.3.5 Timing of informed consent in emergency situations

As urgent as the participation in a clinical trial may be, emergencies are yet another matter with regard to the timing of informed consent.

2.3.5.1 Emergency care

Emergency situations allow the start of treatment. It is the **state of necessity** that overrules the principle of prior consent to treatment. A person unable to consent, has the right to receive treatment. Based on – essentially – the Hippocratic oath, every physician is required to inform the patient before providing treatment, except in cases of emergency or the refusal of the patient. For the latter exception we refer to the section on the right to know and the right not to know in this deliverable[48]. The exception for emergency care is usually found in national patients' rights regulations.

2.3.5.2 Emergency data processing

In case of an emergency the Data Protection Directive does not require an informed consent for the processing of personal (sensitive) data. In this case the processing of data is allowed under article 6 2. (d) for normal personal data and article 8 2. (c) for health data.

When the emergency cease to exist, this **legal ground** for data processing will simultaneously extinguish. Consequently for further processing the data an informed consent will have to be obtained or the processing should be allowed under one of the other exceptions as provided by the DPD.

2.3.5.3 Emergency trials

After a decade of absence in the Clinical Trials Directive, the current Proposal for Regulation includes a section on clinical trials in an emergency setting. But, albeit the silence of the current Clinical Trials

[46] M. Eder et al., "Improving Informed Consent: Suggestions from parents of children with leukaemia", Pediatrics 2007, 119, e849.
[47] A. Angiolillo et al., "Staged informed consent for a randomized clinical trial in childhood leukaemia: impact on the consent process", Pediatrics Blood Cancer 2004, 42:433-437.
[48] See section 2.6

Directive a number of Member States did adopt legislation regarding informed consent in emergency situations, including the field of tension between informed consent to clinical trials and emergency situations often listing a limited number of situations in which consent is not needed[49]. In France the Huriet law (L209-9) for example includes a provision on the conduct of clinical trials in emergency situations and states that biomedical research activities may be pursued when due to matters of urgency the informed consent of the participant cannot be obtained if the protocol, as approved by the Ethics Committee, allows so and informed consent is obtained from the participant's relatives if they are present. As soon as possible the participant needs to be informed and consent needs then to be asked for the continuation of the trial.

According to the ICH Good Practice Guidelines and as also clearly required by this French law, "**delayed consent**" should however be obtained in case prior consent from the subject is not possible and the legal representative is not available as soon as possible and consent to further participation in the trial should be requested at that moment. The Guidelines furthermore impose that all measures to protect the rights, safety and well-being of the subject should be taken and in order to ensure compliance with regulatory requirements these measure need to be described in the protocol and a documented approval thereof or favourable opinion of the Ethics Committee has been obtained in that matter.

The new Proposal for Regulation of Clinical Trials refers in its Article 32, 1 under (a) to a *sudden life-threatening or other sudden serious medical condition* to define an emergency trial. One of the criticisms which may be formulated with regard to this new provision is that the word 'sudden' may be an ill-chosen term. Let's imagine a situation in which a cancer patient's condition slowly deteriorates and finally becomes life-threatening. The patient is too weak to act. Is this 'sudden'? This raises the questions what constitutes an emergency.

- In Belgium urgency is tied to the fact that the condition has become life-threatening or at least serious enough to leave severe and permanent damage. In other words, it is the qualification of the condition as life-threatening that appears crucial to the assessment of an emergency situation. Does that make the wording of the Belgian Act broader than that of the Proposal of Regulation? Not necessarily, as the relevant provision further stipulates that the experiment needs to be of *essential importance to the confirmation of experiments on persons who are capable of consenting or those of other research methods*[50].
- In France, emergency is not defined by the quality of the condition, nor by the moment such quality presents itself. The Huriet law (Article L 209-9) simply speaks of emergency situations that do not allow the obtaining of prior informed consent. In case the subject

[49] Ethical considerations for clinical trials on medicinal products conducted with the paediatric population, Recommendations of the ad hoc group for the development of implementing guidelines for Directive 2001/20/EC relating to good clinical practice in the conduct of clinical trials on medicinal products for human use, ftp://ftp.cordis.europa.eu/pub/fp7/docs/ethical-considerations-paediatrics_en.pdf

[50] Article 9, 1 Belgian Act concerning experiments on the human person

cannot consent, it is up to the family to consent (or not) *if they are present*, which suggests that a protocol is authorized to commence without consent.[51] However, this can only be the case if the protocol, as approved by the Ethics Committee, contains the option that in such case no informed consent is needed, and that the patient will be informed as soon as possible.

- The Declaration of Helsinki (World Medical Association) nowadays also contains a provision on research involving subjects who are physically or mentally incapable of giving consent. Its section 29 takes unconscious people as an example. The words 'urgency' or 'emergency' are not used, but *if the research cannot be delayed, the study may proceed without informed consent* (be it under certain conditions, cf. infra). This wording remains very vague and is therefore even broader than the Belgian or French legal texts.

Most of the aforementioned documents require the **absence of a legal representative** so that the protocol can start without the consent of the subject. In France, reference is made to the patient's family. The Guideline on Good Clinical Practice, the Proposal for Regulation and the Declaration of Helsinki literally state that first the consent of a legal representative needs to be pursued.

Only the Proposal for Regulation additionally speaks of possible **previous objections** as known to the investigator. This additional prerequisite may seem redundant but is essentially beneficial to the patient's rights as it excludes abuse of the absence of a legal representative. It is however clear that, given the emergency situation, no physician or investigator can be burdened with a thorough check of such possible objections and should therefore only rely on what is personally known to him, through – for example - past oral objections or notes thereof in the patient's medical records.

A vital condition that is often included regards the **direct relation** that needs to exist between the condition that is life-threatening and leads to the state of emergency. It limits the applicability of such provision to protocols that can actually be beneficial to the subject by acting against the primary concern: the underlying condition. Such limit excludes the possibility of performing protocols which fall out of the urgency condition and for which an investigator could well have the patience to obtain consent from the subject or its legal representative or which has no direct benefit for the patient's condition. Both the Proposal for Regulation and the Belgian Act have specific wording for that. The Declaration of Helsinki is more implicit as in accordance with its section 29 clinical trials may only be performed on subjects who are physically or mentally[52] unable to give consent *if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research population.*

To ascertain that the advantages to the patient outweigh possible **risks and burden** is an extra obligation for the treating physician or the investigator. There are however different ways of

[51] D. Vanpee, J.B. Gillet and M. Dupuis, 'Clinical trials in an emergency setting: implications from the fifth version of the declaration of Helsinki', in *The Journal of Emergency Medicine*, vol. 26, n°1, pp. 127-131, 2004.
[52] Not to be confused with incompetent individuals to which sections 27 and 28 of the Declaration apply.

implementing such obligation. The Proposal for Regulation keeps the wording minimal and states that *the clinical trial poses minimal risk to, and imposes a minimal burden on, the subject*. Clearly, that provision leaves room for case-by-case interpretation and is hence flexible. Another possibility is the wording of the Belgian Act which essentially states the same but is more elaborate and precise: pain, discomfort, fear and any other foreseeable risk in relation to the illness and its development must be limited to a minimum and the foreseeable risks may not outweigh the hoped-for advantage. It furthermore is specifically added that the risk and burden need to be specifically defined and periodically checked. In the wording of the Proposal for Regulation only the continuing minimal risk and burden are implicitly included, and hence a frequent check thereof is necessary. A specific definition and the periodical check of both risks and burden offer first and foremost an extra argument for the Ethics Committee to appreciate in its decision to allow the performance of clinical trials in emergency situations (cf. infra), they also constitute a means *a posteriori* to appreciate the investigator's considerations and thoughts which may be of importance in future disagreement or dispute between the subject and the investigator. Prior approval from the Ethics Committee is probably one of the major safeguards when it comes to the protection of patients' rights and is of paramount importance to the effective control of the necessity for clinical trials to be performed in emergency situations.

Starting a protocol in emergency situations may be acceptable under the above conditions, it should be repeated that this will only remain so as long as informed consent is obtained for continuing the trial as soon as the participant regains ability to consent, or as soon as an authorized legal representative has been identified, whichever occurs sooner.

2.4 Informed consent and contract law?

Introduction

It is clear that an informed consent as such cannot be considered a contract in legal terms. An informed consent is only a declaration of will. For example: a declaration by the patient of his willingness to participate in a clinical trial, to be treated for a medical condition, or to share personal medical data.

However, an issue often signalled in literature is that the process of giving informed consent and signing an informed consent form is not experienced by the patient as a process of expressing will, but as a **process of signing a contract**[53]. A contract which exempts from liability rather than protecting the patient. This feeling can be provoked by to the use of complicated and very long informed consent documents, written by medical personnel in a language not adapted to laymen. It may also be provoked when signing an informed consent document becomes a condition for getting the newest treatments only available through the participation in a Clinical Trial; or when signing an informed consent is presented to the patient as a legal administrative necessity rather than a moment where the physician is available for questions.

Therefore the question whether contract law (should) apply to the informed consent process was asked. We will examine this question on the basis of 1) the nature and qualification of the relationships in the informed consent process and 2) the characteristics of an informed consent form.

2.4.1 Nature of the relationships in the informed consent process

A first element which should be considered in answering the question whether contract law applies to the informed consent process is the qualification of the relationship rising from giving consent. The relationships which arise depend on the subject of the informed consent:

- In case of an informed consent for treatment, it is the treating physician's responsibility to request the patient's consent.
- In case of an informed consent for participation in a Clinical Trial, a special relationship rises between the patient and the investigator and indirectly the sponsor.
- When processing personal (medical) data, the relationship between the data controller and the patient / data subject is crucial to the informed consent process.

The qualifications of the relationships get even more complicated when we not only consider the person directly requesting the informed consent from the patient but also the institutes (hospitals, research labs, etc.) behind them. In many cases and as described in deliverable 3.1. several of these informed

[53] E. Barnett et all, "Informed consent too much of a good thing or not enough?", Professional Psychology: Research and Practice, 2007, Vol. 38, No. 2, 179–186; M. Eder et all, "Improving informed consent: suggestions from parents with children with leukaemia", Pediatrics 2007, 119; V. Jenkins, "What oncologists believe they said and what patients believe they heard, An analysis of phase I Trial Discussions", Journal of Clinical Oncology, 2011, vol 29, 61-68.

consents will often have to be obtained in one patient — doctor relationship. Equal to each of these relationships is the characteristic of unequal distribution of powers. The patient, trial subject or data subject is considered to be the weakest party.

2.4.1.1 The patient-physician relationship

A European wide regulatory instrument governing the patient – physician relationship does not exist. The qualification of the relationship is thus subject to national law. The EuroGentest project[54], in which patient rights of all European Member States are being studied, distinguishes two levels and two types of regulations, as presented in the table below.

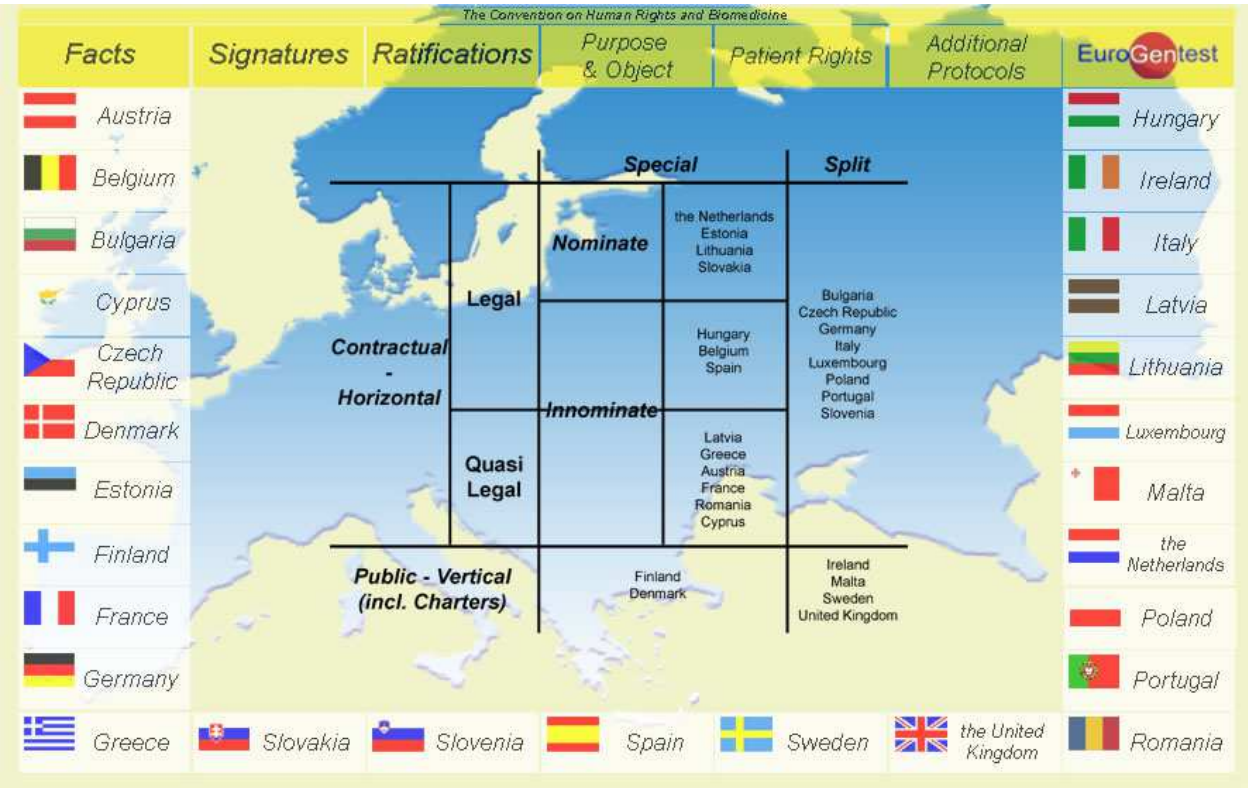


Table 1 Patient Rights Regulations in Europe[55]

Of importance to applicability of contract law on informed consent is the first distinction: the distinction between countries with a contractual – civil law / horizontal approach and those with a public / vertical approach on patient rights.

[54] For more information see: http://www.eurogentest.org/.
[55] Patient Rights in the EU, Centre for Biomedical Ethics and Law KU Leuven, europatientrights.eu .

- Under the **civil law approach** patient rights are well defined rights actionable against specific parties that should be respected with no limitations as to the providers'resources. If violation occurs, compensation and/or sanctions can be imposed.
- Under the **public law approach** the patient has no avenue for direct action against the healthcare provider. There are mainly obligations imposed on physicians and other healthcare providers in legally binding codes of medical deontology.

The authors of the table do however add that "The difference between the civil law and public law approach is mitigated by the recourse possibilities such as disciplinary procedures against medical professionals and complaint procedures against health care providers that exist in both systems. And in a public law or vertical system the civil law way may remain open for the patient in the case of malpractice. Also in a civil law approach additional protection to the patient may be offered in the so called vertical relation, using administrative legislation".

It thus seems that under both systems the doctor-patient relationship may have a contractual nature as well as a non-contractual. Especially in countries where patient rights regulations have a public law character, this results in different means available to the patient in case of a claim. The doctor patient relationship has for example a non-contractual character when it comes to public healthcare and the patient will have to rely on tort law, in particular an act of negligence when a claim is made against the NHS. While, when consulting a private physician, the relationship has a contractual character and the patient will be relying on a breach of contract when a claim is made against a private physician[56].

Without detracting the merits of the research completed under the EuroGentest project, it should however be noted that not in every Member State the categorization of the patient – physician relationship is as obvious.

Two examples of Member States which can easily be categorized are France and the Netherlands. In France the discussion on the categorization was ended through court, in the Netherlands through legislation. The French Court of Cassation marked the physician - patient relationship as contractual already in 1936 in its ruling on the Mercier case[57]. In the Netherlands the discussion on the legal qualification of this relation was ended only in 1995 by the enactment of the "Wet Geneeskundige Behandelingsovereenkomst" – Law on the Medical Treatment Relationship. This law qualifies the physician – patient relationship explicitly as a contract of a special kind[58].

In many member states, especially those under the category contractual – innominate, the qualification is still subject to discussion. This is for example the case in Belgium. Although a study of the current situation in and historical development of all Member States' national laws and regulations would be no longer within the scope of this document, it is interesting to briefly look into the case of Belgium since in

[56] J. Herring, *Medical Law and Ethics*, 3rd ed., Oxford University Press, Oxford, 2010, p.126.
[57] Cass. (Fr.) 20 May 1936, D.P. 1936, vol.1, 88.
[58] Wet Geneeskundige Behandelingsovereenkomst, (Dutch) Staatsblad17 November 1994, nrs. 837-838.

Belgium the Court of Cassation argues that the existence of the consent of the patient gives rise to the existence of a contractual relationship between the physician and the patient[59]. Most legal practitioners nowadays agree largely with this statement, but not everyone thinks it is a useful qualification. Dalq for example stated that "Le consentement doit s'interpréter comme une convention et sa portée se situe sur le plan contractuel et non pas quasi-contractuel. Le consentement fait partie du contrat entre le médecin et le malade. Lorsque le malade consent à l'intervention, il prend à sa charge les risques de celle-ci et lorsqu'il n'y consent pas, ceux-ci restent à charge du médecin"[60]. D'Haese notices that the patient-doctor relationship has evolved from a vertical to a horizontal relationship in which the physician is the expert applying his knowledge to allow the patient to decide about his health in an as informed as possible way. This change shows itself also in the acceptance of the physician – patient relationship as a contractual relationship[61]. Consequently Goffin argues that the consent which gives rise to a valid contract for treatment originates in the offer of a physician to treat the patient in a concrete situation and in the consecutive acceptance of the patient to this treatment[62].

2.4.1.2 The patient – investigator and patient - sponsor relationship

Also in the patient – investigator and patient – sponsor relationship of a clinical trial it has been argued in legal doctrine that although the informed consent as such is not a contract "and participants are immune from any contractual obligations, because of their overriding right to withdraw", a contract nevertheless arises[63]. Humphreys, who studied this question based on English law, refers back to Walter Reeds' yellow fever experiments on human volunteers to support his reasoning. In order to avoid possible claims of immorality Reed required his participants to sign written contracts containing a clear declaration of consent[64]. By including the phrase "The undersigned understands perfectly well that in case of the development of yellow fever in him, that he endangers his life to a certain extent" in his 'consent form', Reed sought to avoid possible claims of immorality[65]. Humphreys does however admit that the term "informed consent" as we know it today was only developed in the '60, long after Walter Reed's experiments. Capron found more precisely that what we know as written consent forms were back then usually called **contracts, waivers or releases**[66] and were used rather to protect the

[59] Cass. (Be.) 4 Octobre 1973, available online at www.cassonline.be

[60] Translation: The consent shall be interpreted as an agreement and its scope is contractual and not quasi-contractual. Consent is part of the contract between the physician and the patient. When the patient consents to surgery, he shall bear the risk of it and while when he does not consent, the risks [of the intervention] remain with the doctor. R. Dalq, "L'evolution de la responsabilité médicale", Bull.ass. 1981, (633)633.

[61] R. D'Haese, "Medische contracten in het licht van het recht op eerbied voor de fysieke integriteit. De informed consent-vereiste als raakpunt", TBBR, 2010, 430-457.

[62] T. Goffin, De professionele autonomie van de arts, Proefschrift ingediend met het oog op het verkrijgen van de academische graad van doctor in de rechten, KU Leuven Faculteit Rechtsgeleerdheid, 2011.

[63] S.J. Humphreys: Entering a clinical trial: consent and contract – a consideration. *The* Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd

[64] Walter Reed and the Yellow Fever Experiments IN Emanuel et al. (eds): The Oxford Textbook of Clinical Research Ethics. 2008; Oxford: Oxford University Press ch.1, pp. 9-18

[65] S.J. Humphreys: Entering a clinical trial: consent and contract – a consideration. *The* Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd

[66] Capron AM: Legal and Regulatory Standards of Informed Consent in Research IN Emanuel et al. (eds): The Oxford Textbook of Clinical Research Ethics. 2008; Oxford: Oxford University Press ch.57,

investigator from liabilities than the trial subject from harm. A similar finding has been described by Manson and O'Neil, only they do refer to current practice: "A focus on the communicative transactions by which consent is sought, given and refused [in clinical trials] provides a much clearer view of the reasons why consent is important and of the relations between consent and other significant ethical standards. Informed consent transactions are used to waive other requirements in specific ways and for specific purposes. So informed consent has a role to play only where certain underlying requirements such as ethical, legal and professional obligations and legitimate expectation of various sorts are accepted"[67].

