CONTRACT

CONSENT IN A TRIAL & CARE ENVIRONMENT

D2.2 – Collation and systematisation of questionnaire responses

Update – data up to 5th September 2011

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ABSTRACT:

The present deliverable is a report on the results of the questionnaire developed in CONTRACT and presented in D2.1. These results of the questionnaire will serve as the necessary input for WP3 (Evaluation of the status in Europe).

KEYWORD LIST: Questionnaire, results, best practices of consent

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Contents

Executive Summary

The present deliverable is a report on the collation, systematisation and results of the questionnaire developed within CONTRACT and presented in D2.1. This questionnaire was made available via the CONTRACT website and other project websites as well as direct contact to different stakeholders.

In parallel to the results of this questionnaire the identification of best practice cases are described for relevant stakeholders.

The results of the questionnaire serve as the necessary input for WP3 (Evaluation of the status in Europe).

This is an updated version with data collection up to 5th of September 2011.

1 Introduction

1.1 Purpose, context and scope of this deliverable

The present document is a summary of the response of the questionnaire. It also tries to describe best practice cases.

1.2 Background

As given in D2.1 we have identified the following main stakeholder groups for the survey:

- Clinicians / Care providers
- Chairpersons of research projects / trials
- Basic Researcher / Molecular biologists
- Computer Scientists
- Legal Practioners / Ethicists
- Data Manager / Statisticians
- European Policymakers

Patients or patient groups were not the target of the questionnaire. The link to the questionnaire was sent to the targeted projects and other stakeholders as given in D2.1 for distribution to their members.

2 Collation of questionnaire responses

2.1 Targeted projects and individuals

Altogether 221 projects were actively contacted and asked to participate in the survey. The list of the projects is part of D 2.1. Coordinators and Chairmen/Chairwomen were asked to spread the information about the link to the members of their project.

The questionnaire was made available at the 25th of March via the website of CONTRACT. People who had given their consent in taking part in the survey were notified by email with the link to the questionnaire. Some of the targeted projects put the link to the questionnaire on their website, like GPOH, SIOP Europe, p-medicine, ContraCancrum, TUMOR, STaRC.

A reminder to answer the questionnaire was sent to the same projects and individuals 3 weeks after the start time. The collation of answers for this analysis ended at **5th of September 2011**.

2.2 Statistical analysis of the responses

For statistical analysis the data were uploaded in IBM SPSS Statistics 19. For comparison of results between different stakeholders and in dependence of single parameters discriptive statistical methods were used. T-Test was used for the calculation of significant differences.

Altogether 203 individuals participated in the survey. 58 of them completed the questionnaire completely and 145 only a part of the questionnaire. Most of the partcipants who did not complete the questionnaire stopped after the first 2 pages (Fig. 1).

Figure 2a shows the age distribution of all participants and figure 2b of only those who completed the questionnaire. In part of the participants age is missing.

49 (24,1%) particpants are female and 63 (31,0%) are male. In 91 (44,8%) participants' gender is missing. In the group of participants who finished the survey 20 (34,5%) were female and 34 (58,6%) male. In 4 (6,9%) the gender is missing.

The highest professional degree of participants is given in table 1. Their country of origin is listed in table 5.

Most of the questionnaires were answered by people from Universities (67; 33,0%) (Tab. 2).

Answers are from 24 different countries including 3 countries outside of Europe (from North America, Asia, Africa).

Highest professional degree	Number of responses [all]	Number of complete responses
Primary school	1	0
High school	6	1
Bachelor	9	4
Master or equivalent	32	15
MD	11	7
PhD or other	37	18
State Exam	3	1
Professor at a University	11	7
Other	3	2
Missing	90	3

***Tab.1**: Professional degree of participants*

Employment at	Number of responses [all]	Number of complete responses
Government (public) service	16	8
Large industry	11	6
Self-employment	5	1
SME	10	4
University	67	35
Other	12	4
Missing	82	

***Tab.2**: Institutes of employment of participants.*

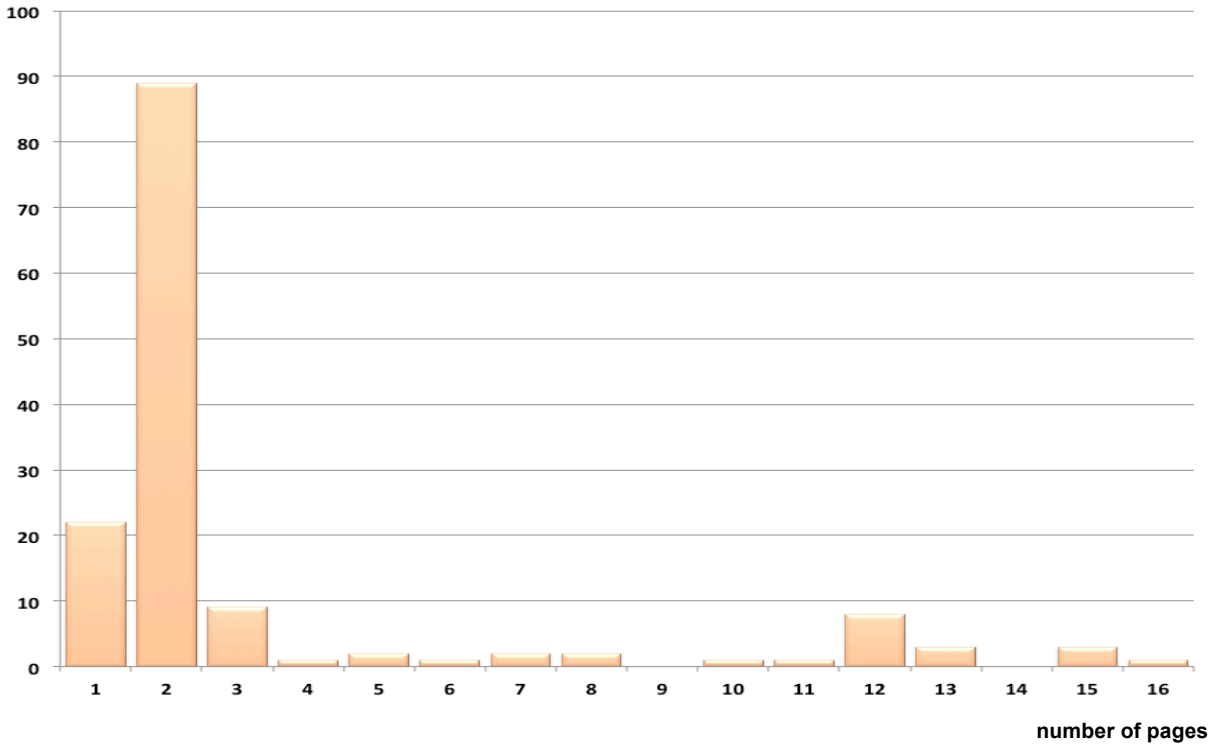


Fig. 1: *Number of participants quitting the survey after* ***x*** *number of pages.*