Humphreys however notices a difference in asking the consent of a **patient or a healthy volunteer**. He states that the term 'contract' is more appropriate for clinical trials involving healthy volunteers because this emphasizes the distance between the researcher and their subjects. He says it emphasizes that "what they are engaged in is research, and the care they may be getting is perhaps really more like 'customer service' than patient care", "When the subject is however also a patient, there is hope of medical benefits and consent to treatment governs the relationship, rather than contract law". Although Humphreys may be right when he states that by labelling the informed consent form as a contract, "an unpleasant and contextually inappropriate overtone of legalese" may be created, but it should in the light of the above paragraph be noted that also when the participant is a patient and the informed consent form is not labelled as a contract, under most legal systems a contractual relationship will arise.

Kosta on the other hand notices a difference in the concepts of informed consent under the Clinical Trials Directive and other international documents describing informed consent: "In the context of the Clinical Trials Directive, the informed consent of the individual to take part in a clinical trial is approached as a written decision of the individual, duly dated and signed", while in for example the Data Protection Directive consent is the expression of the agreement of the individual and thus a mean for the data subject to indicate his wishes[68]. Kosta relates this different approach to the respect for the **autonomy** of the patients and research subjects: "The quintessential role of consent in medical and research ethics is justified on the basis of respect for autonomy […] and is needed in order to secure respect for autonomy, which is presumed to be fundamental to ethics". We will come back to the link with the autonomy of the patient when discussing the right to withdraw[69].

2.4.1.3 The data subject – controller relationship

The data subject – controller relationship is of a different kind compared to the patient – doctor relationship or the patient – investigator relationship.

pp. 613-632

[67] Manson, Neil and O'Neill, Onora, Rethinking informed consent in bioethics (Cambridge University Press, Cambridge 2007), 70.

[68] Kosta, E., Unravelling consent in European data protection legislation - a prospective study on consent in electronic communications, Leuven, 2011 (unpublished doctoral dissertation, KU Leuven).

[69] See 2.4.2.1

As already indicated above[70] the consent of the data subject under the Data Protection Directive 95/46 EU is an expression of the **agreement** of the individual to the processing of his personal data. The EU Charter of Fundamental Rights specifies in article 8 (2) that personal data can be processed "on the basis of the consent of the person concerned or some other legitimate basis laid down by law". Therefore, consent is recognised as an essential aspect of the fundamental right to the protection of personal data. At EU level and from the very beginning informed consent has thus been a criterion for legitimising data processing operations, but as the article 29 working party describes: it is also just one of several (under the current Directive six) legal grounds that can be used to legitimize data processing[71]. The working party continues: "In some Member States it is the preferred ground, sometimes close to a constitutional principle, linked to the status of data protection as a fundamental right. Other Member States may see it as one of six options, an operational requirement that is no more important than the other options". No matter how preferred or not, obtaining consent will never negate the controller's obligations with regard to fairness, necessity and proportionality as well as data quality or allow the circumvention of other provisions. Therefore, the working party concludes that consent should not be regarded "as an exemption from the other data protection principles, but as a safeguard", "it is primarily a ground for lawfulness and it does not waive the application of other principles". Contrary to the conclusion of Manson and O'Neill that informed consent transactions are used to waive other requirements in specific ways and for specific purposes, informed consent as it is included in the Data Protection Directive today is not a waiver nor a contract in itself, but a safeguard to ensure that data are processed whilst protecting the data subject. As such the criteria to the validity of the consent for data processing and to the validity of a contract under civil law are complementary.

The idea that consent is **a safeguard, not a waiver** is further supported through the articles 7(a) and (b) of the Directive. The Article 29 Working Party indicates: "The choice of the most appropriate legal ground is not always obvious, especially between Article 7(a) and 7(b). Under Article 7(b), the processing must be necessary to perform a contract, or in order to take steps at the request of the data subject prior to entering into a contract, and no more. A data controller using Article 7(b) as a legal ground in the context of the conclusion of a contract cannot extend it to justify the processing of data going beyond what is necessary: he will need to legitimise the extra processing with a specific consent to which the requirements of Article 7(a) will apply. This shows the need for granularity in contract terms. In practice, it means that it can be necessary to have consent as an additional condition for some part of the processing. Either the processing is necessary to perform a contract, or (free) consent must be obtained".

In the light thereof it makes sense that the Data Protection Directive foresees in the specific role of the data controller as the person responsible for the data processing in the broadest sense. As the article 29 working party indicates in the same opinion: "The data controller may want to use the data subject's consent as a means of transferring his liability to the individual. For instance, by consenting to the

[70] See.2.4.1.2
[71] Article 29 WP Opinion 15/2011 on the definition of consent, 13 July 2011, http://ec.europa.eu/justice/policies/privacy/index_en.htm.

publication of personal data on the Internet, or to a transfer to a dubious entity in a third country, he may suffer damage and the controller may argue that this is only what the data subject has agreed to. It is therefore important to recall that a fully valid consent does not relieve the data controller of his obligations, and it does not legitimize processing that would otherwise be unfair according to Article 6 of the Directive".

2.4.2 The process of consenting and informed consent form

A second aspect which could be considered in the question whether contract law should or should not apply on the informed consent process are the characteristics of the informed consent form and the informed consent process.

At first sight the processes of obtaining informed consent and of concluding a contract look very similar and seem to have similar results: two parties sign a document by which they are legally bound and through which they create rights and obligations. However, as we will discuss, some typical characteristics of the informed consent do render this reasoning more difficult.

A complicating factor in this comparison is again **national law**. Since there is no European-wide basis governing the process of concluding a contract, the conditions to the validity of a contract very much depend on national law. Some of these conditions differ quite substantially (e.g. between common law approach and civil law approach) but others seems to recur in more or less all national legal systems. And so while the precise legal approach may differ, similar concepts are used in many modern law jurisdictions. As a starting point to this common basis we turn to the General Principles of European Contract Law, as drafted by the Commission on European Contract Law in 1998. Although not legally binding, these principles are intended as a basis for parties in the European Communities wishing to have their contracts governed by this common set of principles rather than national law[72].

In many national legal systems the first conditions to the rise of a contract are that an 'offer' is made by one capable party and this is 'accepted' by another capable party[73]. Under the PECL a contract is assumed to be concluded when:

- parties intend to be legally bound
- they reach a sufficient agreement[74].

The intention of a party to be legally bound by the contract is to be determined from the party's statements or conduct as they were reasonably understood by the other party. Sufficient agreement is reached when the terms of the contract have been sufficiently defined by the parties so that the

[72] The Principles of European Contract Law, Parts I and II revised 1998, Part III 2002, available online at www.jus.uio.no/lm.
[73] S.J. Humphreys: Entering a clinical trial: consent and contract – a consideration. The Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd
[74] Article 2:101 PECL

contract can be enforced or can be determined and no specific matters on which one of the parties requested agreement, is left open to discussion[75].

When comparing these requirements to the requirements of a valid informed consent as described in deliverable 4.2.[76], similarity can indeed be noticed.

- Both parties, the patient on the one hand and the physician, investigator or controller on the other hand, wish to be legally bound.
- They reach an agreement on the chosen treatment, the participation in a clinical trial and / or on the participation in data processing.
- One could thus argue that an 'offer' is made by the party asking for the informed consent and 'acceptance' is expressed by the party giving informed consent[77].

It is also for most informed consents true that the **intention of the parties** is to be determined from the parties' statements of conduct. For some informed consents, like for the participation in a clinical trial or the processing of sensitive personal data, a written and signed form is required, but then again, a requirement as to the form of the contract is also in contract law not unusual. Moreover a signature and a written document are often also convenient evidence of the existence of agreement and will thus be helpful to both the informed consent process and the fact of a contract. Nevertheless an - in our opinion pertinent - remark is made by Humphreys: "A consent form is not consent. The form may only be evidence of consent being discussed and perhaps obtained […]. A signed consent form will not actually prove that the signatory understood what was signed. A contract signed and dated, by contrast, is itself evidence of the fact of there being a contract"[78]. D'Haese also agrees with this remark and therefore suggests differentiating the evidential value: with regard to the appointments and arrangements such as time, place, treating physician… the general rules of contract law can be applied. A signed informed consent form thus proofs the existence of a contract and the appointments and arrangements included herein. The singed informed consent form does however not proof the legitimacy of the actual informed consent since the form may never replace the personal oral discussion[79].

It is quite remarkable that the PECL recognize in Article 2:104 that contract terms which have not been negotiated individually always have to be brought to the other party's attention before the contract is concluded and a mere reference to these terms in a contract document, even when signed, is not sufficient. This is striking because in many national contract law systems, this rule is only recognized with regard to consumer protection, not in general contract law and exactly here the informed consent may differ from a contract since it is a specific characteristic of the informed consent that the physician,

[75] Article 2:102 and 103 PECL.
[76] CONTRACT Deliverable 4.2. Final report and guidelines on good practice cases.
[77] T. Goffin, "De professionele autonomie van de arts", 2011, Katholieke Universiteit Leuven.
[78] S.J. Humphreys: Entering a clinical trial: consent and contract – a consideration. *The* Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd
[79] R. D'Haese, "Medische contracten in het licht van het recht op eerbied voor de fysieke integriteit. De informed consent-vereiste als raakpunt", TBBR, 2010, 430-457.

investigator and controller are **obliged to fully** inform the patient before a valid informed consent can actually originate. The patient needs to be able to make an "understanding and enlightened decision"[80]. Under general contract law the conclusion of a contract is quite a rigid action. It binds both parties upon agreement, even so where a party did not properly understand the contract. Or as Drabiak-Syed describes it: "Ordinary principles of contract law are designed as an incentive to comply with contractual terms […]. Contract law assumes parties are autonomous, equal and that individuals must comply with their stated intentions and promised actions". Consequently, contract law usually assumes that what has been put in writing is what has been agreed between parties, even so where one party can demonstrate they did not properly understand what they were signing or even if they did not bother to read it[81].

Two other aspects of the informed consent process remain to be discussed with regard to application of contract law:

- Providing informed consent is an on-going process not so much a fact. The patient is always free to withdraw and may do so freely at any time without having to justify. He or she may furthermore never be forced, persuaded or coerced.
- A third difference could furthermore be noticed with regard to representation. While a contract can under certain circumstances be signed or entered into on behalf of someone else with appropriate mandate or power of attorney, an informed consent cannot be given by any other person than the patient himself or his legal representative.

In the following paragraphs we will take a closer look at these two possible differences.

2.4.2.1 Right to withdraw

Contrary to the basic idea behind a contract is the feature that the person giving informed consent can at all times **unilaterally decide to withdraw** his consent and so to speak terminate the contract, without any cause or compensation[82]. A right to withdraw as it exists today, without time limit, would be of an unprecedented nature in contract law. Not even consumer protection regulations grant such a right.

As already mentioned above, this right to withdraw informed consent is often linked to the idea that the informed consent is an act of autonomy, a derivation from the right to self-determination. As Kosta describes: the relations between patients and physicians are characterised by the self-determination of the patient, the relation between the data subject and data controller is characterised by the right to

[80] Nuremberg code
[81] S.J. Humphreys: Entering a clinical trial: consent and contract – a consideration. *The* Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd
[82] See CONTRACT Deliverable 3.1. Initial report and guidelines on good practice cases, 2.3. Introduction to Informed consent in Clinical Trials.

informational self-determination[83]. Faden and Bauchamp found that informed consent is from a moral point of view closely linked to the autonomous choices of patients and subjects[84]. It is the decision of the patient acting intentionally, with understanding and without controlling influences that legitimates actions that would otherwise be unacceptable[85]. It is not an agreement reached between two parties. Respect for the individual autonomy, entails the recognition of the right of individuals to make their own choices and means taking consents and refusals seriously[86]. Kosta therefore concludes that the consent of the individual is still the main mean to empowerment and should be examined under the light of autonomy, especially with regard to data protection, as this is in line with the European commitment to respect for human rights[87].

Vansweevelt and Vandenberghe tend to agree with this conclusion, but argue that this should not prevent the informed consent from being subjected to contract law. They argue that contracts which affect the physical integrity of a person will always be revocable. The patient or trial participant cannot be forced to being treated. He himself decides thereto, and he himself can always revoke this decision. Vansweevelt and Vandenberghe therefore argue that the right to revoke or the right to withdraw should be considered a ground to terminate the contract and "since a ground to terminate the contract can be authoritative when invocable by the creditor" this is not a problem[88]. The right of the patient to not give his consent at all or to withdraw it later should thus be considered merely a ground to terminate the contract.

Humphreys too agrees with this conclusion, though he adds that this makes the informed consent in fact a unilateral contract where only one party is really obliged to fulfil its obligations and does in fact not bind the patient/participant[89]. He therefore questions whether the offeror (the physician or investigator) should not be allowed the right to revoke his offer at any time too. Informed consent forms often include paragraphs on prematurely termination of the trial when for example:

- The drug has been shown to be so beneficial that it would not be ethical to continue a trial where subjects might not receive the drug;
- The overall trial enrolment was met, so all sites are being closed, even if some sites have not completed their enrolments;

[83] Kosta, E., Unravelling consent in European data protection legislation - a prospective study on consent in electronic communications, Leuven, 2011 (unpublished doctoral dissertation, KU Leuven).
[84] Faden, R. and Bauchamp, T., A history and theory of informed consent (Oxford University Press, New York, Oxford, 1986), 7.
[85] Manson, Neil and O'Neill, Onora, Rethinking informed consent in bioethics (Cambridge University Press, Cambridge 2007), 1.
[86] Brownsword, Roger, Rights, regulations and the technological evolution (Oxford University Press, Oxford 2008), 72.
[87] Kosta, E., Unravelling consent in European data protection legislation - a prospective study on consent in electronic communications, Leuven, 2011 (unpublished doctoral dissertation, KU Leuven).
[88] T. Vansweevelt, De civielrechtelijke aansprakelijkheid van de geneesheer en het ziekenhuis, Antwerpen-Apeldoorn, Maklu, 1992, 52; H. Vandeberghe, "Medische aansprakelijkheid" in De professionele aansprakelijkheid, Brugge, die Keure, 2004, (1)12.
[89] S.J. Humphreys, "Entering a clinical trial: consent and contract – a consideration." The Internet Journal of Law, Healthcare and Ethics. 2010 Volume 6 Number 2. DOI: 10.5580/9bd

- The sponsor finds that the investigational drug presents an unreasonable and significant risk to subjects;
- The treatment was not effective, so there is no reason to continue the trial;
- The sponsor finds that they are unable to manufacture the drug appropriately for marketed use (can not obtain needed materials, formulation problems, etc.);
- The sponsor determines that they are unable to continue the investigation for a business reason, such as lack of funds, lack of adequate market potential, competing drugs have received marketing approval ahead of the test compound, etc;
- Or for safety reasons.

When incentives, such as payments, are promised for the participation in clinical trials (e.g. to healthy participants in phase III trials) it may seem only fair that these incentives are only given when the trial is completed. Humphreys observes two main opinions on this question: "Some argue that once there has been substantial performance the offer cannot be withdrawn. Other academics see the offeror as making two offers – the express or main offer that payment will be made upon completion, and an implicit offer which accompanies the main offer that the main offer will not be revoked once performance has begun"[90].

D'Haese however, notices that in the patient – physician relationship the argument of Humphreys does not count because it is a contract of duration. In contracts of duration the agreement giving rise to a contractual relationship will not necessarily coincide with the consent to treatment, he argues: "The initial agreement will give rise to a contractual relationship between the physician and the patient, but the physician will be required to obtain an informed consent from the patient for every treatment he wishes to start as part of the contract of duration"[91].

Legal doctrine seems to largely agree on the impossibility to waive the right to withdraw. Kosta studied the right to withdraw mainly from a data protection point of view and states that because the right to withdraw is derived from the right to informational self-determination it cannot be waived for the future[92]. Goffin, who studied the right to withdraw especially in treatment relationships tends to agree with this and concludes that a patient can waive his right to informed consent in general on two conditions: the waiver must be voluntarily and true, but he or she may nevertheless always recall this waiver since rights affecting the physical integrity are always revocable. Drabiak-Syed who looked into the right to waive informed consent with regard to prenatal screening and diagnosis also agrees. She

[90] Ibid.
[91] R. D'Haese, "Medische contracten in het licht van het recht op eerbied voor de fysieke integriteit. De informed consent-vereiste als raakpunt", TBBR, 2010, 430-457.
[92] Kosta, E., Unravelling consent in European data protection legislation - a prospective study on consent in electronic communications, Leuven, 2011 (unpublished doctoral dissertation, KU Leuven); See also Simitis, Spiros (ed.), Kommentar zum Bundesdatenschutzgesetz, 6th edn Nomos Verlagsgesellschaft, Baden-Baden 2006.

states that if a contract contains a provision that the parties agree in advance to waive the right to withdraw consent "this jeopardizes the patient's autonomy, psychological well-being and bodily integrity that are normally protected by the mechanism of informed consent.", "Such a waiver is incompatible with both the comprehension necessary for consent and the ability to make a decision free from coercive external influence."[93] One should moreover be careful that the adherence to a waiver for informed consent is not put under the threat of damages since in that case the process of consenting would no longer be without coercion.

2.4.2.2 Representation

Contracts can under certain circumstances be signed or entered into on behalf of someone else with appropriate mandate or power of attorney. In contract law the person entering into the contract on behalf of someone else is however appointed by the principal or the person who is to be bound by the contract. Informed consent can as a rule only be given by the patient, participant or data subject himself unless he or she is not capable to do so. When he or she is not capable, consent must be obtained from his or her legal representative. In contrast to what is the case under contract law legal representatives cannot be appointed by the subject himself, but are appointed by law. Incompetent adults will mostly have someone appointed by court, parents act under normal circumstances for their children, and so forth[94].

Also in the case of an emergency, when no informed consent is obtained, or the informed consent is at least delayed, national law foresees a system of representation in which the physician is often indicated as a last resort. As mentioned in the contribution on the timing of informed consent, the state of necessity overrules the necessity of prior consent to treatment[95]. Which means that, from a contractual point of view, the patient receives treatment he did not consent to. The same goes for clinical trials as a number of Member States have adopted legislation which allows the conduct of clinical trials in cases of emergency, as does the Proposal for a Clinical Trial Regulation (CTR) 2012/0192[96]. According to Goffin however, this is no reason for not applying contract law. He states that from the point of view of contract law the contract which arose from admitting emergency is voidable, but it is up to the patient / participant to, after having been treated, decide whether or not he wishes to confirm or annul the void contract[97]. In Germany however, most scholars do not agree with this argument. They state that there is no contract because core personality rights are affected. In Germany the general opinion is that informed consent is a unilateral withdrawable statement of will. The right to withdraw is a constitutional right to protect the personal rights of a subject. No legal capacity is needed, but only the ability of understanding. A contract needs in Germany as a minimum two corresponding statements of will and

[93] K. Drabiak-Syed, Waiving informed consent to prenatal screening and diagnosis, Journal of Law, Medicin and Ethics, 2011, 559-564.
[94] See CONTRACT Deliverable 3.1. Initial report and guidelines on good practice cases, Legal Age and Majority as discussed for Belgium, Germany, Poland and the UK.
[95] See section 2.3
[96] With regard to clinical trials there is no such option yet under the current Directive. The proposal for a new clinical trials regulation has included such a provision in article 32.
[97] T. Goffin, De professionele autonomie van de arts, 2011, Katholieke Universiteit Leuven 302-303

will bind both parties, so that the right to withdraw at any time would be excluded. So a contract is in Germany the opposite from a unilateral statement of will.[98]

2.4.2.3 Conclusion

We have to conclude that arguments can be made to apply contract law to the process of consenting, but **no consensus can be found in Europe**. Whether or not national courts will be likely to apply contract law to the process of consenting seems to very much depend on national legislation and case law, especially national legislation and case law on the patient – doctor relationship. From the legal doctrine as included in the above analysis it appears that when it is accepted that the patient–doctor relationship is subject to contract law, also the process of consenting to treatment, to the participation in a trial and correlatively the consent for data processing is regarded subjected to contract law, even though the patient – doctor relationship is clearly a relationship in which the patient in entitled to extra protection mechanisms.

[98] Simitis in: Simitis, BDSG, § 4a Rn. 20 ff; Nink in Spindler/Schuster, Das Recht der elektronsichen Medien, § 4a BDSG, Rn. 1a

2.5 Is consent negotiable or not? / Where is the choice in informed consent?

2.5.1 Consent as a mean of executing choice

The true nature of concept of consent represents the power given to an individual over his or her own body and over his/ her life choices – it is stemming from one of the four main principles of medical ethics - the **principle of autonomy**. With increase of intensity and personality of the consequences of a choice increases the claim to autonomy in the making of a given decision.[99] Consent seemingly serves two primary values – the above-mentioned autonomy and well being of interested individual.[100] In his/her different roles: as a patient, research subject, or data subject, the individual is given control, which he/ she exercises by taking choices in those spheres of life. The choices individual is supposed to take should enhance his/ her autonomy and should be respected by all persons involved. However, hospitals and physicians have not only a mere responsibility to respect the choice taken by individuals, but rather have an obligation to the patient /trial subject to make consent.[101] The outcome of such an autonomous choice in the form of consent is morally transformative for the action in question.

By its transformative nature consent can be understood as a way of **executing choice**, and giving individual a choice is a true goal of informed consent.[102] When considering autonomous choices consent can be seen as having a positive and facilitative function or a negative and protective function – a positive function disallows enhancement of any medical procedures before the consent is given, while the negative function is securing that no intervention occurs without the consent.

The connection between consent and choice is so close that numerous historical justifications enlist cases where instead of the phrase "informed consent" a phrase "informed choice" is being used.[103]

Choice is, according to the Oxford Dictionary, understood as "an act of choosing between two or more possibilities"[104] and to choose, explains further Oxford dictionary, is to „pick out (someone or something) as be ing the best or most appropriate of two or more alternatives."

This is where the actual framing of the problem becomes visible – the crucial for exercising choices are the alternatives between which the individual can select. That is also what informed consent is aiming at: giving patient **control over alternative possibilities**. But the choice which is offered to a patient is a Hobson's one – the patient is standing before a take it or leave it option – or he or she will accept

[99] Marjorie Maguire Shultz, "From Informed Consent to Patient Choice: A New Protected Interest," *The Yale Law Journal* 95, no. 2 (December 1, 1985): 221.
[100] Franklin G Miller and Alan Wertheimer, *The ethics of consent: theory and practice* (Oxford; New York: Oxford University Press, 2010), 92.
[101] Ruth R. Faden and Tom L. Beauchamp, *The History and Theory of Informed Consent* (New York :: Oxford University Press, 1986), 17.
[102] Ibid.
[103] Ibid., 56.
[104] Catherine Soanes, *Compact Oxford English Dictionary of Current English*, New ed of 3rd revised ed. (Oxford University Press, 2008).

whatever the physician proposes in terms of treatment, research or data processing, or in most cases he or she will refuse to consent and by that will not receive (the proposed) treatment, will not take part in a clinical trial and finally his/her data will not be processed which results, as the alternative before, in not taking part in the clinical trial. Following Berg's line of thoughts[105] - informed consent aims at enhancing autonomy and it is critical for the process to expand individual choice – however when choice is not available no informed consent can effectively bring it.

The property of making a choice is rooted in one of the defining attributes of both **autonomy** and consent – the **voluntariness**.[106] According to standard definitions it is one of four preconditions of consent: disclosure, competence, voluntariness and understanding.

The condition of voluntariness was enlightened by the Nuremberg Code:

This means that the person involved should (...) be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over- reaching, or other ulterior form of constraint or coercion."

A voluntary consent is therefore one executed with no constrain and coercion – and these can be imagined as existing due to influence exerted by third parties, or as already mentioned above, created by the fact that there are no real viable option and therefore no genuine choice exists.

What has to be carefully differentiated here is the legal understanding of voluntariness in consent and the other accounts of role of voluntariness. In the legal account voluntariness is lack of coercion, duress, force, or constrain which are imposed by others. Whenever a consent has been given by individual where there was no constrain or coercion by a third person such a consent should be considered valid.

However, in a more ethical understanding of voluntariness of choice an account by Olsaretti[107] should be considered. Olsaretti[108] argues for dividing choices into free choices and voluntary ones – free being those given without coercion, or other influence from people, while voluntary choices are those where an individual has choice between acceptable alternatives, or at least the only option which he has is of his liking and he/she would have chosen it also if more choices would be available.

The situation is considered in more detail separately for the three consents.

[105] Jessica W. Berg, Paul S. Appelbaum, and Lisa S. Parker, *Informed Consent: Legal Theory and Clinical Practice*, 2nd ed. (Oxford; New York: OUP USA, 2001), 308.
[106] Faden and Beauchamp, *The History and Theory of Informed Consent*, 274.
[107] Serena Olsaretti, "Freedom, Force and Choice: Against the Rights-Based Definition of Voluntariness," *Journal of Political Philosophy* 6, no. 1 (1998): 53–78.
[108] Ibid., 56.

2.5.1.1 Consent for care

Consent for care is very diverged as daily care routine varies immensely – from diagnostics, through daily practice, until the complex surgeries the setting of consent is very different. Also the conditions for consent differ: from presumed consent in a general practice to written consents and more complex informed consent processes in case of surgeries. Nonetheless, what is important in every of those settings is the attribute of **choice** patients can have. That choice will be dependent on the actual alternatives existing in particular situation, but the second aspect influencing it will be the physician (or any other caregiver) himself. When assessing choice two situations are imaginable: the patient can choose from a number of alternatives for diagnostics, or care which are although of similar efficacy, or a particular one being more effective than others. After being introduced to the possibilities patient is requested to choose one, or none of them. A second possibility will take place when the patient is brought before an alternative – a single available treatment, or no treatment possible at all, where the choice is limited to accepting the diagnostics or therapy suggested. The latter is the one where choice, or voluntariness (as understood by Olsaretti) is limited.

2.5.1.2 Consent for clinical trial participation

Negotiability of informed consent and rules of participation is **even more limited** in case of clinical trials.

Clinical trials are guarded by very strict rules and the repeatability of certain actions and accuracy in executing research as well as identical course of trial among the trial centres and their research subjects are a precondition of success – only when those conditions are fulfilled the results of trial can be regarded as credible. Hence, the trial conduct is subject to very specific rules described in the study protocol.

One of the aspects of the aforementioned repeatability is the handling of research subjects. Usually the treatment and medicaments offered in the course of the trial are double-blinded – meaning that both the researcher and the trial subject neither are aware of what are the critical aspects of treatment and medication, neither can influence those in any way.

As a result of those conditions patient's consent can hardly be subjected to specific negotiation and give patient the possibility to determine the exact course of research (and by that influence the particularities to which he or she is consenting to and therefore is willing to agree on).

Furthermore, the position of the researcher in clinical trial has to be considered – for him/her first of all, informed consent is a non – negotiable (moral) obligation.

In order to ensure safety and integrity of patients/ research subjects and also comparability and exploitability of study results, all participating patients and trial subjects have to be treated according to the study protocol. The equal treatment of all patients/ study subjects ensures that data generated in clinical trials is reliable and robust which is a basic requirement of ICH – GCP.

Furthermore, the Clinical Trials Directive Article 3(g) stipulates that prior to the commencement of a clinical trial, the adequacy and completeness of the written information to be given and the procedure to be followed for the purpose of obtaining informed consent have to be evaluated by an Ethics Committee. That is only approved consent forms must be used in clinical trials.

In clinical research, patients and research subjects have only the choice between accepting all study specific requirements and take part in the study or reject participation and are treated according to alternative (routine) methods. Additionally, patients/ research subjects may, without being subject to any resulting detriment, withdraw from the clinical trial at any time by revoking his informed consent. This will not affect their ordinary treatment or the care given to them.

The crucial point regarding consent is not the choice whether to take part or not, but the fact, if such a decision has been taken fully **voluntarily** after full disclosure of potential risks and benefits and a well-executed informed consent process .

Sometimes within a clinical trial there are so called voluntary sub studies, often dealing with genetic issues. The participation is not mandatory. But as with clinical trials, the participation is voluntary in these studies but the content (procedures and interventions) of the consent is not negotiable.

In certain exceptional circumstances, issues that do not affect the objectives of the study may be discussed with the sponsors, like expense allowances e.g. travel expenses if patients live very far from the study site.

In clinical care the requirement complexity and intelligibility of IC, is less codified and often varies between countries and is also influenced by case laws, institutional policies or hospital interpretation of recommendations from professional and specialty groups.

Although the details of the laws, regulations and guidelines regarding IC in clinical care may differ considerably, the bottom line is that failure or deviation from informed consent renders any physician liable for negligence or battery and constitutes medical malpractice. And therefore physician will rather not negotiate legally defensible consent templates.

2.5.1.3 Consent for processing of personal data

The lack of choice is the most visible in the case of data processing where, to quote after Berg, “because of the realities of a situation choice is not available, no informed consent procedure can create it”.[109] Whenever patient is to participate in a clinical trial and so becomes a research subject, he or she will also have to consent for the processing of his/ her personal data. Therefore the patient / research subject has not one consent (and so choice to make) – whether he or she is willing to participate in a

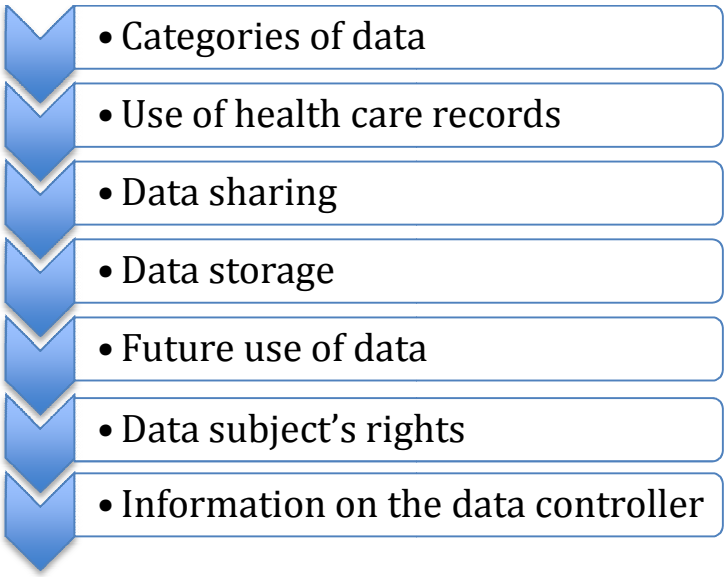
[109] Jessica W. Berg, Paul S. Appelbaum, and Lisa S. Parker, *Informed Consent,: Legal Theory and Clinical Practice*, 2nd ed. (Oxford; New York: OUP USA, 2001), 308.

trial, but also a second one whether he/ she is in accord with processing of his/her personal data. However, if the patient is willing to take part in a trial (and often that is the best possibility for treatment, given the survival rate in trial vs. in treatment only) the choice which he/she can take as to data processing is in fact **illusory**. A clinical trial cannot be conducted without processing of the personal data of the trial subjects, if therefore law requires obtaining from the trial subject also consent for data processing the patient /trial subject no patient can be admitted to a trial without such consent.

2.5.1.3.1 Negotiating consent for data processing

As much as consent for data processing in general is a sine qua non condition for the clinical trial participation and therefore trial subject's choice is to certain extent limited, as much it is the one which scope could eventually be a subject to negotiation.

In order to understand in how far the provisions of an informed consent form for processing of data can be subject to negotiation a differentiation between them is needed. Based on the CONTRACT D3.1 the following summary of kinds of provisions to be included in an informed consent for processing of data is provided:



Out of the list above most of the categories cannot be subject to negotiation e.g. categories of data which are needed for a particular trial are defined in the trial protocol – in order to successfully conclude the trial certain information needs to be provided (certain health or genetic information needed for particular tests etc.) – therefore providing it is not subject to negotiation, as without them the trial cannot take place. What however could be negotiated is in how far certain samples (who are also to be understood as bearing information) are to be included or shared with other institutions. Furthermore, trial subject could negotiate in how far his/ her personal information should be stored for future research, determining both the time of retention (above the legal minimum), as well as the scope for which the personal data shall be used.

2.5.2 Practical consequences

The idea of negotiable consent is from an ethical point of view very appealing, as it would broaden, or even implement individual's control into the informed consent. As such the idea is worth striving to. However, in practical terms a negotiable consent would be a **problem in a multitude of levels**. Firstly the process of obtaining consent is already now taking a considerable amount of **time** for the physician and requires effort in order to inform the patient – in case of negotiable consent it would possibly be more time consuming and more effort would be required. Secondly administrating negotiable consent would be a considerable **administrative burden** – considering that patients/ trial subjects would each make different choices following every individual and making sure that the physicians and medical stuff is acting accordingly with patient wishes, formulated in the consent form, would require manpower.

Technological solutions could support the negotiability of informed consent:

- Negotiable points within the IC can be supported in the preparation phase of the IC form by technological tools like the IC generator, which can provide a degree of flexibility in terms of providing e.g. multiple check boxes of available choices that would refine the consent. Of course, as mentioned above, it would be nearly impossible for clinicians and researchers to manage and act accordingly to a set of non-unique consents even if they were initially taken for a single trial. This would require checking for IC conformity for each data subject, every time his/ her data are being processed. A possible solution to this problem is offered by e-consent. The EnCoRe architecture[110] for example aims at allowing data subjects define and re-define, *at any time*, the purpose for which their personal information is used. Data subjects are encouraged to provide their privacy preferences when disclosing personal data by dictating a variety of constraints in the form of choices. These privacy preferences are: Allowed/disallowed purposes for using personal data; Consent for disclosing data to third parties; Allowed/disallowed lists of entities with which data can be shared or not; Notification preferences; Deletion Preferences; Other preferences related to data handling (e.g. data minimisation, etc.). Driven by the data subjects' privacy preferences an access control component is in charge of enforcing security & privacy policies on personal data every time access is requested. The above mentioned privacy preferences are stored alongside with other "metadata" in a repository, managed by a data registry manager component. In total, these metadata include: data subjects' preferences (determined by their consent and revocation choices);
- associations of privacy preferences to the actual personal data, stored in organisations' data repositories;
- information about the whereabouts of personal data, i.e. where the personal data has been disclosed to;
- additional information about personal data, such as provenance;

[110] See existing e-consent solutions: 3.1.4

The privacy policies are enforced by a trusted and secure agent or an interception point, which ensures that access to personal data is consistent with stated access control policies and data subjects' preferences. It handles data access requests coming from a variety of requestors such as people (employees), applications, services, other components etc.

Access to the data is either granted or not, based on the information of an access request (requestor's identity and/or role; identity of the data subject for which an access to their personal data has been requested; list of attributes (related to the data subjects' personal data) that the requestor wants to access (e.g. credit card, address, etc.); purpose of the request).

Since, as stated above, the privacy preferences can be changed at any time, such an e-consent implementation supports a form of negotiable consent. An obligation management system is responsible for notifying the data subjects about usage or disclosure of their personal data, dealing with transformation and minimisation of personal data, or with data deletion. Changes in privacy preferences (e.g. data deletion request) are propagated to relevant third parties, to whom data were already disclosed.

2.6 The right to know vs. the right not to know

2.6.1 Background

On the first view discussing both: right to know, as well as right not to know may seem contradictious to the main scope of a project which focuses on *informed* consent. That contradiction is derived from the sole reasoning of consent, especially with the addition of the adjective informed, which is stressing the importance of patient's right to be informed about possibly all of the consequences of the treatment / research he or she is going to undertake and on that basis take a conscious choice when it comes to treatment, research, data processing, or any other of his life choices (as consent in principle is a concept which appears not only in the medical law, but is also recognised in the other areas of human life, and therefore in other areas of law). The debates surrounding informed consent focus to greater extent on the quality and amount of information which the patient should be made aware of, than on the patient's choice whether he or she wishes to receive said information.

Nevertheless, the question whether patient has **a right, or rather an obligation to receive information** on his / her own condition has to be examined. It is even more so, as the new discoveries in the medicine and genetics area make it possible to reveal extensive information about one's genetic status and consequently may create a burden for the patient himself / herself. That burden may go as far as to become a psychological problem, where the so much argued concept of patient's autonomy can turn against the patient himself when the excess of information compromises patient's well being with the "burden of knowledge".

That stands in opposition to the general philosophical believe that knowledge is a marketable good with a value of itself.[111] Albeit the main objection against the consideration of the right not to know is that the duty to inform the patient is almost universally recognised both in ethical, as in legal sense. Legal acts, as well as non binding ethical guidelines pose an obligation on the health-care professionals to provide a thorough information to the patient / research subject, and lack of information is seen as negligence, results in void informed consent. Therefore, a double function of providing patient with information has to be assumed – one is that of securing that patient receives information (and the question posed here is whether he or she can discharge that right), but the second one is the legal obligation of the health-care-professional to provide such information to the patient; for fulfilling of that duty the professional will be held liable.

In order to argue the status of right (not) to know underlying concept(s) have to be analysed. At the outset the concept of **autonomy** will be analysed for this aim.

[111] The debate on the value of knowledge started by Socratese, quoted by Plato: Plato, Alexander Sesonske, and B. N Fleming, *Meno; text and criticism.* (Belmont, Calif.: Wadsworth Pub. Co., 1965).

2.6.1.1 Autonomy as a basis of right not to know

Autonomy is a notion rooted in the liberal Western tradition[112] that focuses on the importance of individual's choice and freedom – that concept underpins all the levels of individual's life and, as reason i.a. Faden and Beauchamp[113] it is strongly connected with other notions like privacy, voluntariness, self-mastery, choosing freely, and responsibility for one's choices.[114]The principle of autonomy represents the trend which moves away from the patriarchal model, where the choices are made not by the concerned individual, but by a superior third person, who due to their special position or knowledge should be more capable of making a reasonable decision.

Accepting autonomy as a core value in healthcare requires that the health care providers respect individual's power and individual's perspectives to make their own choices, which are often not based on objective knowledge, which in typical cases is more extensive on the side of health care provider, but rather on the subjective understanding, which individual has, of his / her own life, views and preferences. That at the final stage also means that the concerned individual is capable of better judging how the choice he or she is making will affect him / her and his / her life.

The concept of autonomy is largely derived from Immanuel Kant's work.[115] Humans, according to Kant, are agents who are morally self- governed, and so are to be seen as autonomous.[116] Furthermore, Kant argued that people are ends, and not solely means to an end, and therefore, are beings capable of judging and taking choices on their way of life. Because of that individual should not be subject to the mere decisions of a third persons and he / she are not to be treated as ends of others.[117]

For an action, or a choice, to be considered autonomous, it requires fulfilling certain preconditions. According to Faden and Beauchamp[118] there are three conditions which need to be fulfilled for the action to be considered so. Those three are intentionality, understanding and non-control (voluntary choice). For considerations of right (not) to know the question of understanding is the crucial one as it determines what sort of understanding on the side of individual is needed in order to secure that the choice taken by him / her is still autonomous.

2.6.1.1.1 Understanding as a condition of autonomous actions

Faden and Beauchamp commence their dwellings on condition of understanding by stating: "An action cannot be autonomous if the actor fails to have an understanding of his or her action."[119] Further in the

[112] Faden and Beauchamp, *The History and Theory of Informed Consent*, 7..
[113] Ibid.
[114] Ibid.
[115] Immanuel Kant and H. J Paton, *Groundwork of the metaphysic of morals* (New York: Harper & Row, 1964). Compare i.a. Emanuel, *The* Oxford *Textbook of Clinical Research Ethics*, 606; Faden and Beauchamp, *The History and Theory of Informed Consent*, 8..
[116] Jerome B. Schneewind, *The Invention of Autonomy: A History of Modern Moral Philosophy* (Cambridge University Press, 1998), 483.
[117] Faden and Beauchamp, *The History and Theory of Informed Consent*, 8.
[118] Faden and Beauchamp, *The History and Theory of Informed Consent*, 241.
[119] Ibid., 248.

discussion the authors argue that there is surprisingly little on "understanding of understanding", they also elaborate on the variability with which patients or subjects understand information provided to them on the treatment, research, risks and consequences. However, they do not consider what should be the subject of understanding. And the subject of understanding, it could be argued, can be although the aforementioned information about diagnosis, prognosis, research, risks, but it could also be the understanding of the pure fact of taking an autonomous choice and autonomously choosing to do so without all the available information, but maybe with, in the subjective view of the individual, sufficient amount of information.

That would result in the health care subject only to be aware that he / she is to make a choice, while the health care professional would be responsible for supporting that choice and offering as much, or as little information as required by the individual.

Similarly Andorno,[120] and O'Neill[121] state that the decision about receiving the information should be respected to the same degree as any other autonomous decision in health care and that "the amount and level of information given should be dictated by the patient, donor, or research subject, not by the physician"[122].

However, also an opposite view is represented: "autonomy analysis does not permit us to respect a person's state of non-knowledge. Autonomy requires choice and choice requires information through disclosure"[123]

2.6.1.2 Other grounds for individuals right (not) to know

Next to autonomy as a basis of right not to know there are also other views on the background of this right – Laurie[124] argues that the autonomy model is deficient and argues for privacy as fitting for the model better. The respect-for-autonomy-paradigm, values a patient's right to know, claims Laurie, but places little value on a patient's right not to know. The latter, he posits, can be assured by privacy.