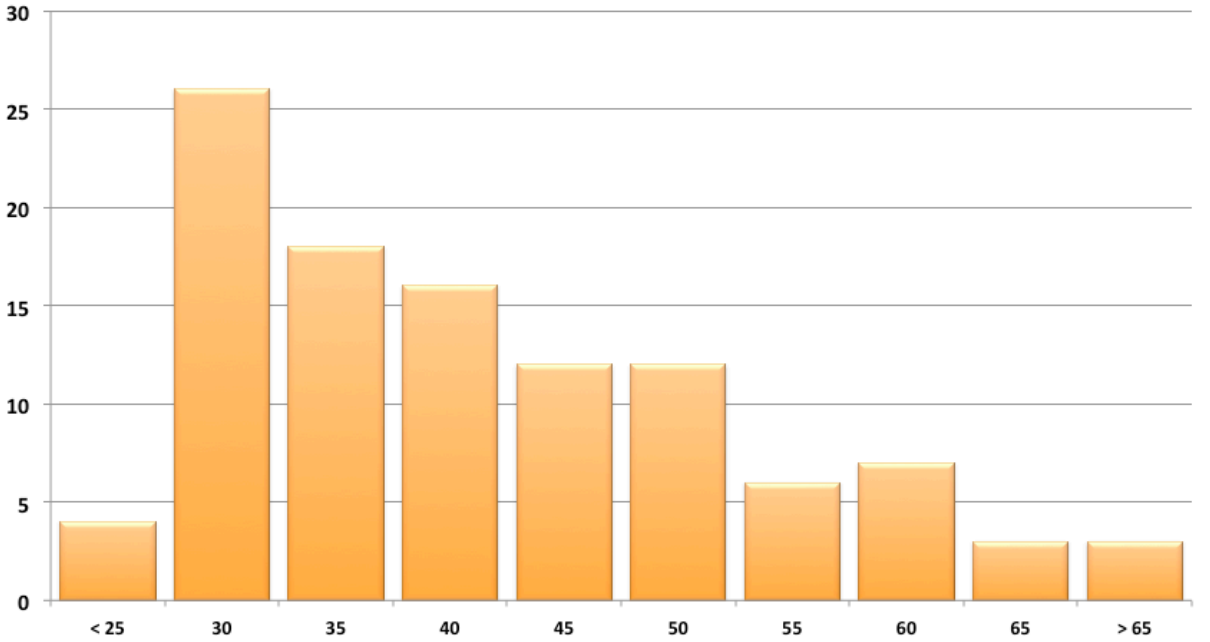


Fig. 2a: *Number of all participants given according to age.*

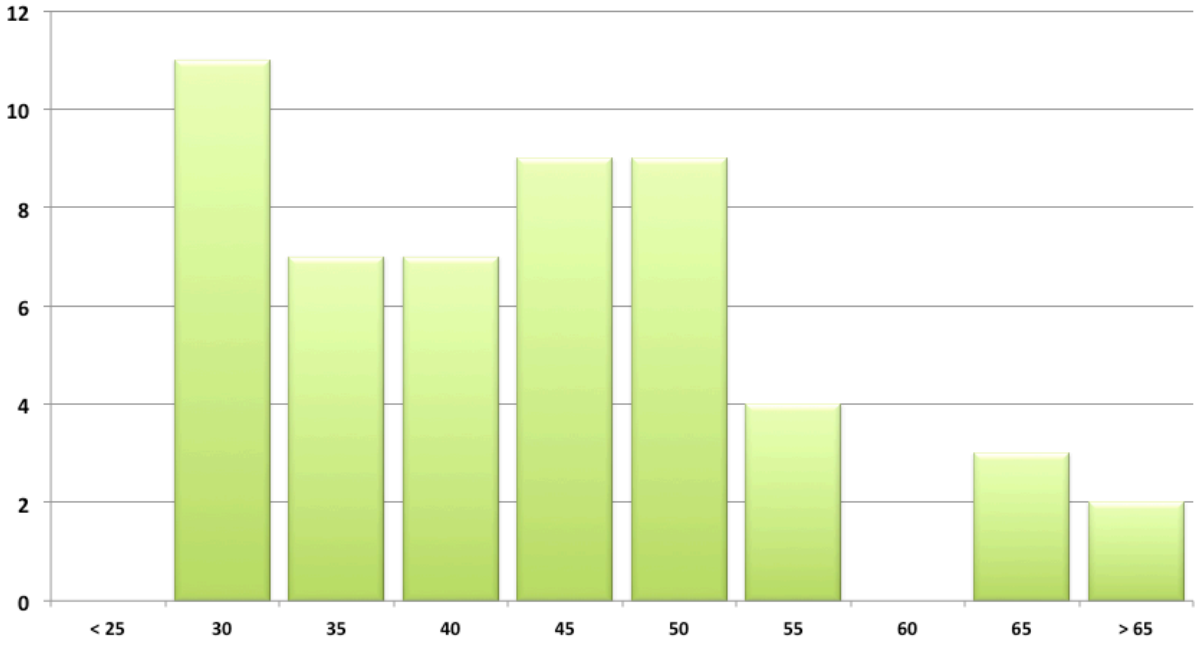


Fig. 2b: *Number of participants with completed questionnaires given according to age & participants without known age.*

3 Systematisation of questionnaire responses

3.1 Responses over time

The number of responses over time of the completely answered survey is given in figure3.

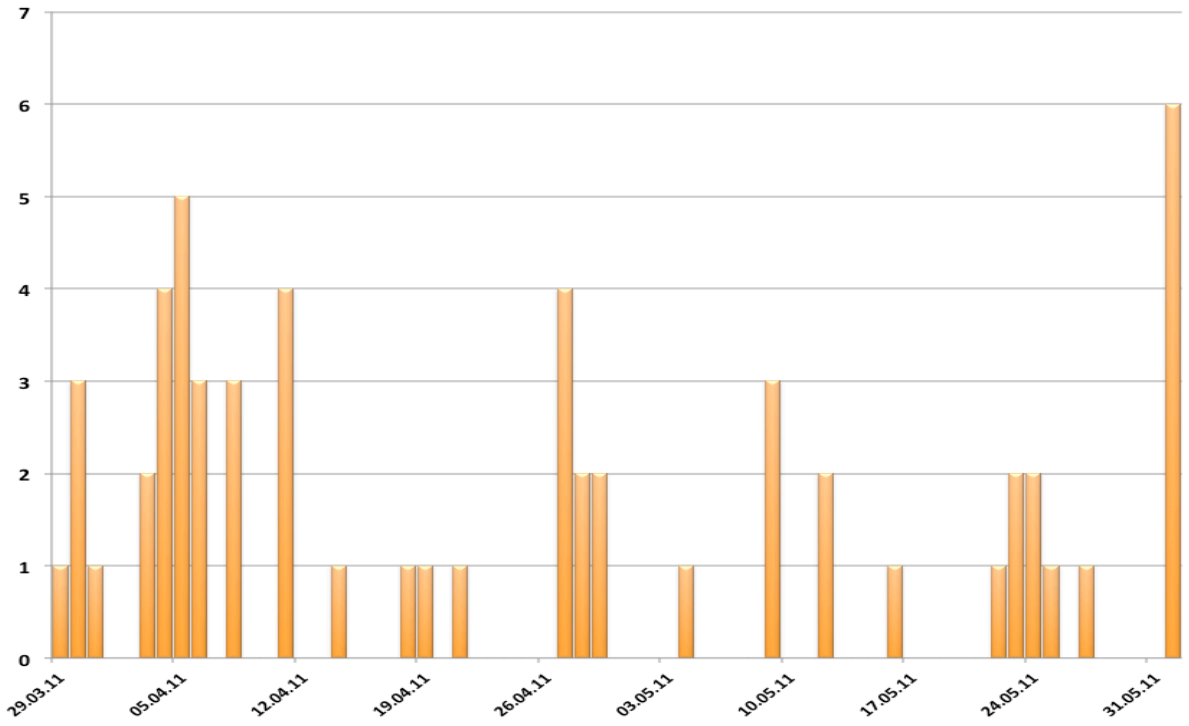


Fig. 3: *Number of participants over time. Last column is a summary of answers after the 31st of May.*

3.2 Responses from different stakeholders

The number of responses according to the main stakeholders as defined in D2.1 is given in table 3:

Stakeholder	Number of responses [all]	Number of complete responses
Clinicians / Care providers	13	9
Chairpersons of research projects / trials	21	10
Basic Researchers / Molecular biologists	19	11
Computer Scientists	17	5

Legal Experts / Ethicists	20	10
Data Manager / Statisticians	7	4
European Policymakers	1	0
Other	21	9
Missing	84	

***Tab.3**: Number of responses from different stakeholders.*

3.3 Responses according to different professions of participants

The number of responses according to the main stakeholders as defined in D2.1 is given in table 4:

Profession	Number of responses [all]	Number of complete responses
Physicians	27	18
Manager	9	5
Molecular biologists	2	2
Computer Scientists	17	6
Ethicists	1	0
Lawyer	19	10
Statisticians	1	0
Bioinformatician	9	4
Other	36	13
Missing	82	

***Tab.4**: Number of responses according to different professions of participants.*

3.4 Responses from different countries

The number of responses according to different countries is given in the following table 5:

Country of origin of participants	Number of responses [all]	Number of complete responses
Austria	1	
Belarus	1	1
Belgium	7	5
Bulgaria	3	3
Denmark	2	
Estonia	2	1
Finland	2	
France	1	
Germany	59	30
Greece	13	7
Ireland	1	1
Italy	1	
Lithuania	2	1
The Netherlands	1	
Norway	1	1
Poland	1	1
Slovenia	1	1
Spain	4	1
Sweden	1	
Switzerland	6	2
United Kingdom	7	1
Africa	1	
Asia	1	1
North America	1	1
Missing	83	

***Tab.5**: Number of responses from different countries.*

3.5 Responses of different sections of the questionnaire

The questionnaire is divided into 6 different sections. These sections are listed in table 6 showing also the number of questions and which stakeholders did answer them. The number of responses ist listed as well.

	Section	number of questions	to be answered by	Number of responses
1	General	35	all	up to 120
2	Clinical care	11	all	up to 80
3	Research	3	researchers	25, 25, 47
4	IT related Clinical care context Clinical trial context	 21 11	 IT experts IT experts	 up to 10 up to 17
5	Legal and ethical issues Data Protection Authority	22 9	all DPA	up to 75 3
6	Handling	6	all	up to 69

***Tab.6**: Number of responses in different sections.*

As the number of responses is in main parts of the questionnaire up to now relatively low only general answers are provided. Differences between different stakeholders or participants with different professions or from different countries are not given due to too low numbers.