Autonomy is, as describes Laurie[125], rather ill-equipped to provide solution, as it relies on the individual's ability to control various aspects of his/ her life and therefore patients are often placed in "the invidious position of having to make choices that they might otherwise have avoided". [126]

[120] R. Andorno, "The Right Not to Know: An Autonomy Based Approach," *Journal of Medical Ethics* 30, no. 5 (October 1, 2004): 436.
[121] O. O'Neill, "Some Limits of Informed ConsentR. Andorno, "The Right Not to Know: An Autonomy Based Approach," *Journal of Medical Ethics* 2930, no. 5 (October 1 (February 1, 2003): 4–7, 2004): 436.
[122] Ibid.
[123] Graeme Laurie, *Genetic Privacy: A Challenge to Medico-Legal Norms* (Cambridge University Press, 2002), 189.
[124] Laurie, Genetic *Privacy*.
[125] G. Laurie, "Commentary," *Journal of Medical Ethics* 30, no. 5 (October 1, 2004): 443.
[126] Ibid.

Laurie argues that the sole act of asking a patient about his will of knowing or not knowing, already compromises the right not to know, as in cases it will already give the information to the patient. Therefore, an assumption should be made that, whenever genetic testing is done and there is no reasonable assumption about person's wishes the interest in not knowing should be recognised. [127] Laurie argues that there is a need to weight against each other the interests of individual and his relatives, against the decision not to disclose information and by this protect individual's privacy. Such an approach is rather moving away from the autonomy and choosing to act paternalistic instead, but according to Laurie, that is the one, which allows for sufficient individual's protection.

Further account of right not to know suggests that although autonomy is ill-fitted to provide individuals with right not to know the right to liberty may serve the cause instead. It is so, write Harris and Keywood, as liberty allows limiting autonomy: "right to liberty where liberty includes the right to make free, but non-autonomous decisions or autonomous but autonomy-limiting decisions."[128]

2.6.2 Right to know, right not to know and consent

The question whether when thinking about right to know, and so also speaking about informed consent we speak about the disclosure or about comprehension of information has to be asked. Is it enough to make the information available to the patient and leave him with the possibility to choose – to read, giving the chance to meet the doctor and speak about doubts, require more information etc. or rather to decide – that information is available to me but I choose to decide freely without it and I choose not to know.

That touches also the very basic question of consent – the question how the "informed" consent should be understood. Is it understanding as giving all the available information or is it the possibility of receiving as much information as one is willing and capable of adopting? If autonomy starts with the very first question which health care subject is to ask himself: "how do I take that choice?" – "how do I choose to be informed?" – "in how far I want to receive information?" That is what should be considered true autonomy – to accept that the patient can take a choice not only purely subjective (which he does by sole fact of being himself and taking a choice in his own case) but also eventually an irrational choice based on no objective information – if he or she chooses to do so.

The question reaches also further – the right to know and not to know may be considered on a first stage as a question about one's state of health. But on a second level it can be asked whether patients and research subjects can choose to take uninformed choices – to choose to undergo treatment or research without realisation of their full risks and consequences.

[127] Laurie, "Commentary," 441.
[128] J Harris and K Keywood, "Ignorance, Information and Autonomy," *Theoretical Medicine and Bioethics* 22, no. 5 (September 2001): 426.

2.6.3 Legal standing of right not to know

The debate about right not to know is taking place between the legal scholars, next to that the right not to know is, or is not being recognised by the binding legal laws.

2.6.3.1 Recognition of the right not to know in various international legal instruments

Despite the controversy and the philosophical debate which surrounds the right not to know, this right has been recognised in a number of legal instruments of various level. The most important international documents that consider it are shortlisted here.

Council of Europe Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo Convention) – Dated 04.04.1997[129]

Article 10 – Private life and right to information

1. *Everyone has the right to respect for private life in relation to information about his or her health.*

Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed.

In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient.

UNESCO Universal Declaration on the Human Genome and Human Rights – Dated 11.11.1997[130]

Article 5

(c) The right of each individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected.

World Medical Association Declaration of Lisbon on the Rights of the Patient – Adopted 1981, amended in 1995 and 2005.[131]

Article 7 – Right to information

[129] Available online: http://conventions.coe.int/Treaty/Commun/QueVoulezVous.asp?NT=164&CL=ENG
[130] Available online: http://portal.unesco.org/en/ev.php-URL_ID=13177&URL_DO=DO_TOPIC&URL_SECTION=201.html
[131] Available online: http://www.wma.net/en/30publications/10policies/l4/

a. The patient has the right to receive information about himself/herself recorded in any of his/her medical records, and to be fully informed about his/her health status including the medical facts about his/her condition. However, confidential information in the patient's records about a third party should not be given to the patient without the consent of that third party.

b. Exceptionally, information may be withheld from the patient when there is good reason to believe that this information would create a serious hazard to his/her life or health.

c. Information should be given in a way appropriate to the patient's culture and in such a way that the patient can understand.

d. The patient has the right not to be informed on his/her explicit request, unless required for the protection of another person's life.

e. The patient has the right to choose who, if anyone, should be informed on his/her behalf.

2.6.3.2 Recognition of the right not to know in Clinical Trials Directive

The question to ask is whether the Clinical Trials Directive envisages or at least accepts a right of the patient not to know when deciding to participate in a trial.

The Directive strongly underlines the duty of providing trial subject with information prior to obtaining his/her informed consent. The objective of providing information is not only mentioned in Article 2 (j) which defines "informed consent" but also reinforced in Article 3 where protection of clinical trial subjects is the focus.

Definition in Article 2 stresses importance of information given to the patient for the decision in question. Informed consent can only be taken:

"after being duly informed of its (clinical trial) nature, significance, implications and risks."

The wording suggests that this duty is obligatory and that patient cannot discharge it in any manner. Support for this interpretation can be drawn from the commentators of German AMG law that transposes Directive into German legal grounds. Deutsch states[132] that certain information "unconditionally have to be provided to the subject." Also the Polish law, which literally translates Article 2 of the Directive, does not provide the possibility to omit any information to the patient on his/her request. Rather, as notes Kondrat at all. "the subject or his statutory agent must be informed"[133] about all aspects of the trial.

[132] Erwin Deutsch, *Medizinrecht: Arztrecht, Arzneimittelrecht, Medizinprodukterecht Und Transfusionsrecht* (Berlin ::: Springer,, 2008), 926 and 964.
[133] Mariusz Kondrat et al., *Prawo Farmaceutyczne Komentarz* (Warszawa: Wolters Kluwer Polska, 2009), 37f.2.

However, the wording of Article 3 could be interpreted in opposing manner. This Article states:

2. A clinical trial may be undertaken only if, in particular:
(b) the trial subject or, when the person is not able to give informed consent, his legal representative ***has had the opportunity****, in a prior interview with the investigator or a member of the investigating team, to understand the objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted and has also* ***been informed*** *of his right to withdraw from the trial at any time;*

What should be noted here is the difference between the wording of the two parts of this article: the first one speaking about **opportunity to understand** and the second one referring to **being informed**.

Such a construction could be interpreted as dividing the information which has to be provided to the patient in two groups. The first one consisting of "objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted" the second one being the right of withdrawal.

If one is to take the wording of the Directive literally the two groups are treated differently. The information included into the first group should be accessible to the person in question – the trial subject should have a chance to understand the topics as the Directive requires "**opportunity (…) to understand**." However, for the second group where a sole opportunity to understand is not sufficient – the patient has to be **successfully informed** about the right to withdraw.

From the abovementioned a certain degree of trial subject's freedom in determining the scope of information could be concluded. If subject has "opportunity to understand" then it can be understood that he/she has also a "right not to know" (as he/she chooses not to use the opportunity) – on the other hand information about the right of withdrawal is inalienable and patient has to be made aware of possessing the right. In such understanding the patient could decide whether and in how far he/she wishes to obtain information on the research questions of the trial and eventually make a use of the right not to know and remain ignorant.

The opposing understanding of both articles makes it unclear what was an intention of the European legislator. Was it to award patient with control over the amount of information he/she is willing to receive, or should Article 3 rather secure that the health professional gives trial subject a possibility to discuss clinical trial, while at the same time having no obligation of making the clinical trial subject understand its objectives. When considering the wording of Article 2 and its word-for-word understanding the latter seems to be the case.

In light of the above mentioned it seems that the right to be informed, as the right to consent for a clinical trials cannot simply be discharged by a person – seen as such in the scope of Directive the clinical trial subject has an obligation to be informed about the trial he or she is going to take part in and therefore the Clinical Trials Directive does not provide a right not to know.

This can constitute a serious drawback of when considering a joint trial and treatment possibility – national legislations provide a possibility to refuse information about ones state of health (e.g. according to Polish Act from 6 November 2008 on Patients' Rights and the Commissioner for Patients' Rights patient has a right to request from the doctor not to receive information about his / her health condition (art. 9(4))), however this right cannot be executed whenever treatment shall be part of a clinical trial.

2.6.3.3 Recognition of the right not to know in national legislation

Next to the international documents also the national legislations award patient with the possibility to refuse information concerning his health situation (more insights on the patient's right in the national legislation of four chosen European legislations can be found in CONTRACT D3.1 Initial report and guidelines on identified good practice cases).

2.6.4 Interests of third persons

Whenever an individual is to choose not to be informed a question in how far third persons are to be affected by such a decision arises. That applies mostly in case of genetic information, which by its nature discloses vital information about relatives of the concerned individual, as Chadwick notes the move from "I" to "we" is needed, whenever considering any choices over genetic makeup. The information which is obtaining during testing is firstly subject to the medical secrecy, secondly it is also personal data of the individual, therefore the decision about receiving this information and about sharing it with other persons lies with the person himself / herself. However it should be considered in how far concealing information from the people who are indirectly concerned with it can be considered unethical.

The interests of patient have to be weighed against the interests of the "broader public" – an evident case where the two interest clash is of HIV positive patients: whenever during blood testing the doctor I adiscovers that his/her patent is HIV positive –not only the patient has interest in that knowledge, but also his relatives and close ones have a vital interest in knowing. However, patient may deliberately refuse to know and even more refuse to share such information with third persons.

2.6.5 Summary

Both in the ethical and moral debate, as well as in the legal recognition of right not to know there is no clear stance on whether and if yes on what grounds this right exists and arguments for both exists.

The ethical debate about right to know and not to know is focused with finding justification of individual's ignorance, finding it within autonomy, liberty or privacy, additionally it tries to weight against each other risks and benefits of granting such a right to humans.

The legal recognition on the other hand differs depending on the scope of consent and legal framework. The right not to know is widely recognised in many international sources, with

special focus to genetic information, on national level the right not to know one's medical condition is given recognition as well. However on the European landscape the Clinical Trials Directive does not recognise the right to refuse information.

Whether a change in this respect is needed is disputable – a clear possibility to refuse information with which individual cannot cope can contribute to well-being, however, it can also cause his/her lesser participation in decision-making.

However it seems arguable that in pursuit of patient's freedom in decision-making also the scope of information should be left to patient's discretion. .

2.7 Clinical Problem Analysis

Clinical trials are essential to achieve better treatments for patients. As a result of the Clinical Trials Directive 2001/20/EC (EU CTD) the conduct of clinical trials throughout Europe has changed. Brandon Keim writes in Nature Medicine: "The cost of academic cancer trials has doubled since 2004, according to Cancer Research UK, the country's largest sponsor of academic cancer research". [134] The European Organization for the Research and Treatment of Cancer estimates that expenses have risen by 85% and says the number of trials it supports has dropped by 63%. The Save European Research campaign, which represents more than 3,000 scientists, says academic drug trials have dropped by 70% in Ireland and 25% in Sweden. The number of Finnish academic drug trials shrunk by 75%". Kathy Pritchard-Jones summarizes in the European Journal of Cancer key issues for Cancer Trials. [135] Though this article deals with clinical trials for children, most of these points are also relevant for clinical trials in adults.

The following table is extracted from this article.

[134] Keim B: Tied up in red tape, European trials shut down. Nature Medicine 13:110, 2007

[135] K. Pritchard-Jones: Clinical trials for children with cancer in Europe – Still a long way from harmonisation: A report from SIOP Europe. Eur J Cancer 44 (2008), pp2106-2111

Issue	Experience of European paediatric study groups running investigator-led ('non-commercial') trials in childhood cancers
Definition of an interventional clinical trial	'Standard of care' regimens often include medicines used 'off label' Variation in acceptance by national regulatory authorities of such use as 'background medicine' or whether it falls outside the definition of an 'interventional clinical trial'
Sponsorship	National variation in whether a single European sponsor is required or a national co-sponsorship arrangement is accepted Complex contractual negotiations required between partners
Insurance and Indemnity	Large variation in costs and in whether 'no fault' indemnity is required Insurance costs increased 100-fold with no perceptible change in risks between consecutive trials of the same study group Premiums may be paid by fundraising efforts of childhood cancer parents' associations
Definition of an IMP	Hugely variable for use of old drugs with no or limited paediatric information in their marketing authorisations IMP definition has major impact on bureaucracy of pharmaco-vigilance
Pharmaco-vigilance	Hugely bureaucratic with no noticeable improvement in patient safety (which was in any case very good in childhood cancer trials) National variation in onward reporting requirements for SUSARs when drug is used in more than one trial Inconsistency in inspection findings of regulatory processes for the same trial
Sponsor obligation to provide free drug	Large national variations in how this is absorbed into national health insurance schemes or whether this must be paid for by sponsor Required for IMPs, whose definition is also variable
Drug formulations adapted for children	Lack of appropriate formulations for young children for many oral anti-cancer drugs Strict definition of 'manufacturing' excludes young children from some clinical trials when no appropriate formulation exists
Ethical considerations	Ethical committees need appropriate expertise to evaluate appropriateness of new drug trials in children Timelines to receive the 'single' national ethical approval highly variable Institutions have created other hurdles to opening a trial, variably labelled 'R & D' approval

Table 2: Key issues for Paediatric Cancer Trials in relation to the EU Clinical Trial Directive 2001/20/EC

The availability of clinical trials to children in Europe is threatened as investigator-led, non-commercial trials struggle to find the resources necessary to comply with the EU CTD. [136] The overall aims of the directive were to standardise the regulation and quality of trials and ensure patient safety. The EU CTD has had a disproportionately negative impact on trials in childhood cancer. This is because nearly all trials require international participation in order to achieve necessary recruitment. [137]

[136] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001, <http://www.eortc.be/Services/Doc/clinical-EU-directive-04-April-01.pdf>; J. Hearn, R. Sullivan: The impact of the clinical trials directive on the cost and conduct of non-commercial cancer trials in the UK. Eur J Cancer, 43 (1) (2007), pp. 8–13; C. Mitchell: Clinical trials in paediatric haematology–oncology: are future successes threatened by the EU Directive on the conduct of clinical trials? Arch Dis Child, 92 (11) (2007), pp. 1024–1027; A.J. Baeyens: Impact of the European clinical trials directive on academic clinical research. Med Law, 23 (1) (2004), pp. 103–110.

[137] K. Pritchard-Jones: Clinical trials for children with cancer in Europe – Still a long way from harmonisation: A report from SIOP Europe. Eur J Cancer 44 (2008), pp2106-2111

In detail the following problems in clinical care of patients do exist today:

- There is a **time lack for physicians** being kept informed about all the new developments in medicine, even in their specialized field. Every week hundreds of new papers are published. To find the most relevant, to read them all and to judge them as important for the own work is impossible.
- Today **teamwork** is of utmost importance. No physician is able to treat a patient with cancer by his own. He always has to **communicate and work together** with other specialists in medicine. As a result a lot of so called Cancer Comprehensive Centres are established to facilitate the interdisciplinary work. But up to now no IT infrastructure is supporting this by storing all relevant data in a database, so that every treating physician will have immediate access to the history, diagnosis, treatment and other relevant data of patients in an anonymous and secure way.
- Physicians **do not get feedback of how efficient they are working**. They do not have any statistics regarding the survival of their patients compared to the survival of all patients with that kind of cancer. There is no benchmarking telling them they are doing good or bad.
- Physicians do not know about the possibilities of modern IT technologies that could help them to support them in daily care of patients, or in developing new clinical trials. The lack of this knowledge leads to a lack of requests and requirements to IT people for the creation of new and user friendly tools in this respect.
- Only a **minority of patients are enrolled in prospective clinical trials**. The reason for this is manifold:
    - Physicians do not (want to) enter patients in clinical trials because
        - they fear the burden of workload by entering patients (documentation, regulatory and administrative necessities, etc.)
        - they are not well informed about the meaning and impact of clinical trials (fear of experiments with their patients, simply not used to enrol patients in clinical trials, etc.)
        - in most curricula of Medical Schools Clinical trials are missing, so that students will not learn about the beneficiaries of clinical trials
    - Patients do not want to enter a clinical trial
        - they are not informed at all about clinical trials
        - they are not well informed about the meaning and impact of clinical trials (fear of taking part in an experiment, etc.)
    - There is no financial and/or administrative support to cover the overhead of clinical trials
        - the burden of European regulations contrasts the available resources to increase the number of new clinical trials
        - infrastructures in hospitals or outpatient facilities are lacking (no data manager, etc.)

- Today patients do use the **internet** to get information about their disease. There is no way how a patient can **trust** such information. Often information is contrary and alienates patients.
- Even if patients do find relevant information, they may not understand the medical language used in these information.

More patients are asking for second opinions regarding their disease. This is time consuming for physicians, expensive for the health care system and often unsatisfying for patients. They often get different and contrary answers resulting in the question: “And what should I do now?”

3 Outcomes and alternatives to consent: what is the way to go?

3.1 e-Consent

3.1.1 Introduction

Through the whole of CONTRACT project it was argued that despite the crucial role of consent in the recent medical ethics and the importance this process is given in the law many constrains appear when seeking to obtain meaningful consent from patients and trial subjects.

E-consent, or electronic consent is to be understood as automated tool(s), which with the help of new technology aid the physician in the informed consent process of the patient / clinical trial subject. The e-consent solutions should lead to obtaining consent of the same value as the conventional paper consent forms, but should do so with the help of mobile devices, working stations, tablets etc. The gain should be two-fold – on one hand it should support patient's comprehension of information given and understanding what procedures and in what course will be offered to him/her, on the other hand the management of consent should improve. The improvement in management expected should help to reduce the time and money invested in the procedure, support physicians and trial monitors in keeping an overview of consents given, as well as enable audit of consent.

E-consent is sometimes seen as an answer to the problems raised in the analysis above. Health care providers consider e-consent as a technological solution that should assist them in delivering meaningful consent, and at the same time a tool supporting them in fighting the rising costs and timing problems surrounding the procedure.[138] The first implementations are already in place and some of them demonstrate a significant growth in patient's comprehension of presented information.[139] To demonstrate this, this deliverable provides in first instance an overview of these technical solutions. In a second instance the deliverable deals with the legal aspects of an electronic consent process.

However, in assessing whether e-consent is a possible solution for the future not only practical issues and possible gains have to be taken into account. Consent is, among other, a legal act, which nature and requirements have to be considered and evaluated.

[138] Haruhisa Fukuda et al., "The Subjective Incremental Cost of Informed Consent and Documentation in Hospital Care: a Multicentre Questionnaire Survey in Japan," *Journal of Evaluation in Clinical Practice* 15, no. 2 (April 2009): 234–241.

[139] A „Patient- Friendly System for Informed Consent via iPad® Application" proposed by Mytrus company (from San Francisco, US) should improve patient's comprehension. Mytrus webpage states: „Twenty-four hours after completing the informed consent process, 76 percent of patients using the iPad application successfully passed a comprehension quiz; only 52 percent of patients using traditional paper-based forms„ demonstrated an understanding of the informed consent procedure." See: http://www.mytrus.com/news/article/20120409-ipad-icd , Retrieved: 5 August 2012.

Advance of Information Communication Technologies (ICTs) furnish health care providers with the opportunity to improve patient care by streamlining clinical processes and creating a seamless flow of information. It is very common that the scope of this information varies from organization-wide Electronic Medical Records (EMRs) to Electronic Health Records (EHRs) shared between different organizations. Although, this can improve the effectiveness of the information exchange, coordination and usage, it also can raise patient privacy challenges and issues[140].

In most cases, the primary purpose of gathering patient information is to provide healthcare for a specific episode related to that patient. Using this data for alternative purposes, must be in accordance with the patient's consent. It has been argued that patients should be aware of all the systems that are collecting their information, and should be able to specify how this information will be used[141]. Furthermore, each patient should be able to choose a consent policy that reflects his/ her wish of how the information is to be processed. Ideally, an electronic information system would automatically grant or deny permission to access a patient's record according to the corresponding consent policy. Therefore fine grained privacy rules on information usage, with exceptions for emergency access are needed. However, it is often difficult, if not impossible, to predict all future-use scenarios and enforce patient consent in an appropriate manner. As illustrated, e-consent is at the confluence of Healthcare, Information Technology and Law.