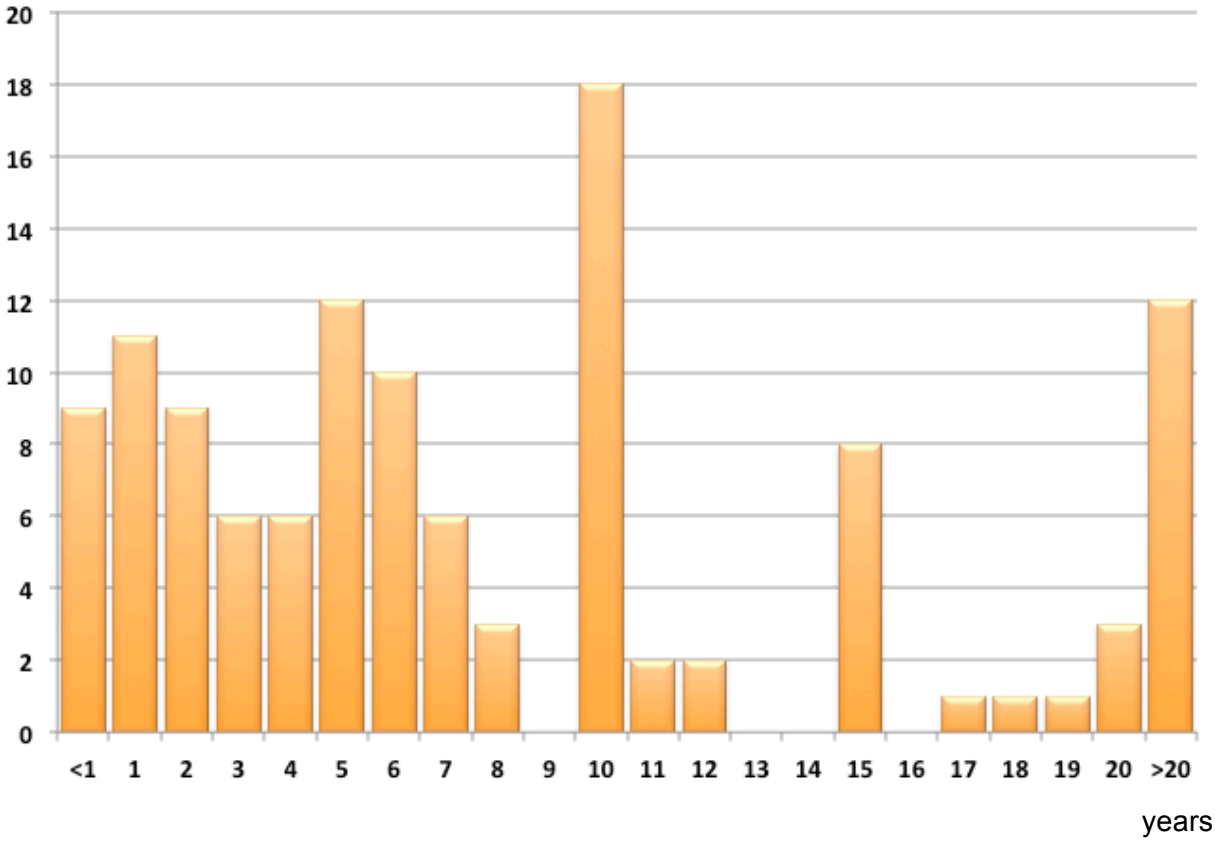
4 The results of the questionnaire

The main results of the questionnaire will be made available via the website of CONTRACT and its newsletter. The results will also be published in high ranked journals and presented on International Meetings and Conferences in Europe and elsewhere. A poster is accepted to be presented at the SIOP Congress of Pediatric Oncology and Hematology in Auckland/New Zealand in October 2011. People who have given their consent in being contacted to receive the results of the questionnaire will be informed about them by sending them anoutcome document via email.

4.1 General results

In the general section of the questionnaire altogether 35 questions were asked. These questions were answered by up to 120 participants.

How long have you been involved with dealing with informed consent in your work?



The mean of 9.1 years shows that most of the participants are experienced with consent.

Did you ever sign an informed consent form as a patient or for someone else?

	Number of responses [n=120]
yes	45
no	75

If yes, for whom did you sign?

	Number of responses [n=45]
for someone else as a legal guardian	2
my child	1
myself	41
missing	1

If yes, have you retained a copy of the informed consent form?

	Number of responses [n=45]
no, I did not receive a copy	16
No, I did receive a copy but did not keep it	9
yes	19
missing	1

If yes, how comfortable were you in general with the process of informed consent?

	Number of responses [n=45]
not at all - 0	1
1	6
2	6
3	10
4	13
perfectly satisfied - 5	6
missing	3
Mean: 3.10	

If yes, did you feel that the informed consent form you filled out explained the medical information sufficiently?

	Number of responses [n=45]
not at all - 0	1
1	4
2	17
3	14
4	4
too detailed - 5	2
missing	3
Mean: 2.52	

If yes, did you feel that the informed consent form you filled out explained the legal information sufficiently?

	Number of responses [n=45]
not at all - 0	5
1	5
2	15
3	10
4	6
too detailed - 5	0
missing	4
Mean: 2.17	

If yes, how did the process of giving informed consent influence your concerns related to the subject of the informed consent?

With respect to the medical procedures to be undertaken

	Number of responses [n=45]
no concern - 0	6
1	14
2	6

3	11
4	2
maximal concern - 5	2
missing	4
Mean: 1.88	

If yes, how did the process of giving informed consent influence your concerns related to the subject of the informed consent?

With respect to the sensitivity and handling of your data

	Number of responses [n=45]
no concern - 0	3
1	16
2	8
3	10
4	3
maximal concern - 5	1
missing	4
Mean: 1.93	

Are you familiar with legal requirements regarding the content of the informed consent procedures?

	Number of responses [n=91]
not at all familiar - 0	7
1	7
2	8
3	14
4	32
very familiar - 5	23
missing	112
Mean: 3.38	

In how much detail should an informed consent form/procedure explain medical information?

	Number of responses [n=91]
not at all detailed - 0	3
1	0
2	8
3	28
4	37
very detailed - 5	14
missing	112
Mean: 3.49	

In how much detail should an informed consent form/procedure explain legal information?

	Number of responses [n=91]
not at all detailed - 0	1
1	5
2	14
3	28
4	29
very detailed - 5	14
missing	112
Mean: 3.33	

Should there be different practices of obtaining informed consent for medical care and research environments?

	Number of responses [n=91]
yes	74
no	17

Which of the following aspects do you consider should be included in informed consent forms for clinical trials?

The focus of the trial is always research and not medical care

	Number of responses [n=91]
yes	50
no	41

Purpose of the trial

	Number of responses [n=91]
yes	85
no	6

Trial treatment(s)

	Number of responses [n=91]
yes	76
no	15

Trial procedures

	Number of responses [n=91]
yes	74
no	17

Data protection

	Number of responses [n=91]
yes	78
no	13

The participant's responsibilities

	Number of responses [n=91]
yes	75
no	16

Experimental trial aspects

	Number of responses [n=91]
yes	47
no	44

Foreseable risks or inconveniences

	Number of responses [n=91]
yes	81
no	10

Expected benefits for patients

	Number of responses [n=91]
yes	76
no	15

Expected benefits for general public

	Number of responses [n=91]
yes	71
no	20

Alternative procedure(s) or treatment(s)

	Number of responses [n=91]
yes	71
no	19

Compensation and/or treatment available in the event of trial-related injury

	Number of responses [n=91]
yes	57
no	34

Payment to participants

	Number of responses [n=91]
yes	46
no	45

Expenses to participants

	Number of responses [n=91]
yes	60
no	31

Information about liability issues

	Number of responses [n=91]
yes	66
no	25

Participation is voluntary, and the participant may refuse to participate or withdraw from the trial at any time

	Number of responses [n=91]
yes	84
no	7

The monitor(s), the Ethical Committee, and the Regulatory Authorities will be granted direct access to participant's medical records

	Number of responses [n=91]
yes	56
no	35

Records identifying the participant will be kept confidential to all parties with the exception of those specified before

	Number of responses [n=91]
yes	73
no	18

The participant or representative will be informed if information becomes available that may be relevant to their willingness to continue participating in the trial

	Number of responses [n=91]
yes	72
no	19

Person(s) to contact for further information regarding the trial, rights of trial participants, and in the event of trial-related injury

	Number of responses [n=91]
yes	75
no	16

Circumstances and / or reasons under which participation on the trial may be terminated by the sponsor

	Number of responses [n=91]
yes	53
no	38

Expected duration of trial participation

	Number of responses [n=91]
yes	72
no	19

Approximate number of participants involved in the trial

	Number of responses [n=91]
yes	38
no	53

Which of the following aspects do you consider should be included in informed consent forms for clinical care?

Purpose of the trial

	Number of responses [n=91]
yes	85
no	6

Data protection

	Number of responses [n=91]
yes	66
no	25

The participant's responsibilities

	Number of responses [n=91]
yes	72
no	19

Foreseable risks or inconveniences

	Number of responses [n=81]
yes	83
no	8

Expected benefits for patients

	Number of responses [n=91]
yes	76
no	15

Alternative procedure(s) or treatment(s)

	Number of responses [n=91]
yes	69
no	22

Treatment available in the event of side effects

	Number of responses [n=91]
yes	70
no	21

Information about liability issues

	Number of responses [n=91]
yes	55
no	36

Participation is voluntary, and the participant may refuse to participate or withdraw from the trial at any time

	Number of responses [n=91]
yes	67
no	24

Records identifying the participant will be kept confidential

	Number of responses [n=91]
yes	64
no	27

Person(s) to contact for further information

	Number of responses [n=91]
yes	71
no	20

Expected duration of the treatment or diagnostic procedure

	Number of responses [n=91]
yes	73
no	18

Approximate number of patients undergoing the diagnostic procedure by the specific physician doing the procedure

	Number of responses [n=91]
yes	24
no	67

Approximate number of patients with this disease being treated by the specific physician

	Number of responses [n=91]
yes	23
no	68

Are you familiar with the re-consent procedure?

	Number of responses [n=89]
yes	34
no	55

If yes, how important is obtaining re-consent from a legal point of view?

	Number of responses [n=34]
not important at all - 0	1
1	6
2	3
3	5
4	14
very important - 5	5
missing	0
Mean: 3.18	

If yes,in your opinion should obtaining re-consent be obligatory?

	Number of responses [n=34]
no	10
yes, for all the patients	15
yes, for under-aged patients	9
missing	0

If yes, when should a re-consent be obtained in your opinion?

	Number of responses [n=34]*
never	3
once a patient turns 14	6
once a patient turns 16	7
once a patient becomes legally adult	17
4 weeks after the begin of a trial treatment	4
At the end of the trial	7
Every time data or biological material is needed for a new research topic	12

Every time biological material is used	4
After every amendment of a trial	10

*more than one answer is possible

How important is the role of the physician to the project when asking for informed consent?

	Number of responses [n=89]
not important at all - 0	2
1	3
2	2
3	13
4	29
very important - 5	40
missing	0
Mean: 4.07	

How important is the attitude of the physician to the project when asking for informed consent?

	Number of responses [n=89]
not important at all - 0	2
1	0
2	4
3	16
4	23
very important - 5	44
missing	0
Mean: 4.13	

How much previous experience in clinical care should a physician obtaining informed consent have?

	Number of responses [n=89]
no experience at all - 0	1
1	6
2	11
3	23
4	38
high level of experience - 5	10
missing	0
Mean: 3.36	

Is it possible in your opinion to obtain informed consent without speaking to the patient, e.g. Using only paper based or electronic mailing methods?

	Number of responses [n=89]
yes	19
no	70

How important is it to provide an information sheet for the patient to allow him/her inform him/herself about the project?

	Number of responses [n=89]
Not important at all - 0	1
1	3
2	8
3	8
4	32
very important - 5	37
missing	0
Mean: 3.97	

Should this information sheet always be followed up with a face to face consultation in any case?

	Number of responses [n=89]
yes	63
no	26

Do you think that patients have difficulties in general to understand informed consent forms and procedures?

	Number of responses [n=89]
yes	75
no	14

How many patients do you think understand all items addressed in informed consent forms and procedures?

	Number of responses [n=89]
< 10 %	2
10 – 20 %	15
20 – 30 %	14
30 – 40 %	13
40 – 50 %	12
50 – 60 %	15
60 – 70 %	5
70 – 80 %	7
80 – 90 %	4
90 – 100 %	2
Mean: 43.37	

To what extent do the requirements to obtain informed consent pose a barrier to research in general?

	Number of responses [n=89]
not at all - 0	4
1	12
2	16
3	27
4	22
very much - 5	8
missing	0
Mean: 2.84	

4.1.1 Questions only for chairpersons of trials and coordinators of projects

If possible and you are willing to share, could you provide us with the following documents: templates used for informed consent the project or trial protocol (for analysis of the completeness of your informed consent)

Altogether 4 participants uploaded 7 documents of which 4 are consent forms 2 are trial protocols and 1 is about patient information. The documents will be analysed in detail in the upcoming legal analysis of the questionnaire's results.

What kind of project are you running?

	Number of responses [n=23]
Prospective clinical trial	15
Retrospective clinical trial	1
An epidemiological project	2
A research project where only retrospective data are used which does not inflence the diagnosis or teatment of current patients	2
other	3 (biobanking, longitudinal prospective population-based study, validation of an assessment tool with the help of experts)

In case of a prospective clinical trial, specify what kind of prospective clinical trial it is you are running

	Number of responses [n=22]
randomized	13
multicentre	15
International inside Europe	13
International outside Europe	8

Did you compile the informed consent forms for your project/trial by yourself?

	Number of responses [n=23]
yes	11
no	12

If yes, how difficult was it for you to compile the informed consent forms for your project?

	Number of responses [n=11]
not difficult at all - 0	1
1	1
2	1
3	5
4	2
very difficult - 5	1
missing	0
Mean: 2.82	

If no, who compiled it for you?

	Number of responses [n=12]
a collegue	1
applicable to partners only	1
jointly with other scientists	1

lawyers from Estonia and Canada	1
Pharmaceutical institutes	1
Science/Project management: CRA to adapt to EC requirements	1
Sponsor	2
study centre	1
Sub-investigator	1
CRO	2

Did you use a template to write the informed consent forms for your project?

	Number of responses [n=23]
yes	16
no	7

If no, would a template have been helpful?

	Number of responses [n=7]
yes	5
no	2

If yes, would you be willing to pay for such a template / service?

	Number of responses [n=16]
yes	11
no	5

Did you need to change the informed consent forms / procedures after an ethical review of your project?

	Number of responses [n=23]
yes	14
no	9

Do you think you have addressed all items that are legally and ethically needed in terms of informed consent in your project?

	Number of responses [n=23]
yes	21
no	2

Do you know whether patients have difficulties to understand your informed consent forms and procedures?

	Number of responses [n=23]
yes	10
no	13

How many patients do you believe understand all items addressed in the informed consent procedures of your project?

	Number of responses [n=19]
< 10 %	1
10 – 20 %	2
20 – 30 %	3
30 – 40 %	3
40 – 50 %	2
50 – 60 %	3
60 – 70 %	4
70 – 80 %	2
80 – 90 %	2
90 – 100 %	1
Mean: 54.78	

In how many languages do you provide the informed consent forms and procedures in your project?

	Number of responses [n=23]
1	10
2	4
3	1
4	0
5	1
10	1
11	1
12	2
15	2
30	1
Mean: 5.69	

Do you provide an information sheet to patients to inform themselves about the project?

	Number of responses [n=23]
yes	17
no	6

Please specify the minimal and maximal number of different informed consent forms that you provide for a single patient?

	Minimal number [23]	Maximal number [23]
0	1	1
1	18	5
2	3	7
3	1	7
4		1
5		1
12		1
Mean	**1.08**	**2.65**

4.2 Results of the clincal care section

Do you see a discrepancy between actual clinical practice and the legal and ethical regulations for clinical practice?

	Number of responses [n=80]
not at all - 0	3
1	11
2	13
3	24
4	16
a large discrepancy - 5	3
missing	10
Mean: 2.69	

What is the maximum number of different informed consent forms that should be provided for a patient taking part in a trial?

	Number of responses [n=80]
0	1
1	32
2	23
3	14
4	2
5	6
10	2
missing	0
Mean: 2.23	

Should there be a maximum number of pages of written information given to a patient at once?

	Number of responses [n=80]
yes	56
no	24

If yes, how many pages of written information for patients do you think are acceptable?

	Number of responses [n=55]
1	2
2	11
3	8
4	7
5	16
6	2
10	7
15	2
missing	0
Mean: 4.87	

Should there be a maximum number of pages of written information given to a patient for one disease, treatment or diagnostic procedure?

	Number of responses [n=80]
yes	51
no	29

If yes, how many pages of written information for patients do you think are acceptable?

	Number of responses [n=51]
1	3
2	12
3	12
4	5
5	9
6	1
7	1
8	2
10	4
15	1
20	1
missing	0
Mean: 4.55	

In your experience, how useful is this written information for patients to understand what is happening?

	Number of responses [n=80]
Not useful at all - 0	1
1	1
2	5
3	26
4	27
very useful - 5	18
missing	2
Mean: 3.59	

In your experience, how useful is this written information for patients to agree with what is happening?

	Number of responses [n=80]
Not useful at all - 0	1
1	2
2	5
3	27
4	28
very useful - 5	15
missing	2
Mean: 3.50	

How much time should a patient be given to reflect before he has to sign an informed consent form for any kind of procedure or treatment according to your opinion?

	Number of responses [n=70]
< 1 hour	5
1 - 6 hours	7
6 – 12 hours	2
12 – 24 hours	18
24 – 48 hours	26
3 – 5 days	17
> 5 days	5
missing	0
Median: 24 - 48 hours	

Should there be more time given in case of a prospective randomized trial?

	Number of responses [n=53]
yes	24
no	29

Does this match the legal / ethical requirements for informed consent in your country?

	Number of responses [n=80]
I do not know	34
no	5
there are no legal / ethical requirements	4
yes	37

Can you estimate the average time period in hours between diagnosis to the time at which informed consent is given by patients / parents / legal guardians in general today?

hours	Number of responses [n=47]
0	1
0.5	1
1	9
2	1
3	2
6	1
8	1
10	2
12	2
24	12
36	2
48	7

72	1
96	1
100	2
168	2
Median: 24	

What is the time frame in which informed consent forms need to be signed by patients / parents / legal guardians?

	Number of responses [n=55]
I do not know	19
1 day	5
2 days	3
there are no legally binding timeframe	28

What are your suggestions for improvement of obtaining informed consent in clinical care?

	Number of responses [n=26]
clear and simple language standard for one contact person	1
details of the therapy should always be printed, not handwritten by the physician	1
Get IC only before surgery, complex and/or experimental investigations/ treatments (e.g. cancer radio-and chemotherapy, transplantations, genetic investigations). Do not undermine pateint's confidence by asking IC for everything. Have the responsible MD provide information and ask him to get the IC if one is needed.	1
I am not familiar with the process, so I can not make any suggestions.Sorry	1
I am really worried by the framing of these questions - it should be the patient who decides how much information they need/want and in what format that would best suit them. Equally, some will want to make a quick decision and get on with life and others will want plenty of time to consider all the information and come to a decision, perhaps after consulting with family and friends (and the Internet!).This is all geared to producing rules and regulations rather than meeting patients' needs which vary and are not constants - even if we wish they would be.	1

independence of persons informing subjects	1
Less complicated (simplier wording) ICFs. more tables and figures instead of wording. limited amount of pages of ICF. more detailed face - to - face (investigator/study nurse-subject)information regarding the trial, enough time for the subject to think about and discuss (with friends and families, etc.) study participation	1
More time	1
none	1
Patients should have the opportunity to read the information on the consent in their own time (however long that might take), and have the possibility to ask questions regarding the information	1
personal talk between patients and treating physician needs to be more standardized	1
Presence of one parent must be sufficient	1
Restrain too complicated details about diagnostic or therapeutic procedures and focus on practical issues (how diagnosis and treatment is to be performed) the patient's mutual advantage, the most important possible adverse events and complications and contact details of the attending treatment team in case of any question.	1
Simplify	1
Simplify language and reduce detail of information - where treatment is strongly medically indicated, only mention risks that a reasonable patient would consider significant. where treatment is less strongly indicated, mention all risks of serious harm.	1
The main part of any informed consent is the personal talk of the doctor and team with the patient and/or legal guardians. The main problem of formal/written consent papers is that they will never be as complete as formally required unless being so long that it will not possibly managed by normal patients. Thus the basic idea of clinical consenting should be adapted to reality	1
To provide brief but accurate information in an understandable fashion.	1
try to be very understandable and at the same time thoroughly informative	1
use pictures and electronic media!	1
Using photos/ patient stories/ online Q & A, teach-back methods to stimulate better discussion between doctor and patient about the procedure.	1
Videos and other non-written material to obtain a higher percentage of real comprehension in participants.	1

Provide an information desk/telephone number/website in case important questions arise	1
Use of standardized icons for key points of the consent form	1
an authorized physician for obtaining the informed consent in order to explain all the details to the patient and his family	1
Every detail about the procedures to be done, the alternative available, the benefit/risk involved should be explained	1
More oral explanation of key points, potential consequencies and existing alternatives	1

To what extent would such improvements influence the future of clinical trials?