[140] Atif Khan, Sarah Nadi, David R. Cheriton, "Consentir: An Electronic Patient Consent Management System", School of Computer Science, University of Waterloo, Ontario, Canada.

[141] E. Kluge, "Informed consent and the security of the electronic health record (EHR): some policy considerations," International Journal of Medical Informatics, vol. 73, no. 3, pp. 229–234, 2004.

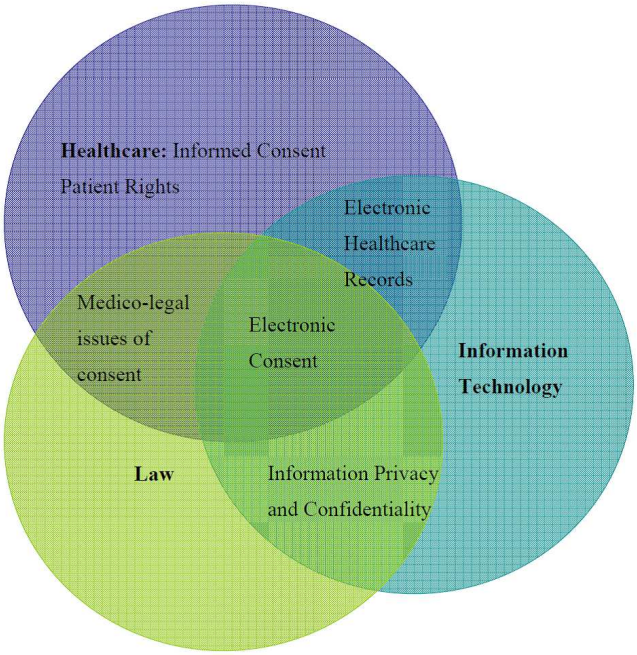


Figure 1 Influences on Electronic Consent[142]

Solution to these challenges and issues can be delivered by e-consent systems that can ensure that patients are informed about the consequences of their clinical intervention and can preserve the privacy of patients' data. This chapter aims in reviewing the existing e-consent solutions and to investigate how they fit within the existing regulatory framework. A study of the various scenarios in which e-consent can be utilized together with a description of the technical and legal requirements for each scenario is included in the CONTRACT deliverable D4.2. Final report and guidelines on identified good practice cases[143].

[142] Sophie K. S. Cockcroft, "e-Consent: provenance, use and future role", International journal of internet and enterprise management: IJIEM. - Olney: Inderscience Enterprises, ISSN 1476-1300, ZDB-ID 21484302. - Vol. 6.2009/10, 4, p. 315-325, 2010.

[143] See Section II, 3. IT and Security systems for informed consent handling.

3.1.2 General requirements for e-consent solutions

Before discussing electronic consent, the underlying health data issue of informed consent needs to be addressed. 'Informed consent' and 'patient consent' are usually used to describe an arrangement between healthcare provider and consumer. The meaning of the term 'patient consent' defines the fact that a patient is willing to share personal health information and where appropriate to receive a course of medical treatment. On the other hand, informed consent has (legally) a very particular meaning, and in many cases was the subject of some controversy. Informed consent requires that the patient is informed, before any request for information, or treatment, about who will access their personal record, how this information will be shared, the actual usage of this information and the risks associated with the prescribed medical treatment or clinical trial[144]. The patient has to be able to decide independently if he/she does want to undergo medical treatment or participate in a trial or not.

A lot of effort has been done to place consent into action in information systems through the concept of e-consent. Four different levels of consent are modelled[145]:

"**Level 1 - General consent:** This level corresponds to an 'opt-out' model, in which a patient is assumed to give blanket consent to any information request so that no further agreement is necessary either for a new episode of care or for the release of information for any other purpose."

"**Level 2 - General consent with specific exclusions:** In this case, a patient accepts a general consent but the permission excludes certain categories of information (e.g. gynaecological or sexual disease information), identified parties (e.g. insurance companies), or disclosure for a particular purpose (e.g. for employment)."

"**Level 3 - general denial with specific consents:** This situation is the analogue of level 2 except that here the patient denies all access to their health data with the exception of certain categories of information (e.g. demographic details related to a specified medical condition), identified parties (e.g. general practitioner), or disclosure for a particular purpose (e.g. for a prostate cancer survey)."

"**Level 4 - general denial:** This case equates to an 'opt-in' model in which a patient is assumed to deny consent for information to be used in future circumstances. Each new episode of care or request to use personal health information therefore requires explicit consent."

[144] Sophie K. S. Cockcroft, "e-Consent: provenance, use and future role", International journal of internet and enterprise management: IJIEM. - Olney: Inderscience Enterprises, ISSN 1476-1300, ZDB-ID 21484302. - Vol. 6.2009/10, 4, p. 315-325, 2010.

[145] Galpottage P. A. B. and Norris A. C., "Patient consent principles and guidelines for e-consent: a New Zealand perspective", Health Informatics Journal March 2005 11: 5-18, doi:10.1177/1460458205050681.

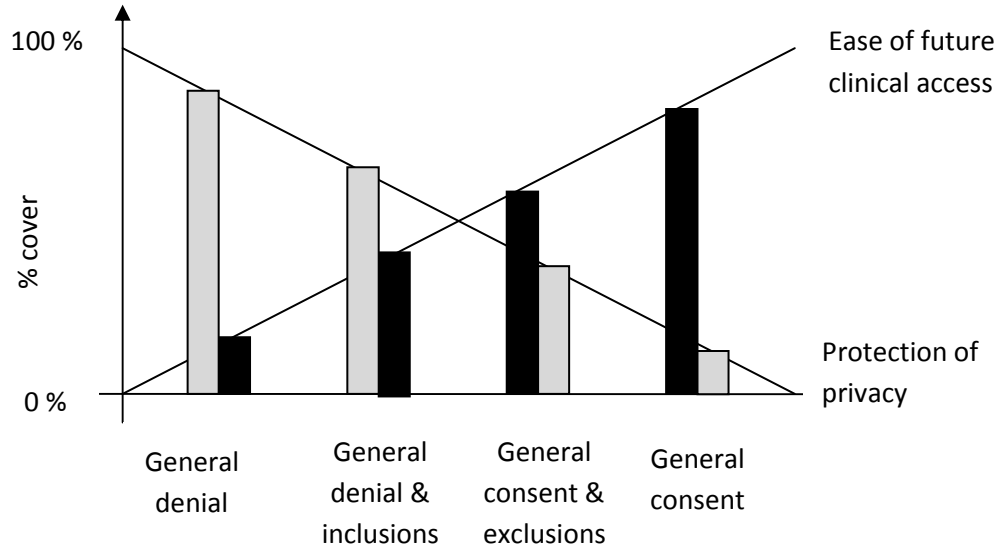


Figure 2 Different forms of consent balance clinical access and patient privacy in different proportions[146]

The following set of principles is proposed as bases for requirements of an e-consent system[146]:

- The system should permit access to confidential patient information by checking that patient consent exists for the information request by invoking methods that check for explicit, inferred, or implied consent.
- It should allow access to patient information to those individuals who have been explicitly permitted by a patient to view their information.
- It should never allow access to patient information to individuals who have been explicitly denied access by a patient.
- It should allow access to patient information to individuals who can be determined to have inferred or implied consent on the basis of their clinical role or responsibility or the clinical circumstance.
- It should not endanger patient safety by denying access to information by clinically approved individuals where consent is either indeterminate or in defined circumstances denied.
- It should not impede clinical work by denying access to information by clinically approved individuals, where consent is indeterminate
- It contains security safeguards that prevent provably unauthorized individuals from accessing patient information by circumventing the consent checking mechanism.

[146] Enrico Coiera, Roger Clarke, "e-Consent: The Design and Implementation of Consumer Consent Mechanisms in an Electronic Environment", Journal of the American Medical Informatics Association Volume 11 Number 2, pages 129-140, Mar/Apr 2004

- It should minimize the number of requests it makes to clinicians and patients to avoid unnecessary impediment or disruption of the clinical process or the private lives of individuals.
- It should not require an expensive or burdensome administrative infrastructure to support the obtaining and determining of consent and performance monitoring of the system.

3.1.3 Legal requirements for e-Consent

3.1.3.1 Formal requirements for consent in care

An exhaustive analysis of requirements of consent for care falls out of the scope of CONTRACT Project as these are subject to national law and differ from country to country, however during the project run a comparative view on the consent for care framework in Belgium, Germany, Poland and UK was offered in Deliverable 3.1. In general, it can be concluded that in many of every day care situations oral consent or any act signifying agreement suffices, while in cases of serious treatment and/or surgery consent in writing is expected. In the setting of requirements for consent for clinical trials the requirement of hand-written signature brought by the Clinical Trials Directive will be analysed in context of e-consent. Therefore, the requirements towards electronic consent will be assessed according to the Directive 1999/93/EC of the European Parliament and of the Council of 13 December 1999 on a Community framework for electronic signatures[147] (Electronic Signatures Directive), these apply also in the case of consent for care given in writing, while additional particular regulations from the national legislation cannot be excluded.

3.1.3.2 Formal requirements for consent in clinical trials

The Clinical Trial Directive defines informed consent in Article 2(j) as: “decision, which must be written, dated and signed, to take part in a clinical trial, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented […].”

While the directive poses many requirements towards consent not all of them will be challenging when moving from the paper-based procedure into an electronic consent. Therefore, it is needed to divide all the requirements, which have to be fulfilled into those which are influenced by the electronic form of consenting and those which are not.

Consent being a free decision, given prior to beginning of the trial and after being duly informed are crucial for the consent, but the shift towards electronic consent will not disable fulfilling those legal requirements. On the other hand the formal requirements of a decision that has to be given in writing, dated and signed have to be analysed with a view on the legal understanding of those terms.

[147] Available online: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31999L0093:en:HTML ; retrieved on 5 August 2012.

Giving a decision in writing is opposed to the oral form of giving consent – which is also foreseen in the Directive, as a way of consenting in special circumstances, when the future trial participant cannot consent in writing (Article 2(j) stipulates: " if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation"). The possible functions of writing requirements would be i.a.: to provide tangible evidence of the informed consent and information which was given to the trial participant; to help the trial participant in understanding that he/she is consenting to take part in the trial; to be of reference to the trial participant later, after the end of the procedure; to allow audit and reference for the persons responsible for the trial on the trial site and by the trial sponsor.

It is therefore to consider, whether Directive's requirement of written form of the informed consent form can be fulfilled by a written electronic consent, or whether it can be fulfilled by a paper-based written document only. As the Directive does not in any sense support rather one over the other it has to be considered whether the above mentioned functions given to the written form of consent can be fulfilled in an electronic written form, as they can be in a paper-based one.

It should be underlined that these functions can be fulfilled in the form of paper-based writing requirements, but, with guaranteeing appropriate technical solutions, can also be secured for written electronic versions (i.e. trial subject should receive a copy of the informed consent he/she had signed; also, as proposed by some already existing solutions a possibility to login in order to retrieve his/her consent).

What shall however be considered is that some of the e-consent solutions propose substituting lengthy consent forms with films, animations or any other form of graphic depictions of what is proposed to the trial subject. That shall aid future subject's comprehension – those materials can be seen as supporting the process of consenting, but replacing the consent form with them would be in breach of the requirement that consent has to be written.

The requirement of dating the informed consent form is not posing any problems for the electronic consents, what more such systems can secure by setting a reminder, that the trial subject will put a date on the informed consent form.[148] What can be problematic in the light of moving from paper-based forms towards the electronic forms is the requirement of signed informed consent forms.

The European Union Electronic Signatures Directive seeks to establish a common framework for the use of electronic signatures and secure that those signatures are commonly recognised. One of its major aims was to assure the non- discrimination principle of electronic signatures, as established by Article 5.2 That principle shall safeguard that electronic signatures are legally effective. However, it has to be considered that the framework proposed by the Directive consists of three different electronic

[148] The Clinical Trials Directive does not explicitly mention that the date has to be written by the subject, however it is a common practice enisaged by the ICH Guidelines E6 that : „prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject**"** (as stated in 4.8.8).

signatures, each of different strength – those three will be shortly overviewed here to establish which of them can be used instead of a handwritten signature on a paper-based informed consent form.

The most plain of signatures for electronic use is the electronic signature, which is defined as data in electronic form which are attached to or logically associated with other electronic data and which serve as a method of authentication. This is the most basic of the three signatures, which however cannot be used for signing informed consent forms, as it is not recognised as equivalent of a handwritten signature. Therefore, a more advanced form will be needed.

The advanced electronic signature (AES) has been defined in Article 2.2 and its main aim is to precisely identify the signatory and the integrity of the document[149]. In order to be considered as an advanced electronic signature, the electronic signature has to meet the following requirements (Article 2.2):

- it is uniquely linked to the signatory;
- it is capable of identifying the signatory;
- it is created using means that the signatory can maintain under his sole control; and
- it is linked to the data to which it relates in such a manner that any subsequent change of the data is detectable;

Despite the fact that the advanced electronic signature can identify the signatory the directive does not give it the legal power of the handwritten signature, therefore AES, just as the electronic signature, cannot be used for signing informed consent forms.

The third and most advanced of electronic signatures is the qualified electronic signature (QES), also called an advanced electronic signature based on qualified certificates created using a secure-signature-creation device. This category of signatures is based on the former advanced electronic signatures, however requires additionally a qualified certificate and a secure-signature-creation device.

The main provision of the Directive states that such a qualified electronic signature satisfies the legal requirements of a signature in relation to data in electronic form in the same manner as a handwritten signature satisfies those requirements in relation to paper-based data, and so it could be used to sign informed consent forms.

Unfortunately, as notes the European Commission itself, in the Report on operation of the Directive: ”Today, users do not have a single electronic certificate to sign documents or transactions in the digital environment in the same way as on paper”[150] – even more most of the European citizens do not have a token which can be used as an qualified electronic signature and therefore is capable of replacing the

[149] Carolina M. Laborde, *Electronic Signatures in International Contracts* (Frankfurt am Main: Peter Lang, 2010), 70.

[150] Report From The Commission To The European Parliament And The Council: “Report on the operation of Directive 1999/93/EC on a Community framework for electronic signatures” published on 15 March 2006. Available online: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2006:0120:FIN:EN:HTML. Retrieved 5 August 2012

handwritten signature – that can be seen as the biggest problem in satisfying the formal requirements for an informed consent, which the Clinical Trials Directive poses.

3.1.3.3 Formal requirements for consent in data protection

The reason for requiring consent for data processing is laid down in the Data Protection Directive – consent is a general ground for lawful processing of data (article 7 DPD) and a specific ground for processing of sensitive data (article 8.2(a) DPD). In the particular case of processing of data in health environment (during a clinical trial) the second of those two cases has to be taken into account.

Consent constituting a ground for lawful data processing is explained in Article 2(h) as "any freely given specific and informed indication of his wishes by which the data subject signifies his agreement to personal data relating to him being processed."

When a clinical trial is being conducted a trial subject has to be asked for consent for processing of his / her sensitive medical data. Therefore, an explicit consent as provided by Article 8 has to be obtained.

Hence Article 2 and Article 8 determine requirements consent has to fulfil: freely given, specific, informed and explicit. Those are however requirements of quality in regard to consent and not formal requirements which are dependent on paper or electronic form of consent. As elucidates the Art. 29 Working Party "there is in principle no limit as to the form consent can take"[151], whenever consent is an indication (in any form – as further states the Working Party) which clearly states what falls within the data processing.

The Directive does not define the form in which data subject should signify his/her agreement to data processing, and so, any indication of wish is acceptable – as long as it is a signal clear enough to be recognised by the data controller.

Additional safeguards were introduced for the special categories of data, which are to be treated as very sensitive and therefore consent for processing of those has to fulfil the additional requirement of being explicit. As explained by the Art. 29 Working Party "explicit consent" has the same meaning as "express consent" and requires that the data subject is proposed a particular way of data processing to which he/ she has to actively agree or disagree on.

The Working Party elaborated also on the form of explicit consent, stating that as a rule it shall be given in writing, both on paper or in electronic form, but that the writing form is in fact not necessary.

What is necessary is a positive action expressing agreement to data processing and in an electronic, or online environment that can be done by electronic or digital signature, but that is not a requirement

[151] Opinion 15/2011 on the definition of consent, adopted on 13 July 2011, available online: http://ec.europa.eu/justice/policies/privacy/docs/wpdocs/2011/wp187_en.pdf. Retrieved 5 August 2012

posed by the Directive – also clicking a button, or an icon should be sufficient as long as it is a clear and positive action on the side of data subject.

However, it should be noted that despite that electronic signature is not required for the sake of valid informed consent the data controller is required to prove that the data subject has given his/ her consent. For that scope data processing consent signed with electronic signature shall be considered of higher value.

Many of already proposed solutions for electronic consent propose opt-out solutions, where individuals can, decide to not allow certain processing – that is however not sufficient in the light of Article 8(2) and such opt out solutions will not fulfil the requirement of explicit consent.

What should be finally underlined is that Directive sets common standards for the level of data protection through European Union, however, as noted by the Art. 29 Working Party[152] the way concept of consent was transposed by the Member States is not consistent: "a general concept is not defined in French data protection legislation, but its meaning has been precisely and consistently explained in the jurisprudence of the data protection authority (CNIL), in relation to the definition contained in the Data Protection Directive. In the UK, it has been developed by common law in reference to the wording of the Directive. In addition, consent has sometimes been explicitly defined in specific sectors, for instance in the context of e-privacy, e- government or e-health." Therefore national legislations would have to be considered when assessing formal requirements posed for a valid consent.

3.1.4 Existing e-consent solutions

3.1.4.1 SecureConsent

Founded in 2005 with offices in Frederick, Maryland and Norwich, Vermont, ConsentSolutions provides innovative approaches to improving the consent process through the use of electronic media. The company has experience in designing multimedia platforms for the potential education of research participants, assuring their understanding of trials. Its main purpose is focused on supporting trial staff and developing interactive, user-friendly software and web sites that help candidates and patients understand and make an informed decision about clinical trial participation. Its software tools are available for institutional licensing.

[152] Opinion 15/2011 on the definition of consent, adopted on 13 July 2011, available online: http://ec.europa.eu/justice/policies/privacy/docs/wpdocs/2011/wp187_en.pdf. Retrieved 5 August 2012

Figure 3 Sample image of the SecureConsent software

SecureConsent[153] is a commercial e-consent Interactive System, specifically developed for candidate and patient consent use with the iPad. The system utilizes interactive media, provides a medical terminology library and integrates a participant-comprehension tracking approach which minimizes the costly expense of ineffective pre-procedure consent. SecureConsent is designed in such a way that it assists the trial candidates to easily acquire the necessary information in order to make an informed decision about the research they are considering. All the candidate actions are captured in an audit trail through electronic document presentation and electronic signatures. Finally, the system provides a simple user interface for the management of the candidate consent and the tracking of the patient for amended consents and signatures.

Some of the main features of SecureConsent are presented below:

The system supports the creation of custom consent to meet the specific desired needs for an iPad or web-based presentation format.

- The touch screen of the iPad is used to present the informed consent to the candidate.
- Each candidate is given a secure, trial specific user ID, which is used for logging in the system.
- The candidate can mark the sections that are not understood for further review with the investigator or the research staff, prior to the signature.
- A multimedia system provides offerings of audio, visual and interactive presentation formats. The multiple options and depth of information enhance comprehension so that the participant should easier make a well-informed decision to participate in a clinical trial and/or medical procedure.

[153] SecureConsent, http://www.consentsolutions.com

- Digital handwritten signatures for subject and witnesses are supported.

All user interactions are recorded immediately into a "real-time" tracking system that automatically creates a trail of timed, dated and usable information across multiple sites and studies. The system also provides a dashboard that allows the monitoring of completion time and status, time spent by question, questions noted and comprehension level, along with trial participant information.

3.1.4.2 iMedConsent

Dialog Medical's industry-leading iMedConsent[154] application enhances the education, discussion and documentation associated with the informed consent process for physicians, ambulatory surgery centres and hospitals. The iMedConsent is a commercial application, trusted by more than 10,000 clinicians to assist with educating and informing patients about conditions, diagnoses and treatments. This novel solution is integral to healthcare organizations' efforts to streamline internal practices, standardize communication across the enterprise and better document informed consent encounters.