	Number of responses [n=27]
not at all - 0	3
1	1
2	3
3	5
4	10
very much - 5	4
missing	1
Mean: 3.04	

4.3 Results of the research section

Did you experience barriers in any of your research projects as a consequence of unclear or lack of informed consent?

	Number of responses [n=49]
yes	25
no	24

If yes, to what extent did these barriers affect the research?

	Number of responses [n=25]
not at all - 0	0
1	2
2	4
3	7
4	11
a large extent - 5	1
missing	0
Mean: 3.20	

How easy is it to overcome these barriers?

	Number of responses [n=25]
not easy at all - 0	3
1	11
2	6
3	5
4	0
very easy - 5	0
missing	0
Mean: 1.52	

4.4 Results of the IT related section

4.4.1 Results of the clinical care context

Is your Hospital Information System (HIS) a monolithic system that serves as access point to the majority of medical data that is available on a patient in the hospital?

	Number of responses [n=10]
Although the HIS is segmented over the hospital (not monolithic), cross department data access is possible	2
No, different information silos exist in the hospital	4
Yes, our Hospital Information System (HIS) comes from single vendor	4

Do you use a commercial Electronic Health Record System (EHR) / Electronical Medical Record (EMR) solution?

	Number of responses [n=10]
yes	3
no	7

If yes, please specify the vendor of your commercial EHR / EMR solution.

	Number of responses [n=5]
SAP	2
Do not know	3

Do patients give care-related consent by signing paper forms?

	Number of responses [n=10]
yes	8
no	2

If yes, do you archive the paper consent forms electronically? (e.g. scanned paper consent forms)

	Number of responses [n=8]
yes	3
no	2
I do not know	3

If consent is archived, is this done centrally?

	Number of responses [n=3]
yes	3

Is the patient consent recorded electronically (other than for archiving purposes) in the EHR or in an independent consent application?

	Number of responses [n=10]
Yes, the patient can give consent using an electronic signature	0
Yes, the data management application requests the physician to record electronically in the application that the patient has given consent (and signed a form)	1
No, there is no electronic recording whatsoever	7
I do not work in a clinic	1
I am not sure	1

Is consent to care-related procedures (e.g. agreement for surgical procedures, sharing of data, ...) recorded separately from data processing consent?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Is electronic consent handled by an eConsent system that is architecturally separate/independent from the Hospital Information System?

	Number of responses [n=10]
yes	0
no	1
I do not know	2
missing	7

Does your EHR / EMR access control system enforce the recorded patient consent with respect to data protection?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Does your EHR / EMR support recording of patients preferences regarding data sharing that LIMIT sharing with respect to the default access policies?

	Number of responses [n=10]
yes	0
no	0
I do not know	3
missing	7

Can a patient express consent about sharing medical data outside of the hospital? (e.g. refuse or enable data sharing with a general practitioner)

	Number of responses [n=10]
yes	0
no	1
I do not know	2
missing	7

Can a patient express consent about secondary use of his EHR / EMR data in specific research projects?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Can a patient express consent about being contacted for possible inclusion into a clinical trial (i.e. consenting to having his medical data scanned for that purpose)?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Can patient consent directives specify "conditions" under which they are valid (e.g. only valid in emergency situations, only for non-commercial research)?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

When consent is given by a legal guardian, is his/her identity recorded and will he/she be identifiable?

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Does the system automatically initiate re-consent or remind the physician to initiate re-consent when a minor patient becomes legally adult or even at an earlier age defined before?

	Number of responses [n=10]
yes	0
no	1
I do not know	2
missing	7

Does the system support functionality for consent life-time limiting (other than age-related time-limiting)? (e.g. expiration of consent possibly followed by automated request for re-consent)

	Number of responses [n=10]
yes	1
no	0
I do not know	2
missing	7

Is the system capable of recording that consent has been revoked?

	Number of responses [n=10]
yes	0
no	0
I do not know	3
missing	7

Can a patient easily obtain a (complete) overview of what he has consented to?

	Number of responses [n=10]
yes	2
no	1
I do not know	2
missing	5

If possible, please describe the procedures and ICT technologies that guarantee the secure process of personal data in your institution?

No answers

Please note down any relevant remarks not covered by the above questions

No answers

4.4.2 Results of the clinical trial context

Is there an electronic system to manage consent related documents for clinical trials (information leaflets, templates, ...)?

	Number of responses [n=19]
no	9
yes, this functionality is provided by the Clinical Trial Data Management System (CTMS) we use	6
Yes, we use a generic document management system	2
I am not sure	1
missing	1

Do patients give trial related consent by signing paper forms?

	Number of responses [n=19]
yes	18
no	1
missing	0

Do you archive signed paper consent forms electronically? (e.g. scanned signed paper forms)

	Number of responses [n=19]
yes	8
no	5
I do not know	5
missing	1

If consent is archived, is this done centrally?

	Number of responses [n=8]
yes, in the clinic	3
yes, in the department only	3
no	0
I do not know	1
missing	1

Is the patient consent recorded electronically (other than for archiving purposes)?

	Number of responses [n=19]
no	0
Yes, the patient can give consent using an electronic signature	1
Yes, the data management application requests the physician to record electronically in the application that the patient has given consent (and signed a form)	7
No, there is no electronic recording whatsoever]	9
I am not sure	1
I do not work in a clinic	1
Missing	0

Is consent to medical related procedures (e.g. agreement to surgical procedures ...) recorded separately from data processing consent?

	Number of responses [n=17]
yes	4
no	0
I do not know	4
missing	9

Is there an electronic system that provides functionality for managing consent given by individual patients (i.e. more functionality than document management) in a more or less generic way?

	Number of responses [n=17]
yes, consent management is provided by the CTMS we use	2
no	2
I do not know	4
missing	9

If yes, does the consent management system offer an overview of the required and obtained consent(s) for each enrolled patient?

	Number of responses [n=2]
yes	0
no	1
I do not know	1

If yes, is the consent management system capable of dealing with trial work-flow dependent consent? (e.g. different treatment trajectories might require different consent)

	Number of responses [n=2]
yes	1
no	1
I do not know	0

Does the consent management system offer support for obtaining re-consent after a study amendment?

	Number of responses [n=2]
yes	2
no	0
I do not know	0

Does the consent management system offer support for initiating a re-consent procedure when the patient becomes legally adult or even at a younger age? (e.g. reminder)

	Number of responses [n=2]
yes	1
no	1
I do not know	0

Is the recorded consent integrated in the investigator trial work-flow? (e.g. data entry is prevented as long as no consent is registered, the investigator is presented with a warning when new consent is needed, etc)

	Number of responses [n=17]
yes	2
no	1
I do not know	5
missing	9

When consent is given by a legal guardian, is his/her identity recorded and will he/she be identifiable?

	Number of responses [n=17]
yes	3
no	2
I do not know	3
missing	9

Does the system allow consent to be revoked?

	Number of responses [n=17]
yes	3
no	2
I do not know	3
missing	9

Can a patient easily obtain a (complete) overview of the consent he / she has given?

	Number of responses [n=17]
yes	4
no	1
I do not know	3
missing	9

Please note down any relevant remarks not covered by the questions...

No answers

4.5 Results of the legal and ethical issues related section

Are you willing to answer a set of questions with respect to legal and ethical aspects of informed consent?

	Number of responses [n=14]
yes	7
no	7

Do you have to deal with different legal sources when organizing informed consent procedures at your organisation?

	Number of responses [n=64]
no	30
yes, because different national sources are applicable to my project	14
yes, because multi national sources are applicable to my project	20

How many forms do you use (without counting languages) to obtain informed consent?

	Number of responses [n=34]
0	2
1	7
2	7
3	9
4	4
5	3
6	1
15	1
Mean: 3.03	

European regulations require different types of consent. At least three of them might be relevant: the patient's consent to treatment, consent to participate in a clinical trial and consent to allow the processing of personal data. Are you aware that by law you might be required to acquire three separate types of informed consent?

	Number of responses [n=64]
No, I am not aware of these regulations	18
yes, I am aware of these regulations and my institution fulfills these requirements	40
yes, I am aware of these regulations but my institution does not fulfill these requirements	6

Are there any specific data security or data protection policies concerning patients' data at your institution?

	Number of responses [n=64]
I am not aware of any	11
no	7
yes	46

Does your institution have a Data Protection Officer (a person in charge of monitoring data protection issues in your institution)?

	Number of responses [n=64]
yes	37
no	14
I do not know	13

In case of clinical trials with participating centers outside of your country do you then also apply requirements arising from foreign legislation to your informed consent procedures?

	Number of responses [n=64]
yes	39
no	25

To what extent have you experienced difficulties within European projects arising from differing National implementations of EU legislation?

	Number of responses [n=64]
not difficulties at all - 0	5
1	8
2	16
3	13
4	14
significant difficulties - 5	8
missing	0
Mean: 2.73	

Has this had a negative impact on your project / research?

	Number of responses [n=64]
yes	22
no	42

If yes, what difficulties have you experienced?

	Number of responses [n=22]
difficulties with the exchange of data between the sponsor and the study centre in France- it was very time consuming to get a version of the study protocol that fitted all needs in the differnet countries. Scotland, England and the Netherlands were the	1
as a reviewer of the ethical part of international research projects I have experienced difficulties related toa)complete lack of relevant legal info by the applicantsb)understanding of legal provisions as simple "bureaucratic" formalities	1
data from some partners might simply not be available or a lot less data becomes available, which significantly impacts the statistical power of any kind of analysis.	1
delay	1
Delays in receiving the [pseudo](a)nonymized data provided by clinicians	1

different approaches in different countries	1
different interpretation of European law in different European countries	1
different requirements in a lot of countries and between ECs. need to adapt for every country of even sigle center if mutliple ECs are inovled.	1
implementation of multi-nation trials	1
legal uncertainty	1
longer time period to start the trial	1
methods to recruitcriterions of breaking	1
overwhelming regulatory affairs, partially silly tripple documentation,financially difficult to resolve adminstratory requirements,	1
protocol amendments were approved in some countries, in others not. study procedures (e.g. number of MRTs done in one study)were handled differentially. some countries took part in a genetic substudy, whereas in other countries the ethic committees refused the participation in generic substudy, in some countries it is obligatory to that investigational drugs are only managed (storage, drug account)by a pharmacy, in other countries they can be managed directly by the site personel.	1
regulatory	1
The actual procedures are too complicated: you have to go through the whole approval system (several IRBs and ethics gremia) for studies that recruit only a few patients and also for amendments. Research killers are fees for the regulatory institutions, insurance, and the data management costs to fulfill all the administrative phantasies. The problem is not to have to few but to have too much and constantly changing regulations.To take care of all legal aspects, costs more than the research project per se!research project itself!	1
time consuming disucssions and costs	1
trying to harmonise different interpretations of consent and data protection requirements	1
Assessment of data security regulations in Member States differ very much due to a lack of harmonisation	1
Timelines not held, IEC stopped work, IEC and CA stopped work due to national problems and restructuring	1
Several	1
Completely different levels of information given from country to countryMajor disagreement with Ethics committee requirements (for example EC was asking to act in contradiction to ICH GCP for reasons related to religion)	1

Would a harmonized one-for-all approach for care and research purposes help you in your research?

	Number of responses [n=22]
not at all - 0	1
1	0
2	2
3	0
4	7
a lot - 5	12
Mean: 4.18	

Does your organization conduct retrospective studies?

	Number of responses [n=64]
yes	28
no	36

If yes, how is informed consent regulated in retrospective studies?

	Number of responses [n=28]
all the previously collected data is being used for the study and additional informed consent of the data subject is not sought	6
former patients are asked for informed consent for the use of the data which was previously collected	9
only data of patients who previously consented to additional studies is admitted to the study	13

In case of vulnerable patients (i.e. subjects possibly not capable of giving legally valid informed consent, such as minors) which of the following is fulfilled?

	Number of responses [n=59]*
a legal representative needs to sign the consent form	55
a vulnerable patient needs to assent	22
Ethic committee might need to be contacted for country specific requirement	1
Incapable patient must get adaptive information	1
signature of the hospital director	1
the patient has to sign an informed consent adjusted to his age group after the age of 12	1

* more than 1 answer possible

Are there any measures taken to measure the vulnerable patientís capability to understand the implications of the assent given?

	Number of responses [n=58]
yes	34
no	24

In case of conflict between the informed consent of the legal representative and assent of the vulnerable patient what further steps are taken?

	Number of responses [n=58]
a ruling of the court is needed	1
such a situation has never occurred in my practice	29
the opinion of the legal representative is binding	8
the vulnerable patient is not admitted to the trial	19
The will of a patient must be considered as much as possible	1

Do you also perform trials on healthy children?

	Number of responses [n=58]
yes	6
no	52

If yes, what is the procedure of obtaining consent and assent in the case of healthy children?

	Number of responses [n=6]
Informed consent of parents/legal guardians and assent of child	1
It depends on age of a child	1
Legal representative gives consent	1
parental consent	1
parental consent and child assent depending on age	1
There is no diffrerence, the procedure is standard	1

Do you also perform trials on mentally ill patients?

	Number of responses [n=58]
yes	8
no	50

What is the procedure of obtaining consent and assent in the case of mentally ill patients?

	Number of responses [n=8]
do not know	1
in case the patient has been assigned a legal representative the latter has to sign the consent	1
informed consent is signed by patient,	1

by legal representative (if has), by two witnesses and by director of the hospital	
It depends on the mental status of the patient (see ICH GCP guidelines, Informed Consent of Trial Subjects) what procedures apply. In cases of ill patients a caregiver should be present as well as a LAR	1
Legal representative	2
the patients are 1 month to 18 years old, parents or caregivers have to agree	1
There is no difference, the procedure is standard	1

Are there any additional good practices, or guidelines you follow in drafting your informed consent forms?

	Number of responses [n=58]
yes	19
no	39

If possible please upload the good practices or guidelines used for drafting your informed consent forms here

No documents were uploaded.

Should informed consent procedures be negotiable or predetermined by one side?

	Number of responses [n=58]
negotiable	21
predetermined	35

How long do you store the informed consent forms?

	Number of responses [n=56]
indefinitely	18
until the end of the clinical care / clinical trial	5

No storage	1
5 years	5
10 years	8
15 years	10
20 years	2
25 years	1
30 years	4
Unknown	2

Is this legally required or is this done for other reasons?

	Number of responses [n=56]
I do not know	18
legally required	32
best practice	1
Estonian Data Protection Act requires that consent forms are stored for 30 years following the participants death	1
institution	1
research	1
safeguard in case of future litigation	1
missing	1

Are you required to obtain accreditation of a governmental or non-governmental institution for your informed consent forms and procedures?

	Number of responses [n=56]
yes	19
no	37

If yes, what governmental or non-governmental institution is this?

	Number of responses [n=19]
Data Protection Authority and National Ethics Committee for Clinical Trials	1
EMEA, Local Ethics-Commitee (our and of each participating institution), BfArM	1
Ethic Committee	12
Executive Director, Executive Agency on Medicines	1
GPOH, GBA	1
regional authorities	1
Swissmedic	1
The Estonian Ministry of Social Affairs, Research Ethics Committee of the University of Tartu	1
missing	5

Can you please describe the accreditation procedure?

	Number of responses [n=18]
all institutions participating in pediatric clinical cancer trials have to comply with all rergulations set by Swissmedic	2
any AMG study has to be accredited	1
by asking for ethical approval of a trial the consent forms are evaluated in detail	1
consent forms are being submitted and reviewed by the IRBs, if they do not approve it changes have to be made	1
GPOH	1
ICFs (togehter with all other essential documents)have to be submitted to the responsible ECs/IRBs and to be approved by these institutions.These institutiosns can request changes to the ICFs.Sometimes the sponsor/investigator has to defend the clinical trial against the ECs/IRBs at a face-to-face meeting. Please refer also to the German Medicines Law and German GCP regulation for further details	1

in both institutions:1. A previous relevant written application describing the informed consent's specific content2. Evaluation of this content by the panel of experts3. Information on necessary changes, to be comply with4. Licensing	1
the Estonian Ministry of Social Affairs, Research Ethics Committee of the University of Tartu	1
see German legislation - 4.(?) Novelle des Arzeneimittelgesetz	1
submission and review	1
submission of application forms and all documentation seen by participants to REC comprised of medics and lay persons	1
submission to Committee	1
submission to the Etical Committee	1
the collaborating Clinician takes all steps so a to provide to basic science researchers the data	1
The Gene Donors Informed Consent Form used in our project is a decree of the Minister of Social Affairs	1
The procedure is specified in the BUlgarian Law on Medicines in Human Medicine	1
The proposal (protocll) including all informed consent forms is sent to the EC and approved, resent for changes or rejected	1
Approved seal is placed	1

Do the informed consent forms require approval by an ethics committee?

	Number of responses [n=54]
yes, by my local and other national ethical committees	26
yes, by my local ethical committee	20
no	8

Do any additional institutions review your informed consent forms?

	Number of responses [n=54]
yes	12
no	42

If yes, please name the institutions

	Number of responses [n=9]
as above	1
Competent Authorities	3
Data Protection Authority (if data protection is an issue for the particular project)	1
Drug control authorities	1
National authority	1
Sponsor QM of the University (University=sponsor of investigator initiated trials)	1
Swissmedic, COG, other national or international institutions depending on the type of study	1
DCGI (Drugs Controller Government of India)	1
Patient organization	1
University Hospital of Crete	1

Do you inform patients about the rights they have concerning informed consent?

	Number of responses [n=54]	
	yes	no
their rights as a patient	46	8
their rights as a clinical trial subject	47	7
their rights as a data subject	45	9

If yes, how do you provide this information?

	Number of responses [n=46]
written consent	24
communication with patients by the physician responsible for the patient	20
missing	2

Do you direct the patient to a non-involved institute/specialist to explain the dangers and aims of the therapy / study?

	Number of responses [n=53]
yes	6
no	47

Can the data subject/patient access their personal data after signing the informed consent form?

	Number of responses [n=53]
yes	29
no	24

If yes, how is this organized? e.g. direct or indirect access, on paper or electronically?

	Number of responses [n=9]
a patient can have access to the chart, reports of exams etc. but not to notes of MDs and nurses.For biological trial or cancer registry data the patient can rerquest to see (and copy) the relevant data	1
according to the Bulgarian law on personal data protection, every individual has the right to access the data related to them	1
by asking the treating physician	2
by direct access and paper	11
electronically	3

they can view their paper-based or electronic data (source data)	
if wished by the patient: on paper	1
only upon specific request supported by the treating physician	1
indirect access, the exact procedure has not been elaborated yet	2
the right is broad and aabsolute and specially regulated in law	1
IMPORTANT GENERAL COMMENT: Since I make use of the pseudonymized data provided by clinicians for basic science research purposes I am not the right person to answer this question. Similar comments apply to several other questions appearing throughout this survey. Apparently the survey is essentially directed to clinicians. THEREFORE, PLEASE NOTE THAT LIMITATIONS IN THE POSSIBLE ANSWERS MIGHT LEAD TO AN INADEQUATE TRANSMISSION OF WHAT EXACTLY THE SURVEY PARTICIPANT WOULD LIKE OR COULD BE ABLE TO ANSWER	1

Do you share non-personal data about trial participants with other institutions?