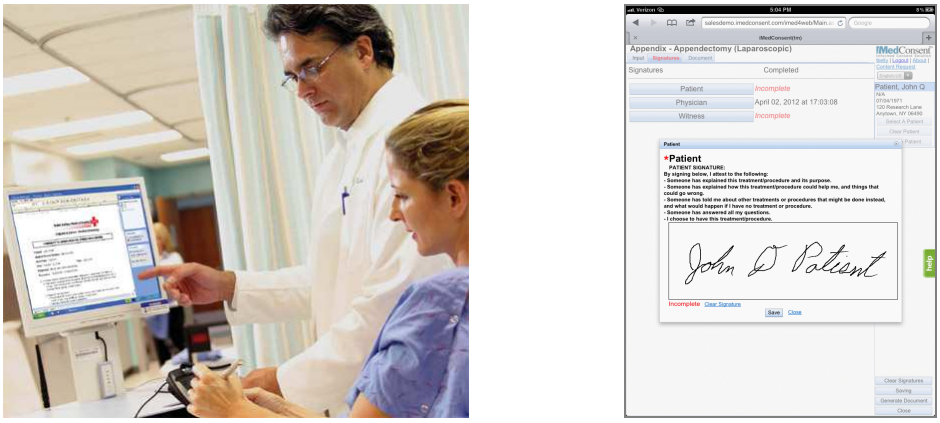


Figure 4 Sample images of iMedConsent software

- Comprehensive content library.
- Integration with other healthcare IT applications including the EMR and document management systems.
- Optional Electronic signature capture for a paperless process.
- Automatic creation of progress note to document encounter.

[154] iMedConsent, http://www.dialogmedical.com

- Advanced directives module.
- "Distributed" program access for affiliated physicians with surgical privileges at the facility (no WAN/LAN access required).
- English and Spanish language documents

The full list of iMedConsent™ Enterprise offerings is presented below:

- Procedure-specific consent forms for over 2,000 treatments and procedures.
- Library of education documents and pre- and post-procedure instructions.
- Anatomical images and diagrams to enhance patient-provider communications.
- Patient monographs for prescription and OTC medications.
- Content available in English and in Spanish.
- Clinical content is updated on a regular basis.
- Remote physician offices can have access to the application to complete hospital required consent forms.
- Providers can create easy-to-access folders of their commonly-used documents.
- Providers can make permanent changes to documents to reflect their unique preferences (if allowed by institution policy.)
- Client can develop custom forms (e.g. unique consent forms, HIPAA forms, patient registration forms, etc.)
- Institution can use the iMedConsent™ application to conveniently manage and distribute the institution's proprietary educational and instructional materials.
- Consent forms and other patient materials are automatically populated with patient information (e.g. name, DOB, medical record number, etc.)
- Consent forms can be prepared in advance for a given patient and stored for later retrieval.
- Eliminates scanning of consent forms and associated costs.
- Ensures no operating room delays due to lost or misplaced forms.
- Automatically delivers a progress note to the EMR eliminating the need for the provider to prepare that note.
- Facilitates actions by the EMR to identify the treatment/ procedure for which consent was obtained and cross-check against procedure ordered.
- Allows for development of complex consents and system interfaces (e.g. consent for tissue banking and research consents).

3.1.4.3 Basic Patient Privacy Consents (BPPC)[155]

Integrating the Healthcare Enterprise (IHE) is an initiative aiming at the integration of information systems of modern healthcare institutions. Within this initiative, the Infrastructure Technical Framework[156] specifies the interactions of a subset of functional components (IHE Actors) of the healthcare enterprise, in terms of a set of coordinated, standards-based transactions. In this context, Integration Profiles have been defined, which specify implementations of standards that are designed to meet identified clinical needs. They enable users and vendors to state which IHE capabilities they require or provide.

Basic Patient Privacy Consents (BPPC) is an IHE profile that was started in May of 2006. It provides a mechanism to record the patient privacy consent(s), and a method for Content Consumers to enforce the privacy consent appropriate to the use. This profile was identified as "Basic", since there is a lack in standards, meeting the complex need of including patient's wishes regarding the access and control of "their" data.

BPPC depends on Cross-Enterprise Document Sharing (XDS), also defined by IHE, which enables a number of healthcare delivery organizations belonging to an XDS Affinity Domain (e.g., a community of care) to cooperate in the care of a patient by sharing clinical records in the form of documents as they proceed with their patients' care delivery activities. Federated document repositories and a document registry create a longitudinal record of information about a patient within a given XDS Affinity Domain.

The BPPC profile complements XDS by describing a mechanism whereby an XDS Affinity Domain can develop and implement multiple privacy policies. It furthermore describes how that mechanism can be integrated with the access control mechanisms supported by the XDS Actors (e.g. EHR systems).

The Affinity Domain organizers create a policy set. Each of the policies is given a unique identifier (i.e., privacy-OID). Each Object Identifier (OID) can clearly identify one of the policies defined by the Health Information Exchange (HIE). This is important, since it allows the Affinity Domain to define their own policies in as clear of language as was necessary for the patients, providers, and systems to understand. This level of policy writing is necessary before one can even hope to commit the logic to computer encoding.

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[155] "Basic Patient Privacy Consents", http://wiki.ihe.net/index.php?title=Basic_Patient_Privacy_Consents, last updated on 13-10-2010, accessed on 20-08-2012.

[156] IHE IT Infrastructure (ITI) Technical Framework Volume 1 (ITI TF-1) Integration Profiles Revision 8.0 – Final Text August 19, 2011

Furthermore, this profile shows how to capture a patient's acknowledgment and/or signature of one or more of these policies. This is done by using a HL-7 CDA document along with an optionally scanned copy or a digitally signature. The scanned copy might be the patient's ink on paper acknowledgment. This capability has been very well received as providers like to see that ink was put to paper.

As soon as a document is used, the document consumer Actors are obligated to enforce the acceptable use. The document consumer Actor is required to block access to documents that are not authorized. Any OIDs that are not understood by the document consumer Actor must not be used to enable access.

The key standards are HL-7 CDA, with optional inclusion of a Digital Signature, and/or Scanned Document (PDF). The intended environment is mainly XDS. It is also possible to use the BPPC Document in other ways[157].

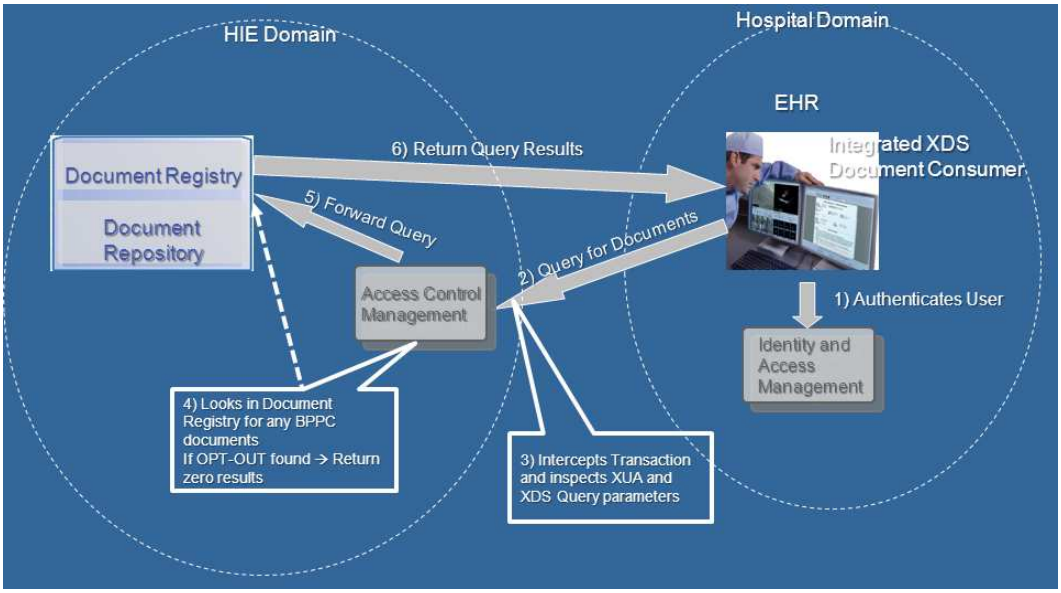

Figure 6 Enforcing BPPC opt-out at the HIE

The figure above illustrates how an opt-out scenario might be implemented using Cross-Enterprise User Assertion (XUA) in an XDS environment that enforces the BPPC consent, in the Health Information Exchange. All accesses shown would also be protected and monitored by Audit Trail and Node Authentication (ATNA) to assure that only trusted systems are involved and that all accesses to sensitive information is recorded in the security audit log.

[157] "IHE - Privacy and Security Profiles - Basic Patient Privacy Consents", http://healthcaresecprivacy.blogspot.gr/2011/08/ihe-privacy-and-security-profiles-basic.html, last updated on 9-8-2011, accessed on 20-08-2012.

Even though, BPPC is "Basic", it does enable communications of the patients' agreement to simple pre-coordinated policies such as Opt-In and Opt-Out. It is also capable of enabling episodic consents that are time limited or specific authorizations such as research projects or clinical trials. It could be used to enable authorizations that are site specific, where the patient might authorize one organization to have access but not others. The profile is designed to be easily integrated into access control environments, yet be on the logical pathway to more advanced consent policy languages.

Supportable Cases	
1	Opt-In to clinical use
2	Opt-Out of sharing outside of local event use, allowing emergency override
3	Opt-Out of sharing outside of local event use, without emergency override
4	Specific document is marked as available in emergency situations
5	Additionally allow specific research project
6	Additionally allow specific documents to be used for specific research projects
7	Limit access to functional roles (e.g.: healthcare) (direct care) providers
8	Limit access to structural roles (e. g. : organizational) (radiologist, cardiologist, billing clerk)
9	Multiple policies apply to each document
10	Change the consent policy (change from opt-in to opt-out)
11	Allow direct use of the document, but not allowed to re-publish
12	When the document is published on media using XDM
13	When the document is published point-to-point using XDR
14	When the document is retrieved across communities using Cross-Community Access (XCA)
15	Individual policy for opt-in at each clinic
16	Individual policy for opt-in for a Personal Health Record (PHR) choice
Possible Cases	
1	Allow access only to care providers with a direct treatment relationship
2	Spouse not allowed access (to all or specific document)
3	Parent is not allowed access (to all or specific document)
4	Restrict access to a specified care-setting
5	All accesses to the data will result in a notification of the patient (e.g.: email or such)
6	All accesses to the data require that a new consent be captured (e.g.: capture new signature)
7	When HL7 v2 or v3 messages are used. This would require further profiling of the use of confidentiality code in those messages.

8	When Digital Imaging and Communications in Medicine (DICOM) is used. This would require further profiling of the use of confidentiality code in those messages.
9	Temporarily allowing a use of a document that would be not allowed by the current policies. This could be done with a new consent being registered that is soon after deprecated, but this is not very good solution.
Not Possible Cases	
1	Patient identifies individuals that have rights to their data
2	Patient identifies individuals that do not have rights to their data
3	Each access of the data must be individually authorized by the patient
4	A document with a mixture of more/less sensitive information thus needing different levels of protection
5	Notification to those that have used a document under consent that is now revoked
6	Pulling back copies of documents that have been used under a consent that is now revoked

Table 3 Supported, possible and not possible cases of BPPC usage along with several policies[155]

3.1.4.4 Consentir

Consentir[158] is a policy (rule) based patient consent management system that utilizes patient consent information along with operational policies as input. The system aims to protect patient information in a real time manner by applying policy based consent management. Each policy is represented by a set of Resource Description Framework (RDF) rules in Notation 3 (N3)[159]. These rules allow or deny access to specified documents. Then an Euler proof mechanism is used to compute the result and the proof of the aggregated rules. The advantage of using this mechanism is that it will be possible in the feature to validate proofs between different systems.

3.1.4.4.1 Technologies Used

RDF is a standard model for data interchange on the Web. Its features can facilitate data merging even if the underlying schemas differ, and it supports the evolution of schemas over time without requiring all the data consumers to be changed[160]. Therefore, RDF is an ideal candidate for management and exchange of medical information where the datasets have a large amount of consumers, are characterised by long life span and are constantly evolving.

[158] Atif Khan, Sarah Nadi, David R., "Consentir: An Electronic Patient Consent Management System", Cheriton School of Computer Science University of Waterloo Ontario, Canada.
[159] "Notation 3 (n3): A readable RDF syntax," Website, http://www.w3.org/TeamSubmission/n3/.
[160] "Resource description framework (rdf)," Website, http://www.w3.org/RDF/.

Notation 3 (N3) is an RDF based standard that uses an analogous syntax to RDF/XML in order to represent the data. In addition to these, N3 has extra features like rules and formulae that are useful when processing data and making inferences from facts in the data. Information in N3 is represented as a set of statements, where each statement is composed of a subject, verb and an object.

Euler is an inference engine that supports logic based proofs and provides high level of integration of the core engine with high level programming languages used to build enterprise systems. The current Euler implementation supports Java, C#, Python, Javascript and Prolog. For the described system, Euler's Java implementation was used, in order to integrate the reasoning engine into the application. Furthermore, Euler can deal with large amount of data by translating data (triples) into SQL.

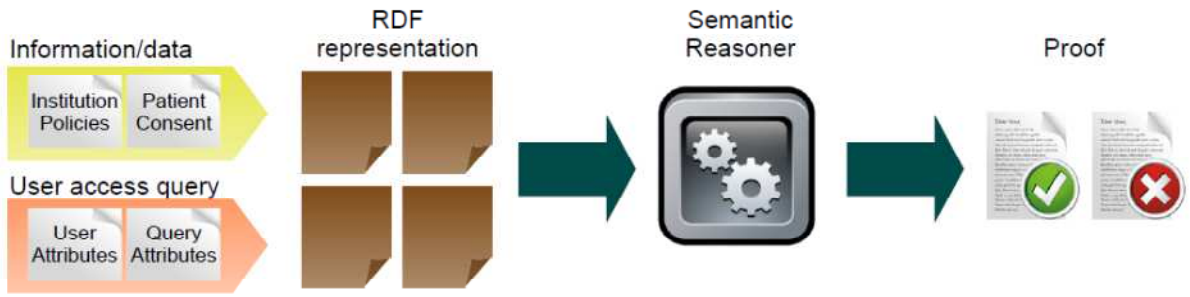

Figure 7 Workflow diagram of the main Consentir actions

The system utilizes information about the patients, their documents and their privacy policies along with information about the different hospitals, physicians and nurses in order to determine who can access a certain document. Initially the facts and the rule set are loaded into Euler in order to create a query which will return whether the document can be accessed. The mechanisms to grant access or not, take into account deny rules as well.

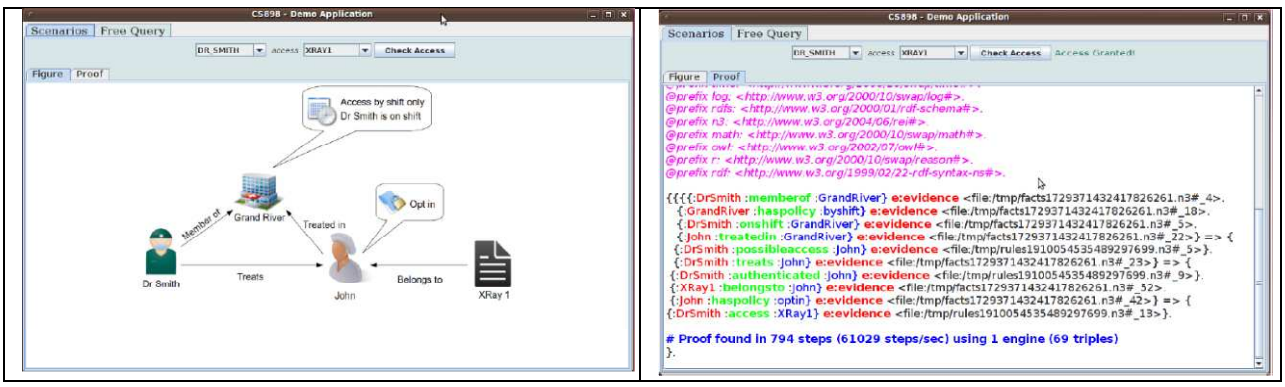

Figure 8 Example scenario and query results (proof of scenario)

3.1.4.4.2 Supported Policies

Consentir, supports both hospital and patient consent policies and might have flexible application in complex health care scenarios.

Hospital policies:

- Members only
- By shift
- Must be treating doctor/nurse (except in emergencies)

Patient consent policies:

- Opt in
- Opt in except for sensitive documents
- Opt in except for certain people
- Opt out[161]
- Opt out with emergency override

3.1.4.4.3 Limitations

The work that has been done so far is a simple prototype that demonstrates the applicability of using ideas from the semantic web to the problem of reasoning with patient consent. Usage of a reasoning engine such as Euler can successfully provide the required results. However, the proposed solution has still some limitations. The system can only answer queries which have one answer. For instance, an answer in the form of list of results, like "Who has access to a specific document?" cannot be returned, since Euler will not look for all possible solutions, but only the first one to be found. Furthermore, the rule set should be expanded in order to be able to address all medical situations. In order for that to be achieved, it is necessary for a rule ontology to be built, capturing all the possible situations. N3 notation supports rule nesting which would support more elaborate policies, which can be used in the future in order to expand the rule set, such that it will include more consent policies. Another useful feature that is missing from the current version is discovering conflicts between different levels of policies. For example, a hospital might have policies that allow access to patient information in a specific

[161] The authors of the respective article understand opt-out as a policy where a patient explicitly denies access to all their information regardless of who is trying to access the data or why they are trying to access it;

situation, while the province policies deny access. Additionally, Consentir only supports "access" or "deny" results. A more sophisticated solution demands more granular access levels.

3.1.4.5 PEHR - Heidelberg University Hospital's approach

The University Hospital Heidelberg has designed the architecture of a Personal Electronic Health Record (PEHR), based on a service oriented architecture (SOA) according to profiles from the initiative Integrating the Healthcare Enterprise (IHE) and international standards like HL7 and DICOM[162]. The architecture of PEHR relies on the patient's consent in order to exchange documents and medical data with other care delivery organizations, with the additional requirement that no opt-out solutions are allowed (only opt-in), as demanded by the German legislation (in order to transfer medical data electronically between different institutions). In order to address this issue, theoretical considerations led to an abstract model for a consent management solution. Two implementable, practical approaches were derived from that model, a centralized and a decentralized approach[163].

With respect to a standardized implementation, the IHE Basic Patient Privacy Consent profile (BPPC)[164] provides opt-in support, but important aspects like e.g. how to structure a consent document and how to make the legal text machine-readable, are not specified. Hence, two additional services were needed in order to solve the consent issue in the Regional Health Information Network (RHIN), namely a Consent Creator Service (CCS) used to create a consent document and the so-called Consent Management Service (CMS) to manage the consent documents generated by the patients.

3.1.4.5.1 Architecture

The CMS consists of a three-layered architecture (Figure 9). The interface layer offers a document listener and a query listener. The document listener can receive consent documents via HL7 v2 Medical Document Messages (MDM) or a Simple Object Access Protocol (SOAP) web service both containing the Clinical Document Architecture (CDA) consent documents. The

[162] Heinze O, Bergh B, "Establishing a Personal Electronic Health Record in the Rhein-Neckar Region", Informatica Medica Slovenica 2009, 14:3-9; Heinze O, Brandner A, Bergh B, "Establishing a personal electronic health record in the Rhine-Neckar region", Stud Health Technol Inform 2009, 150:119.

[163] Birkle M, Heinze O, Bergh B, "Entwurf eines elektronischen Einwilligungsmanagements für ein intersektorales Informationssystem", in eHealth 2010: Health Informatics meets eHealth. Volume OCG Books 264. Edited by: Schreier G, Hayn D, Ammenwerth E. Vienna: Österreichische Computer Gesellschaft; 2010.

[164] IHE, "IHE IT Infrastructure (ITI) Technical Framework Volume 1 Integration Profiles Revision 7", Basic Patient Privacy Consents Integration Profile 2010.

query listener uses HL7 query by parameter (QBP) messages in order to receive queries for consent policies.