	Number of responses [n=53]	
	yes	**no**
yes, in the same country	29	24
yes, abroad, within Europe	27	26
Yes, abroud and outside Europe	20	33

If yes,is the participant informed about this?

	Number of responses [n=33]
yes	29
no	4

Do you create the same level of data security for collected information in all your trial centers?

	Number of responses [n=53]
yes	41
no	12

Are you aware of any legal complaints in your professional or personal environment due to the possible inappropriate handling of informed consent?

	Number of responses [n=53]
yes	13
no	40

If yes, what legal actions were taken?

	Number of responses [n=13]
Alternative dispute resolution /Mediation	5
Lawsuit against the hospital or clinician	6
Other complaint procedure	2

4.5.1 Answers by Data Protection Authorities

Does your institution have a unit which provides specific legal support concerning

	Number of responses [n=3]	
	yes	no
yes, medical law	0	3
yes, scientific research	1	2
yes, clinical trials	0	3

Does your institution offer advice about obtaining valid informed consent?

	Number of responses [n=3]
yes	3
no	0

Does your institution offer specific advice for the processing of health related data?

	Number of responses [n=3]
yes	3
no	0

If yes, please describe in what form the advice is offered

	Number of responses [n=3]	
	yes	no
online	3	0
phone	3	0
mail	3	0
personal	3	0
flyers	3	0
guidelines	2	1
others, not further specified	1	2

If yes, is there an interest from the clinical trial organizers in this offered advice?

	Number of responses [n=3]
yes	2
no	1

Does your institution have any procedure of control (audit) over the collection of informed consent and corresponding data?

	Number of responses [n=3]
yes	2
no	1

Is there a procedure for data subjects to submit a complaint?

	Number of responses [n=3]
yes	3
no	0

If yes, are clinical trials included in such a procedure?

	Number of responses [n=3]
yes	2
no	1

If yes, how is such a complaint handled?

	Number of responses [n=3]
attempt of mediation, and if not possible opinion (with or without recommendations) of the data protection authority	1
internal complaint procedure which is followed by special external complaint procedure (special commission).Special procedure is provided for personal data protection issues	1
this procedure is explained in detail in the Bulgarian law on personal data protection	1

4.6 Results of the handling related section

Should the informed consent process be paper based?

	Number of responses [n=59]
yes	44
no	15

Should a patient be able to sign the informed consent form electronically?

	Number of responses [n=59]
yes	26
no	33

In your opinion what percentage of patients will be able to sign informed consent electronically?

	Number of responses [n=27]
10 %	1
20 %	3
30 %	5
40 %	2
50 %	6
60 %	4
70 %	2
80 %	4
Mean: 40.74	

Should there always be an alternative between paper based and electronic informed consent?

	Number of responses [n=59]
yes	27
no	32

How should a patient be able to withdraw informed consent?

	Number of responses [n=59]
by writing to the treating physician	10
by written application	1
electronically, via Web	5
only by telling the treating physician	5
any of the above	35
by any way he/she wishes	1
by telling or writing	1
informally	1

Do you use paper based informed consent forms or electronic means?

	Number of responses [n=14]
Paper based only	14

Should an electronic informed consent form be based on modules, so that a specific template can be build?

	Number of responses [n=14]
yes	11
no	3

If yes, what kind of Informed consent modules would be needed?

	Number of responses [n=14]
for care	11
for trial	11
for research	9
for biobanking	9
for data storage	9
for data transfer	11

5 Best practice cases

According to the results of the questionnaire 'Best Practice Cases' can be defined in different sections of the questionnaire. Questions in the general section are used for the filtering of responses to find best practice cases. These best practice cases are listed in the following sections of the deliverable.

As GCP criteria for informed consent are important to fulfill, these criteria are taken into account, as well as criteria given by other organizations and by literature.

5.1 Literature review

In general, in the medical sense informed consent is a voluntary, legally documented agreement by the patient to allow performance of a medical procedure/ treatment or research procedure after the potential risks, hazards, and benefits of the treatment have been explained[1].

On the one hand there is informed consent process as it is employed in everyday patient care setting (clinical care), i.e. for surgery, anesthesia, and other invasive or complex medical or radiologic procedures on the other hand the informed consent process for patients volunteering for clinical research.

In clinical care, i. e. when no research participation is involved, the requirement (when is IC needed?), complexity (What needs to be disclosed?) and intelligibility (Does patient understand?) 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[2].

Although the details of the laws, regulations and guidelines regarding IC in clinical care may differ considerably, the bottom line is that failure to obtain informed consent renders any physician liable for negligence or battery and constitutes medical malpractice.

Medical research involving human subjects is much more restricted by law and globally harmonised.

In many countries legal regulations regarding medical research in human subjects are based on the principles of the world medical association declaration of Helsinki[3]and the Guidelines of the International Conference on Harmonisation[4].

Requirements for the conduct of clinical trials in the EU are provided in the "Directive 2001/20/EC" (Clinical Trials directive,CTD)[5]in which the above mentioned guidelines regarding Good Clinical Practice (GCP) are implemented.

In the CTD Informed consent is defined 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,

[1] Mosby's Medical Dictionary, 8th edition. © 2009, Elsevier; McGraw-Hill Concise Dictionary of Modern Medicine. © 2002 by The McGraw-Hill Companies, Inc.)

[2] http://www.templehealth.org/ICTOOLKIT/html/ictoolkitpage1.html)/ Hochberger, J, Einverständnis-erklärung zu endoskopischen Eingriffen

[3] http://www.wma.net/en/30publications/10policies/b3/

[4] http://www.ich.org/

[5] http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm

significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; 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.

A review of legislation and guidelines with respect to the requirements of the informed consent forms for medical research was conducted. The professional regulations applying in different countries of the EU (Austria[6], Denmark[7], France[8], Germany[9], Spain[10], Sweden[11], Switzerland[12], UK[13]), the US[14] and Research Ethics Review Committee of the World health organisation (WHO ERC)[15] were considered.

Throughout all countries and organisations the below listed elements of information about the research study should be provided to the patient or his or her legally authorised representative:

1. An explanation of the purposes of the research
2. A statement that the study involves research
3. A description of any reasonably foreseeable risks or discomforts to the subject
4. A description of any benefits to the subject as well as to others which may reasonably be expected from the research
5. A disclosure of established alternative procedures, treatments
6. A statement about compensation in case of research related injury
7. An explanation of whom to contact for answers to pertinent questions about the research
8. A statement clarifying the implications of research participation for the subject's confidentiality (data protection)
9. The expected duration of the subject's participation in the trial
10. A description of all study procedures and treatments
11. A statement about the voluntary nature of study participation and the right to refuse and withdraw
12. Informed consent must be documented in writing

[6] Formum Österreichischer Ethikkommissionen; http://www.meduni-graz.at/ethikkommission/Forum/index.htm

[7] Ministerial Order No 806 from 12 July 2004 of information and consent at inclusion of trial subjects in biomedical research projects; http://www.cvk.sum.dk/CVK/Home/English.aspx

[8] Institut Nacional du Cancer (http://www.e-cancer.fr/recherche); Comités de protection des personneshttp://www.cppsudest3.com/protocole/infoconsentement.htm/;
http://www.recherche-biomedicale.sante.gouv.fr/pro/comites/accueil.htm

[9] Arbeitskreis medizinischer Ethikkommissionen (http://www.ak-med-ethik-komm.de/formulare.html); Bundesinstitut für Arzneimittel und Medizinprodukte http://www.bfarm.de/DE/BfArM/BfArMService/gesetze/gesetze-node.html

[10] Agencia española de medicamentos y productos sanitarios http://www.aemps.es/actividad/documentos/formularios/home.htm; Ministerio de Sanidad, Política Social e Igualdad http://www.msps.es/profesionales/farmacia/ceic/documentacionEnsayoCli.htm

[11] Central Ethical Review Board http://www.epn.se/start/central-ethical-review-board-documents.aspx

[12] Swissmedic http://www.swissmedic.ch/bewilligungen/00089/00283/index.html?lang=de, Swissethics - Arbeitsgemeinschaft der Ethikkommissionen" (AGEK) http://www.swissethics.ch/templates.html

[13] National Research Ethics Service http://www.nres.npsa.nhs.uk/applications/guidance/consent-guidance-and-forms/

[14] Code of Federal Regulations for the Protection of Human Subjects in Research Department of health and human services (45 CFR 46. 116); FDA CONSENT REQUIREMENTS (21 CFR 50. 20-27); Marcela G del Carmen, Informed Consent for Medical Treatment and Research: A Review; The Oncologist, 2005;10:636–641

[15] Research Ethics Review Committee of the World Health Organisation;HTTP://WWW.WHO.INT/RPC/RESEARCH_ETHICS

Furthermore, in different countries and even in the same country within different institutions responsible for research oversight (e.g. competent authorities, ethic committees, institutional review boards), there are additional elements which should be included in the informed consent, like

- The anticipated expenses, to the subject for participating in the trial
- The provision of information obtained during the study that may affect a subject's willingness to continue
- A statment why the subject has been chosen
- A description of the subject's obligations
- A statment about circumstances and/or reasons under which the subject's participation in the trial may be involuntary terminated
- A listing of legal references
- A description of monetary implications (funding, sponsoring

Also, there are different requirements regarding the layout, length and structure of an informed consent form.

With the questionnaire it was aimed to analyse the current situation concerning the legal, ethical, technical and clinical handling of consent, mainly in European projects.