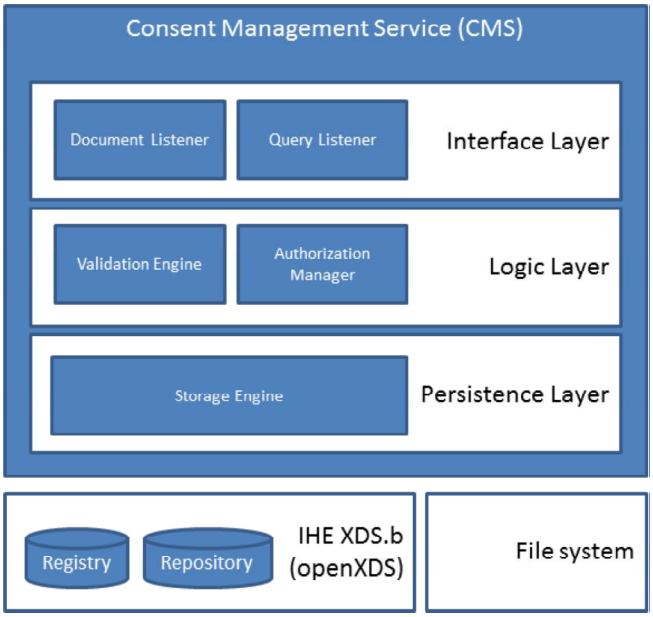

Figure 9 Architecture of the Consent Management Service (CMS)

The HL7 Query/Response conformance statements are used to build the queries. The Message Header (MSH) segment contains meta-data including: the sending and receiving application, time stamps and versions. The essential part of the message is the Query Parameter Definition (QPD) segment which includes the query characteristics. The figure below displays an example of such a query.

```
1 MSH|^~\&|<Sending-Application>||<Receiving-Application>||<Time-Stamp>||QBP^Z04^QBP_Q11|<Message-Control-ID>|P|2.5.1
2 QPD|Z04^CMS query name^CMS0001|<Control-ID>|<Patient-ID>
3 RCP|I||R
```

Figure 10 Example of an HL7 Query to the Consent Management Service.

The validation engine from the logic layer is used by the listener in order to validate the messages, documents and queries. The authorization manager is the core of CMS and implements the Policy Decision Point (PDP) and the Policy Enforcement Point (PEP). This part of the architecture utilizes the storage engine to get the consent documents related to the proper patient from the query. The storage engine is responsible for the storage and retrieval of consent documents either from an XDS.b Registry/Repository using the transactions ITI-41 and ITI-43 or from a file system depending on the configuration of the CMS.

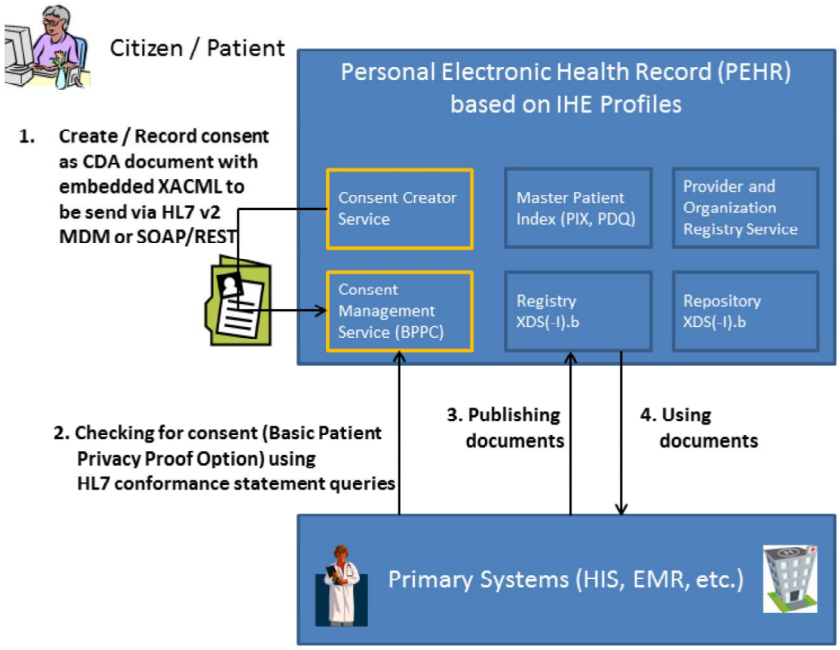

Figure 11 Consent Management Suite (COMS) in the context of a regional health information network (RHIN). Overview of COMS and its services (yellow) in IHE-based regional health networks using the Heidelberg PEHR as an example.

The Consent Creator Service (CCS) is a Java-based application that provides a web-based interface for the creation of consent documents based on CDA and eXtensible Access Control Markup Language (XACML). The web-interface might be integrated into the patient view of the PEHR or into the context of a primary system like a Hospital Information System (HIS). The personal consent documents creation or processing can be applied by the patient such that he/she can manage a) who has access to documents in the record, b) which primary systems, like hospital information systems or practice management systems can add new documents and c) which document types should be transferred to the PEHR.

Then, the consent document is sent to the CMS via an HL7v2 MDM for validation and storage. Consents can also be changed and updated in a similar way. The CCS provides interfaces to the Master Patient Index (MPI) as well as to the Provider and Organization Registry Service (PORS) in order for patients, physicians and organizations to be identified correctly.

The consent document itself constitutes an HL7 Version 3 CDA document based on the definitions of the Basic Patient Privacy Consents (BPPC) profile (Figure below). It contains the necessary text for consents related to a dedicated affinity domain and the essential information about the patient (MPI-ID), the author, the legal authenticator, the involved providers and organizations (PORS-ID) as well as the consent rules chosen by the patient. These rules consist of policies, bundled in a policy set. These policies are represented in XACML inside the body structure of the CDA document. Each policy consists of a human-readable text describing the

effect of the policy and a machine-readable section containing the coding of the policy for retrieving and processing. Furthermore, the CDA document can also include a PDF transformation of the consent and optionally a digital signature. It can be printed for signature by the patient, to ensure legal compliance.

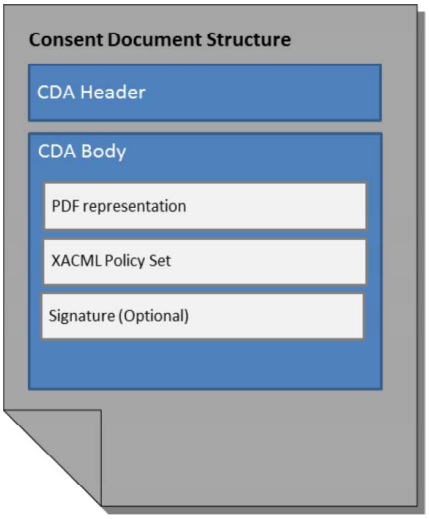

Figure 12 Structure of the consent document. The consent document is based on HL7 version 3 CDA.

3.1.4.5.2 Limitations

The proposed and developed architecture provides an efficient solution for integrating primary systems into the network. The system is capable of supporting opt-out scenarios as well, provides flexibility and can be adapted to other settings in other regions worldwide. However, the COMS may not be considered an out of the box solution. Obviously an adaptation to the respective local requirements and rules of the affinity domain has to be undertaken but this is something that can be fulfilled without a completely redesigning of the general framework, by customization and parameterization. At present the COMS is in alpha release phase and will be open sourced with its first release candidate at the Open eHealth Foundation.

3.1.4.6 The EnCoRe Architecture[165,166]

The EnCoRe project aims to leverage the power of consent in order to allow data subjects to control what happens to the personal information they disclose to organisations (state or non-state). Consent should allow data subjects define and re-define, at any time, the purpose for which their personal information is used, the organisations with which it is shared, and the

[165] EnCoRe Project Deliverable 2.2, Technical Architecture arising from the second Case Study, 2011
[166] EnCoRe Project Deliverable 2.2, Technical Architecture arising from the third Case Study, 2011

duration and place it is stored. Therefore, the project aims to improve the process, through which individuals can **grant and revoke** their consent to the use, storage and sharing of their personal information by others.

In order to achieve these goals, EnCoRe proposed a technical architecture that has been designed to be as generic as possible, based on three different case studies. The first considered usage of employee data in an organisational context, the second was a biobank scenario and the third scenario was based on the Cabinet Office/ Identity Assurance Programme (UK).

One of the main capabilities of the EnCoRe Architecture is the flexible management of privacy preferences. Data subjects are encouraged to provide their privacy preferences when disclosing personal data by dictating a variety of constraints in the form of choices, e.g. on how data should be accessed by the organisation, on notification and disclosure criteria, etc. The privacy preferences, supported by the architecture are the following:

- Allowed/disallowed purposes for using personal data
- Consent for disclosing data to third parties
- Allowed/disallowed lists of entities with which data can be shared or not
- Notification preferences
- Deletion Preferences
- Other preferences related to data handling (e.g. data minimisation, etc.)

The architecture describes the interaction of multiple components. In the next sections the core components are described, based on satisfying the following general use cases that the architecture supports:

An end-user (data subject) discloses personal data along with consent/privacy preferences: the system captures these preferences via user-side plug-ins; the information is sent to a consent and revocation provisioning component for the internal configuration of the policies and the data registry. This also includes setting privacy obligations, driven by user preferences.

Employees and/or applications try to access data for specific purposes (e.g. marketing, transaction processing, research, etc.): a privacy-aware access control policy enforcement component intercepts these requests and grants or denies access based on the evaluation of access control policies. These policies describe security constraints, as well as privacy constraints based on data subjects' preferences (e.g. approved/banned purposes for using data, black/white lists of entities that can handle data, etc.);

Data subject changes their consent/privacy preferences: this triggers a chain of updates of stored privacy preferences within the organisation, including updates of the data registry, access control policies and obligations. If the updated preferences relate to data, which are shared with third parties, these parties will also receive the updates;

Personal data is disclosed to a third party: the system intercepts the attempt of applications to disclose data to third parties via locally deployed agents. If the transfer of data is authorized by the privacy-aware access control policy enforcement component, then the personal data is disclosed to the third party via an external workflow manager, by using the sticky policy mechanisms which bundle data to policies and privacy preferences. The data registry is updated accordingly with the information about where the data has been disclosed.

3.1.4.7 Main components of the architecture

3.1.4.7.1 Consent & Revocation Provisioning Component

This component is the contact point between an organisation's web server/ portal and the EnCoRe framework. It primarily provides workflow-based coordination and provisioning capabilities to the following two cases: data subjects disclose their personal data along with privacy preferences; data subjects change or revoke some of their privacy preferences.

The core engine of this component is the **Internal Workflow Manager**, which orchestrates the sequence of privacy management tasks that need to be executed on personal data and preferences (collection and storage). This includes the initial disclosure of personal data and preferences, along with any subsequent change. This module interacts with various EnCoRe components, such as the internal personal data storage(s) and the privacy-aware access control policy enforcement component. It also interacts with the external workflow manager when personal data are transmitted across the external boundaries of the organization that uses the architecture. The following incoming requests are routed to the relevant component: A new data subject's registration request, a data access request from an existing data subject's web browser (e.g. a returning data subject wanting to check/change their personal data and/or preferences), as well as a request to update personal data and/or privacy preferences by an existing data subject.

3.1.4.7.2 Privacy-Aware Access Control Policy Enforcement:

This component is in charge of enforcing security & privacy access control policies on personal data, driven by data subjects' preferences. These policies take into account preferences, such as purposes for accessing data, entities the data may or may not be disclosed to, etc.

This component is in charge of ensuring that the personal data, stored in a variety of data repositories (any database used by an organization), is accessed based on the fulfilment of privacy-aware access control policies and data subjects' privacy preferences.

It primarily consists of the following components:

- A Contextual Handler: contextual information is related to an access request, such as the purpose for accessing the data, the requestors' role and identification, location, etc.
- A Policy Decision Point: this is the component that, based on access requests and contextual information, grants or denies access to data, based on the evaluation of access control policies and relevant data subjects' privacy preferences.
- A Policy Enforcement Point: this is a trusted and secure gatekeeper which allows or denies access to personal data, based on decisions made by the policy decision point. This component is a distributed component. Multiple local instances of the policy enforcement point are deployed within relevant components such as the internal workflow manager and organisations' applications or services, to locally enforce the access control decisions. These components securely interact with the centralised policy decision point component.

3.1.4.7.3 External Workflow Manager

The External Workflow Manager is in charge of interfacing and interacting with other deployments of EnCoRe systems. Its purpose is to share personal data along with privacy preferences with the help of sticky policy mechanisms and ensure consistency of this information, across all the involved parties, especially when data subjects change or revoke their preferences.

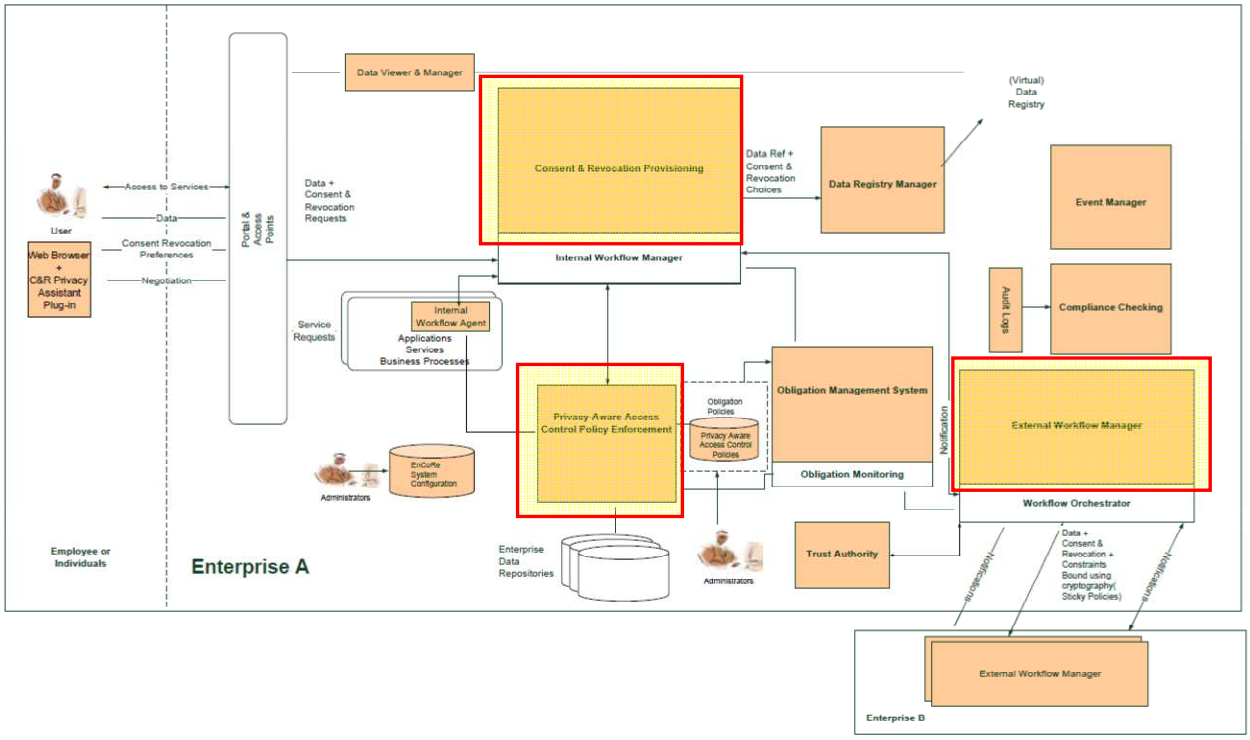

Figure 13 EnCoRe Technical Architecture – Highlighted main component

3.1.4.7.4 Privacy aware policies

The biobank scenario has revealed the need for more flexible privacy aware policies beyond access control. In satisfying that need, EnCoRe introduced the obligation policies.

Obligation policies are implemented by the Obligation Management System, which is responsible for the privacy-aware lifecycle management of data. It enforces constraints and duties that have been defined both by organisational policies and data subjects' preferences. This includes obligations for: notifying data subjects about usage or disclosure of their personal data; dealing with transformation and minimisation of personal data; dealing with data deletion, etc.

Furthermore, sticky policy mechanisms (i.e. the binding of data with meta-data) are implemented by a specific component in the architecture. This is the Flexible Sticky Policy Manager within the external workflow manager. This component is instructed by the external workflow manager about the type of binding to be enforced between the personal data and meta-data (inclusive of privacy choices and a suitable abstraction of the access control and obligation policies). The level of stickiness (simple association or strong cryptographic binding) can be configured.

3.2 Harmonizing legal rules for (e-)consent in Europe

Introduction

In order for e-consent solutions to be implementable, a harmonised legal framework for Europe is an absolute necessity. But such a harmonised legal framework is not only necessary for the implementation of e-consent, it is a need experienced already quite a while in everyday healthcare and clinical trial situations. Moreover, this need was recognised by the European Commission, resulting in the recent publication of two proposals for regulation: Proposal 2012/0011 for a regulation of the European Parliament and of the Council on the protection of individuals with regard to the processing of personal data and the free movement of such data, also called the General Data Protection Regulation (hereinafter DPR) and Proposal 2012/0192 for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (hereinafter CTR).

The Data Protection Directive dates from 1995 and was thus written in times where only 1% of all telecommunicated information was carried over the internet. Today, that figure has risen to about 97%. Consequently, it is no surprise the DPD was in high need of a review. When launching the Proposal for the General Data Protection Regulation commissioner Reding said: "Technological developments are welcome drivers of innovation, growth and jobs creation. However, technological changes also bring about new regulatory challenges.", "Our data races from Munich to Miami and to Hong Kong in fractions of a second. In this new data world, we all leave digital traces every moment, everywhere". "Personal data", Reding continued in her speech, "is the currency of today's digital market. And like any currency it needs stability and trust. Only if consumers can 'trust' that their data is well protected, will they continue to entrust businesses and authorities with it […]"[167]. In the light of this evolution and these findings the DPR aims to enhance opportunities for companies that want to do business in the EU's internal market, while ensuring a high level of protection for individuals.

The Clinical Trials Directive dates from 2001 and was thus not in the first place confronted with an extreme technological evolution, but was reviewed because it was the most heavily criticised piece of EU-legislation in the area of pharmaceuticals, voiced by all stakeholders – patients, industry and academic research[168]. It (partly) caused the number of applications for clinical trials to fall, the costs for clinical trials to increase and the average delay for launching a clinical trial to rise. It thus seems that the CTD could not fulfil its aim to simplify and harmonise the administrative requirements for clinical trials across the EU, whilst ensuring the safety of clinical trial participants, the ethical soundness of trials and the reliability and robustness of data generated[169]. Because the Commission found that the CTD

[167] V. Reding, "The EU Data Protection Reform 2012: Making Europe the Standard Setter for Modern Data Protection Rules in the Digital Age", speech given at Innovation Conference Digital, Life, Design, 22 January 2012.
[168] Explanatory Memorandum to the Proposal 2012/0192 for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, COM(2012)369final, 17 July 2012, 2.
[169] NHS confederation, "The European Commission has published formal proposals to revise the existing EU Clinical Trials Directive", www.NHSConfed.org, last consulted 13 sept 2012.

appears to have hampered the conduct of clinical trials in Europe, they decided to act. The new Regulations therefore aims to again simplify the authorisation procedure allowing for a fast and thorough assessment of the application, simplify the reporting procedures, allow the Commission to conduct controls in Member States and other countries to make sure the rules are being properly supervised and enforced and through the choice of the form of a Regulation ensure that the rules for conducting clinical trials are identical throughout the EU[170].

For both Proposals for Regulation the instrument of Regulation is considered to be the most appropriate European legal instrument to increase harmonisation and decrease legal fragmentation. The Explanatory Memorandum to the DPR by opting for the legal form of a Regulation hopes to "reduce legal fragmentation and provide greater legal certainty by introducing a harmonised set of core rules, improving the protection of fundamental rights of individuals and contributing to the functioning of the Internal Market". The Explanatory Memorandum to the CTR states that: "Only the legal form of a Regulation ensures that Member States base their assessment of an application for authorisation of a clinical trial on an identical text, rather than on diverging national transposition measures".

In this section we firstly further discuss the sections of both Proposals for Regulation important to the CONTRACT project and secondly examine them in the light of the findings and analyses discussed in the first section of this deliverable[171].

3.2.1 Proposal for a General Data Protection Regulation

Three aspects of the Proposal for a General Data Protection Regulation are of crucial importance to the project: the conditions set for consent, the conditions set for the processing of health data and the conditions set for the protection of children.

3.2.1.1 Consent in the Proposal for DPR

Article 4 (8) defines the data subject's consent as "any freely given specific, informed and explicit indication for his or her wishes by which the data subject, either by a statement or by a clear affirmative action, signifies agreement to personal data relating to them being processed". This definition differs from the old definition only with regard to the inclusion of the word "explicit". With the inclusion of the word "explicit" the Commission hopes to set a single and consistent definition of consent[172]. Consequently and in so far this was allowed under national law, an implicit consent is no longer acceptable with regard to data protection. Consideration 25 explains that consent should be given through "any appropriate method" which enables the data subject to indicate his wishes. This can be a statement or a clear affirmative action such as ticking a box. The method can be paper-based or electronic as long as it ensures that individuals are aware that they give their consent to the processing

[170] Proposal for a Clinical Trials Regulation, Questions and answers, http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/12/566.
[171] See 2
[172] Explanatory Memorandum to the Proposal for DPR, 3.4, article 4, 8.

of their personal data. The consideration does however add that "If the data subject's consent is to be given following an electronic request, the request must be clear, concise and not unnecessarily disruptive to the use of the service for which it is provided".

Important to notice is that the Proposal for DPR does not require the consent for data processing to be given separately from other actions, but "If the data subject's consent is to be given in the context of a written declaration which also concerns another matter, the requirement to give consent must be presented distinguishable in its appearance from this other matter"[173].

The consent, when validly given under the above conditions, is accepted as a legal ground for the processing of health data under article 9 (a). The Proposal for DPR does however allow Member States to prohibit the processing of health (or other sensitive data) on the basis of consent in those situations where it is deemed inappropriate to have the general prohibition to process health data lifted by the data subject.

3.2.1.2 Processing of health data in the Proposal for DPR

It has long been pushed for the rules on the processing of health data to be subject to be separate and specific. The current proposal does so only partly. The proposal does now include a definition of 'data concerning health', but health data are on the other hand still considered as one of the categories of sensitive data and so regulated under the more general article 9.

Nevertheless consideration 122 states that "The processing of personal data concerning health, as a special category of data which deserves higher protection, may only be justified by a number of legitimate reasons for the benefit of individuals and society as a whole". It is article 81 which foresees specific legitimate grounds for the processing of health data: for treatment, for public health and for other reasons of public interest. But, the Explanatory Memorandum shifts the further enactment of specific safeguards for the processing for health purposes to the Member states[174].

When the processing of health data is necessary for historical, statistical or scientific research purposes, article 81 refers to article 83, an again more general provision. Article 83 states that "personal data may be processed for historical, statistical or scientific research purposes only if" the purpose of the processing cannot be achieved through the use of anonymised or pseudonymised data and the data are linked to other data as little as possible. As scientific research is considered "fundamental research, applied research, and privately funded research". In consideration 125 the Proposal for DPR a reference is with this regard included to the legislation on clinical trials: "The processing of personal data for the purposes of historical, statistical or scientific research should, in order to be lawful, also respect other relevant legislation such as on clinical trials".

[173] Article 7, 2. Proposal for DPR.
[174] Explanatory Memorandum to the Proposal for DPR, article 81, 15.

3.2.1.3 Protection of children in the Proposal for a DPR

New to the regulation of data protection are the provisions foreseen to protect children. Consideration 29 explains: "Children deserve specific protection of their personal data, as they may be less aware of risks, consequences, safeguards and their rights in relation to the processing of personal data". Even though the protection of children in healthcare and during clinical trials is most likely not the case the Commission wished to address in the first place, it is of great importance to these situations too. If only because under article 4 (18) a child defined as "any person below the age of 18 years". Consequently, in all matters concerning data protection, national regulations on the legal age of majority will now only have subsidiary power.

The Proposal for a DPR does include a special provision on the consent of children, namely in article 8. When children are directly offered information society services, the processing of their data is, according to article 8, only lawful if and to the extent that consent is given or authorised by the child's parent or custodian. Consideration 130 and 131 mention that standard form for the consent of a child can be adopted under the examination procedure.

Apart thereof however, the inclusion of children as a category of data subjects deserving special protection, does not seem to have considerable consequences under the current proposal.

3.2.2 Proposal for Clinical Trials Regulation

As a general principle the Proposal for a Clinical Trials Regulation sets forth the compliance with The EU Charter of Fundamental Rights which in article 3(2)a states that any intervention within the field of medicine and biology cannot be performed without free an informed consent. It is stated on page 6 of the current proposal that "The rules on the protection of subjects and on free and informed consent had been discussed extensively in the legislative process leading to Directive 2001/20/EC.", "The proposed Regulation does not […] change the substance of these rules"[175]. Consequently it can be noticed that adapting the current legal framework on the informed consent for participation in clinical trials to the worries as expressed by many clinicians was not one of the priorities in this proposal. The only issue which is newly addressed is the informed consent procedure in emergency clinical trials.

Next it should be noted that, in contrast to the Proposal for DPR, the Proposal for CTR opts explicitly to not touch upon the subject of legal representation of children. Consideration 22 explains that because the rules on the protection of minors diverge in Member States, it should be left to the Member States to determine the legal representative of minors. Moreover, article 2(16) defines a minor as "a subject, who is, according to the laws of the Member State concerned, under the age of legal competence to give informed consent".

[175] Explanatory Memorandum to the Proposal for CTR, 3.4. Protection of subjects and informed consent, 6-7.

3.2.2.1 Informed consent in the Proposal for a Clinical Trials Regulation

Article 2 (19) provides the following definition of informed consent: "Informed consent is a process by which the subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate". This definition is much shorter than the one provided in article 2(j) CTD 2001/20/EC. However, when looking at Chapter V of the Proposal for CTR, which addresses the protection of subjects and informed consent, the wording of article 2(j) CTD was recovered with only one difference: the informed consent is no longer considered to be 'a decision' but 'a process'. This may seem a little change, but as illustrated in the analyses above, it can have major implications[176].

A new provision now stipulates that "Written information given to the subject […] shall be kept concise, clear, relevant and understandable to a lay person"[177]. This is similar to the provision added in the Proposal for DPT: "The controller shall provide any information and any communication relating to the processing of personal data to the data subject in an intelligible form, using clear and plain language, adapted to the data subject, in particular for any information addressed specifically to a child". It thus seems that the European legislator would like to put an end to the lengthy and over complicated informed consent forms, a complaint often heard also within this project.

3.2.2.2 Informed consent in emergency Clinical Trials

The newly introduced provisions on informed consent in emergency trials are included in article 32 of the Proposal for CTR. By way of derogation informed consent may now be obtained after the start of the clinical trial to continue the trial in case of urgency, when no legal representative is available and the subject has not previously expressed his objections. The clinical trial in which the subject is involved should furthermore relate directly to the medical condition which caused the impossibility to obtain prior informed consent in the first place and should pose minimal risks and burden on the subject.

For a more extensive discussion of this new provision we refer to the discussion above on the timing of consent[178].

3.2.3 Are the Proposals for Regulations of data protection and clinical trials the way to go?

Some of the issues discussed in the first part of this deliverable are (partly) addressed in the new Regulations. However, with regard to informed consent they still have their own approach. It thus seems harmonisation of informed consent is not gained through these two proposals.

[176] See also: 2.3; 2.4.
[177] Article 29, 2. Proposal for CTR
[178] See 2.3

3.2.3.1 The re-use of data

The fragile balance between the autonomy of the patient / data subject and the need for reliable data of researchers / data controllers continues to be an issue under the new Proposals for Regulation, especially the General Data Protection Regulation.

As explained in the analysis an informed consent for the processing of data needs to be specific. This principle is also under the new DPR a cornerstone. Article 4 (8) and consideration (25) require the informed consent to be specific. Article 5(c), (b) and (e) echo the general principle that personal data must be adequate, relevant and limited to the minimum necessary for the specified and explicit purpose of the data collection for no longer than necessary. No further explanation is foreseen on what constitutes a specific purpose or a specific consent.

A specific provision is foreseen for the processing of data for historical, statistical and scientific research, namely the new article 83. Article 83 provides a legal ground for the processing of data when the purpose is research. It is thus important to notice that provision addresses secondary data processing, not primary. The re-use of data originally collected for a different purpose, e. g. on the basis of informed consent, is under this provision allowed only if 1.(a) the purposes cannot be fulfilled by using anonymous or pseudonymous data, (b) the data are as little as possible linked to other identifying data. Article 83, 3. allows the Commission to further specify the criteria and requirements of this provision in delegated acts. Whether or not this provision can meet the challenges researchers are confronted with remains thus to be seen.

3.2.3.2 Timing of consent

When the informed consent needs to be obtained from the patient / data subject is a second issue which to a large extend remains unanswered.

The Proposal for a General Data Protection Regulation does on the one hand specify in consideration (49) and article 14 DPR that the data subject needs to be provided with the information in relation to the data processing "at the time of collection, or, where the data are not collected from the data subject, within a reasonable period depending on the circumstances of the case". This indicates that – as was the case under the DPD – the data subject needs to be informed before his consent is asked, but nothing more. The Proposal for a Clinical Trials Regulation on the other hand does not specify when the informed consent has to be obtained at all. Following article 28 CTR, a clinical trial may only be conducted when (c) the subject has given informed consent and (d) the subject had the opportunity in a prior interview with the investigator to understand. For further details the CTR refers to the ICH good practices[179]. Consequently it can – again as was already the case under the CTD – only be concluded that the information needs to be given prior. When exactly seems to again depend on the case. Although

[179] Consideration (29) Proposal for a CTR

both proposals thus foresee slightly different provisions and do thus not harmonise, they seem to be consonant on this point.

A new difference however is that the CTR does now acknowledge in its new definition of informed consent that informed consent is a process rather than a one-time decision[180]. However, what consequences this shall have is not further explained and remains unclear. The concept of staged informed consents is also not mentioned in the current proposal. This provision is in contrast with the definition of informed consent under the DPR which considers the informed consent to be an "indication" of the data subject's wishes, and implicitly makes it a one-time thing.

3.2.3.3 Informed consent and contract law

Also on the application of contract law to informed consent the Proposals for Regulations do not provide a clear answer.

The Proposal for DPR does foresee that "when the processing is based on the data subject's consent, the controller should have the burden of proving that the data subject has given consent to the processing operation"[181], but a reference is subsequently only made to the right to withdraw without detriment[182].

Also under the Proposal for CTR the right to withdraw remains a key principle. Article 28, 3. specifies that a clinical trial may only be conducted when "any subject may, without any resulting detriment, withdraw from the clinical trial at any time by revoking is his or her informed consent".

Although the right to withdraw does thus clearly remain an important mechanism to protect the data and/or clinical trial subject, it is remarkable that the consequences of such a withdrawal are not equal under both proposals. Under article 28, 3. CTR it is clearly stated that "the withdrawal of consent shall not affect the activities carried out based on consent before its withdrawal", while under the newly introduced rights to be forgotten and to erasure of the DPR, the withdrawal of consent may have much larger consequences. Article 17 specifies that the controller is obliged to erase personal data and abstain from further dissemination of these data when the data subject withdraws his or her consent or the storage period consented to has expired. When the controller furthermore has made the data public, he shall have to take all the reasonable steps to inform the third parties which are processing these data that the data subject requests them to erase any links to, copies or replications of that personal data. The erasure needs to be carried out without delay, except in 5 cases foreseen in article 17, 3. among which the processing for research. In that case the data may be kept for as long as necessary in accordance with the purpose of the research as specified in the informed consent form.

[180] Art 2, (19) Proposal for a CTR.
[181] Consideration (32) Proposal for a DPR.
[182] Consideration (33) Proposal for a DPR

3.2.3.4 e-consent

To obtain informed consent electronically is now explicitly allowed under the Proposal for DPR. Article 4 (8) requires "a statement or clear affirmative action" and consideration (25) explains that consent should be given explicitly by any appropriate method which can ensure that individuals are aware that they give their consent to the processing of personal data, "including by ticking a box when visiting an Internet website". Next thereto consideration (25) only requires that when the informed consent is given following an electronic request "the request must be clear, concise and not unnecessarily disruptive to the use of the service for which it is provided". This is good news in the light of the findings and recommendations described above[183].

Unlike the Proposal for DPR, the Proposal for a CTR does not in any way mention e-consent. The Proposal for CTR only stresses that informed consent shall be written, dated, signed and appropriately documented[184]. It is next required that the written information should be concise, clear, relevant and understandable to a layperson[185]. But, whether it should be on paper or not is not further clarified. It is certain that due weight should be given to the prior interview with the investigator and the possibility to ask questions orally[186].

[183] See Section 2
[184] Article 29, 1. Proposal for a CTR
[185] Article 29, 2. Proposal for a CTR
[186] Article 28, (d) Proposal for a CTR

4 Recommendations to the Commission - Conclusion

If one conclusion can be the result of the analysis of the questions presented above, it should be that the concept of informed consent is used to reflect a balance between the subject's right to autonomy and the subject's need for protection. The autonomous choice of the subject can have a positive and facilitative function or a negative and protective function: a positive function disallows enhancement of any medical procedures before the consent is given, while the negative function is securing that no intervention occurs without the consent.

Through history and across the domains of treatment, clinical trials and data protection, the concept of informed consent has always been linked to the concept of autonomy. Since Western society left the doctor-knows-best doctrine autonomy has moreover been one of the main concepts in medical law. Also since Western society left the doctor-knows-best doctrine the empowerment of the patient has been stressed. And so it is no surprise that a tight link exists between autonomy and empowerment. An intrinsic condition for the patient to be autonomous and to be empowered is that the patient or subject is informed. The patient, the clinical trial participant, the data subject, each and single one of them need information in order to be able to make well grounded decisions and to subsequently indicate their wishes through the provision or denial of their informed consent to treatment, participation and/or data protection. If informed consent should aim at enhancing autonomy, it is crucial for the process of informed consent that the individual's choice is expanded through information.

Next thereto the obligation to obtain "informed consent" from the patient, trial participant or data subject as a formal requirement which needs to be fulfilled before the physician administers treatment, the investigator and sponsor start a clinical trial or a data controller processes data, is also observed as a legal instrument to protect the autonomous individual. It safeguards that the well informed and autonomous individual's opinion is actually asked and respected. Furthermore, whoever needs to obtain informed consent from an individual should not only respect the autonomous choices made by this individual, he or she also has an obligation to guide that individual.

The latter is also reflected in the finding that autonomy is not an absolute concept, but relational. Decisions, even those autonomously taken by an individual, will be influenced by the connections and networks of that individual, the environment he or she lives in and the information which is provided to him or her by the professionals surrounding him. This is especially true in medical practice since the decision to consent or not depends on possibly difficult to understand and a maybe overwhelming amount of information, often given at unpleasant times, namely after having been given bad news. The second key recommendation of the CONTRACT project is therefore too much more than what is the case today reflect the patient's view in the regulations on informed consent.

In this it is important to realize that consent as an autonomous decision made by the patient is a process. Several steps should be completed when obtaining informed consent: the first step is to provide information, the last to obtain a signed consent form. Consequently an informed consent form does not equal informed consent. A form signed and dated may proof that the consent has been

discussed but does not proof that the subject understood what he was signing. In this respect the current Clinical Trials Directive does appropriately stress the oral conversation with the investigator. In the process of consent it is of crucial importance to keep in mind that the primary goal of the different steps leading to valid informed consent is the protection of the patient, not shrinking liabilities. Informed consent as it is included in the Data Protection Directive and the Clinical Trials Directive today is not a waiver but a safeguard to ensure that data are processed and clinical trials are being run whilst protecting the subject. The feeling that informed consent forms are used as an instrument protecting the physician rather than the patient is provoked by long forms, using language not adapted to laymen, presented as an administrative necessity or as a condition to participate in a clinical trial. Instead forms should be as concise, precise and clear as possible. It is the consortium's opinion that this is not enough reflected in the European regulations as they stand today, nor in the published Proposals for Regulations on clinical trials on medicinal products for human use 2012/0192 and on the protection of individuals with regard to the processing of personal data and on the free movement of such data 2012/011.

Following this second recommendation of the CONTRACT project - reflect the patient's view in informed consent regulations - the emphasis should be on the quality and amount of information. One has to be careful that the concept of patient autonomy doesn't turn against the patient because the excess of information comprises the patient's wellbeing with a burden of knowledge. It is therefore important to not only respect the right to know, but also the right not to know. However, it showed from our research that the balance between the right to know and the right not to know is a delicate one. On the one hand it could be argued that it should be the subject who instructs on the amount and level of information he is provided with. But on the other hand it has also been argued that autonomy requires choice and choice requires information through disclosure. Under the Clinical Trials Directive the subject is even considered to have the obligation to be informed about the trial he or she will participate in. We concluded that this balance should always be judged weighing the possible harm to the well-being of the subject and his or her ability to still actually participate in the decision-making.

That consent is a process rather than a one-time thing seems to gain support, but it is not equally reflected in the new Proposals for Regulations. Obviously informed consent has to be obtained before action is taken (before starting treatment, before enrolling in a clinical trial or before collecting data) but it showed from our research that a true need for either staged informed consents, two-step informed consents with a pre and a full consent, re-consenting or an active right to withdraw exists. Also the issue of fully informing the subject before the commencement of an (emergency) clinical trial and before re-using data for research purposes relates back to this. Emergency enrolment in clinical trials has now been regulated by the Proposal for a Clinical Trials Regulation, based on the concept of delayed informed consent. But for all other cases clarity is not provided. The Proposal for a General Data Protection Regulation on the one hand specifies that information has to be provided "at the time of collection, or, where the data are not collected from the data subject, within a reasonable period depending on the circumstances of the case". The Proposal for a Clinical Trials Regulation on the other hand does not specify when the informed consent has to be obtained at all, it only indicates that the informed consent and the prior interview are two requirements which have to be fulfilled before a trial can be commenced. Furthermore, while the Proposal for a Clinical Trial Regulation does acknowledge

the informed consent to be a process, the Proposal for a General Data Protection Regulation does still define informed consent as an 'indication' the data subjects wishes, a one-time thing.

This being said, the CONTRACT consortium would like to reiterate the recommendation and repeats the need for harmonization of the concept of informed consent used in different regulatory instruments, both on European an on national level. It is unfortunate that the Proposal for Clinical Trials Regulation now indicates under the new authorisation procedure that the informed consent forms for both the participation in a clinical trial and for the processing of personal data has to be assessed by each "Member State concerned" individually. While the goal of the Proposal to ensure a smoother authorisation procedure is absolutely necessary, the CONTRACT consortium questions if the reference to national authorisation and thus national legislation for all matters concerning informed consent and data protection is actually aiding. A final example of this lack of harmonization constitutes the consequences of the withdrawal of consent. Under both Proposals for Regulation the right to at all times withdraw consent is clearly kept as an important protection mechanism for the subject. But while the Proposal for a Clinical Trials Regulation states that withdrawal does not affect the activities based on consent before its withdrawal, the Proposal for a General Data Protection Regulation now emphasizes the right to be forgotten, implying that collected data may have to be fully erased.

Another tangible aspect of informed consent in translational research is the re-use of data. The balance between the autonomy of the subject and the need for reliable data of researchers / data controllers is a fragile exercise to make and which continues to be an issue under the new Proposals for a General Data Protection Regulation and a Clinical Trials Regulation. The European Union has been supporting the "bench to bedside approach" where the two-way data flow - from the researchers to the physician and the patient and vice versa - should support treatment and research. But when these data flows depend on informed consents of the patient, this touches again upon the fragile balance between the autonomy of the subject and the need for protection of the subject. The current Data Protection Directive and the Proposal for a General Data Protection Regulation protect the subject by requiring an informed consent to be given for purpose specific data processing. A broad consent allowing future use of the data for research is not allowed under this principle as it is not intelligible. Furthermore it is argued that in case of such a broad consent the consent is no longer informed since the researchers cannot yet inform the subject on the scope of the consent. Often the research the data will be used for is not yet defined. The Proposal for a General Data Protection Regulation only foresees a new article 83 which allows the processing of personal data for historical, statistical and scientific research. The re-use of data originally collected for a different purpose, e.g. on the basis of informed consent, is under this provision allowed only if (a) the purposes cannot be fulfilled by using anonymous or pseudonymous data and (b) the data are as little as possible linked to other identifying data. Since this provision seems to only address the secondary use of data, it only partly solves the problem.

A third and final recommendation and key finding of the CONTRACT project is that e-consent can help when balancing the right autonomy and protection, as well as the right to be informed and the right not to know. One of the criticisms of the current consent procedure is that the pre-eminence of autonomy outshines valued aspects. Although it is sometimes argued that e-consent would decrease valuable

contact with the physician or investigator, it is the opinion of the consortium that e-consent should be understood as an automated tool which with the help of technology aids the physician or investigator in obtaining the subject's consent, not which replaces the paramount face-to-face contact. e-consent solutions should and can lead to obtaining informed consent of the same value where the gain is two-fold: supporting the participation of the patient in the decision making process and improve the management of informed consent, reduce time and money for the physician or investigator. We therefore welcome the fact that under article 4 (8) the Proposal for a General Data Protection Regulation allows to obtain informed consent electronically for the processing of data. The Proposal for a Clinical Trials Regulation has not included such a provision. It is the consortium's recommendation to still do so.

Three key messages summarize it all:

- The regulatory framework on informed consent needs harmonization;
- The patient's view should be reflected in these regulations;
- And electronic consent should be supported.