Below the best practice cases are summarized.

5.2 Summary of the results of the questionnaire

In the following part a summary of the results of the questionnaire is given. Table 7 gives a summary of mean scale values of those items dealing with best practice features.

	Mean of a scale from 0 (lowest and worst score) **to 5** (highest and best score)
General Section	
Satisfaction with consent process	3.10
Sufficiency of medical information	2.52
Sufficiency of legal information	2.17
Rise of concerns related to the subject of IC	
Medical procedures	1.88
Data handling	1.93
Familiarity with IC procedures	3.38
Detailed medical information needed	3.49
Detailed legal information needed	3.33

Re-consent is important from a legal point	3.18
Role of the physician getting IC	4.07
Attitude of the physician in getting IC	4.13
Experience in clinical care of a physician for getting IC	3.36
Importance of an information sheet	3.97
Extent of barriers for research by IC	2.84
Difficulty to compile the IC by oneselve	2.82
Minimal number of different IC forms for a single patient	1.08
Maximal number of different IC forms for a single patient	2.65
Clinical Care Section	
Usefullness of written information for understanding	3.59
Usefullness of written information for agreeing	3.50
Discrepancy between clinical practice and ethical regulations and clinical practice	2.69
Extent of influence of clinical trials by improvement of IC	2.65
Research Section	
Extent of IC affecting research	3.20
Overcome of IC related barriers in research	1.52
IT related Section	
No items	
Legal and Ethical Issues related Section	
Difficulties within European projects from differing National implementations of EU legislation	2.73
Help in research by a harmonized one-for-all approach for care and research purposes	4.18
Handling related Section	
No items	

***Tab.7**: Mean scale values of items from the questionnaire gathered according to the main sections.*

5.2.1 General section

Participants have a high experience with consent. 38 % have signed informed consents (IC), mainly for themselves, only one for a child and 2 as a legal guardian. 38% of them did not receive a copy of the consent. Only 42 % kept the received copy. There is a high satisfaction rate with the informed consent process of 3.10 on a scale from 0 (not at all) up to 5 (perfectly satisfied). The medical information provided by the informed consent was less sufficient (mean rate: 2.52). The legal information on the other hand was even a bit worse (mean rate 2.17). The information provided did not rise concerns related to the subject of the informed consent eather medical procedures (mean 1.88) nor data handling (mean 1.93). Most of the

participants are familiar with the informed consent procedures (mean rate 3.38). The medical and legal information explained should be detailed (mean rate 3.49, 3.33). There should be different practices between IC in clinical/medical care and research environments. Re-consent is important from a legal point of view (mean 3.18) and should be obtained in view of about half of the participants. At least this needs to be done once a patient becomes legally adult. About 40% of participants ask for taking re-consent if data or biological material is needed for a new research topic. The physician plays an important role in getting IC. The physician needs to speak to the patient during the process of taking IC. Using only electronic methods is regarded as sufficient by only 25% of participants. To provide an information sheet is of high relevance. Most patients have difficulties in understanding IC forms and procedures. Less than 45% understand all items addressed in IC forms and procedures. Participants see barriers to research in general by IC (mean 2.84). This is worse if researchers are asked (3.20).

5.2.2 Clinical care section

Half of the clinical participants, coordinators or chairpersons of a project compiled their ICs by themselves. Most of them (69%) use templates or would like to use (71%). 69% of participants would pay for templates or a service to provide them with IC forms. About 60% of the participants had to change the IC forms after an ethical review. Nearly all participants (91%) believe that they have addressed all legally and ethically needed terms of informed consent in their project. They believe that 54% of patients understand all items addressed in their IC form. An information sheet is provided by 74% of these participants. A maximum of 3 different IC forms for a single patient is recommended. IC forms should not exceed 3 pages and written information for patients should not exceed 5 pages. This written information is useful for understanding what is happening (3.59) and for signing the IC (3.50). A median of 24 to 48 hours needs to be given to the patients between signing informed consent and treatment. This is in accordance with daily practice today. Nearly half of the participants (45%) want to prolong this time in case of prospective trials. Only 46% of the participants do know, that this fits with the legal or ethical regulations in their country, 43% do not know.

The five most important topics to be included in IC forms for clinical trials are purpose of the trial (93%), voluntary participation (92%), foreseable risks (89%), data protection (86%), benefits for patients (84%). Number of participants involved in the trial (42%), experimental trial aspects (52%), focus on research (55%),payment to participants (51%), circumstances to terminate a trial (58%) are less important to include in IC forms. There are only minimal differences to topics needed in clinical care forms. Data protection is less important (72%) and voluntary participation does not play a role in clinical care. On the other hand most of the mentioned topics are regarded to be part of the IC by more of half of the participants.

26 concrete suggestions for improvement of obtaining IC are given on page 40 to 42. These suggestions are dealing with simplification, standardisation, time frame and the personal needs of patients. It is stated that IC have to meet patient's needs rather than producing 'rules and regulations'.

5.2.3 Research section

25 out of 49 researchers (51%) have experienced barriers in their research projects as a consequence of unclear or lack of informed consent. To overcome these barriers is not easy (1.52).

5.2.4 IT related section

As the number of participants in this section is as low as 10, it is difficult to draw precise conclusions.

Clinical care context

Only 2 of the participants have a hospital information system (HIS) coming from a single vendor (SAP). If patients give paper based IC the paper consent forms are rarely stored electronically (3/8). But if this is stored then it is done centrally. Only 1 participant mentioned that IC given by a patient is recorded electronically in HIS. Information is given by only 1 participant that care related procedures are recorded seperately from data processing consent. In others this is unknown or no electronic recording done.

Clinical trial context

An electronic system to manage consent related documents for clinical trials is used by 8 out of 19 (42%) participants of the questionnaire. Most of the patients still sign paper forms. In 41 % these paper based IC are stored electronically, in part centrally. The patient consent can only be signed electronically by 1 participant's institute. The data management application of 37% of participants can record electronically that the patient has given consent. Only 2 times (12%) a consent management is provided by the CTMS. In these cases re-consent is also possible to be done electronically but not always automatically if the patient becomes legally adult. The recorded consent is rarely (12%) integrated in the investigator's trial workflow. The identity of legal guardians can only be recorded in 18%. Only in 4 cases (24%) patients can easily obtain an overview of the consent he / she has given.

5.2.5 Legal and ethical issues related section

In mean 3 forms are used to obtain IC. 34/64 (53%) of participants have to deal with different legal sources when organzing IC procedures. Most of them (63%) are aware of European regulations regarding IC and fulfill these requirements, whereas 11% are aware and do not fulfill. 72% have specific data protection policies at their institution. Fewer have an own Data Protection Officer (58%) in their institute. If centres outside the own country are participating in clinical trials requirements from foreign legislation are applied in 61%. This causes difficulties and has an impact on projects in 34%. 18 specific difficulties are given on page 56 and 57.

Only 6 participants perform trials on healthy children and 8 on mentally ill patients. Because of the small number definite conclusions can not be drawn in these cases yet.

19 additional good practices or guidelines are used for drafting IC forms. Unfortunately none of these guidelines is mentioned.

21 participants (36%) want to have negotiable IC procedures. Accreditation of a governmental or non-governmental institution is required by 19 (34%) participants. A description of the accreditation procedure is given on pages 63 and 64. Only few (11%) participants direct patients to a non-involved institute/specialist to explain the dangers and aims of a therapy/study. In 55% of institutions patients can access their personal data after signing the IC form. The way how this is organized is given on page 66 and 67.

Non-personal data is shared within the same country in 55%, within Europe in 51% and outside Europe in 38%. In most of the cases (88%) the patient is informed about this. None of the institutes has specific legal support in medical law, only 1 institute has such support in scientific research. 3 institutes offer advice about obtaining valid informed consent.

5.2.6 Handling related section

Nearly half of the patients are considered to be able to sign IC electronically. An alternative between paper based and electronic IC is required by 46% of participants to be always available. An electronic form should be based on modules (79% requests). Possible modules are for care, trial, research, biobanking, data storage and data transfer. Patients should be able to withdraw IC by any way he/she wishes as mentioned by the majority of participants.

5.3 Best practice case in clincal care

Clinicians, coordinators or chairpersons of a project want to compile their IC by themselve using templates or a service. These templates need to be modular based and should help to pass Ethical Committees and other Regulatory Bodies in the first run. An information sheet needs to be provided that is easily understandable and allows patients according to their abilities and wishes to get as much information as they want to get. The number of information sheets should not exceed 5 and the number of different IC forms at one time should not be more than 3. A median of 24 hours needs to be given to the patients between signing informed consent and respective treatment.

5.4 Best practice case in research

Informed consents need to include topics of research and biomaterial in an understandable clear and explicit way.

5.5 Best practice cases in IT

As the number of participants in this section of the questionnaire is very low, it is difficult to draw precise conclusions from the survey.

5.5.1 Best practice cases in the clinical care context

There should be the possibility to store signed informed consent forms in the HIS.

5.5.2 Best practice cases in the trial care context

An electronic system to manage consent related documents for clinical trials should be made available. Even if patients will sign ICs in the future on paper, IC should be made available also electronically. The patient can decide what he/ she prefers. Re-consent should be made available automatically according to rules that are trial dependend. The identity of legal guardians need to be recorded. Patients have to be able to easily obtain an overview of the consent he / she has given and they have to be able to reject IC at any time.

5.6 Best practice cases in legal and ethical issues

IC forms should be able to handle different legal surces from different European countries. They should be standardized. The IC process should be negotiable and modular based. Patients should be able to access their personal data after signing the IC form. Sharing of data and biomaterial should be made possible between different countries within Europe.

5.7 Best practice cases in the handling of informed consent

Patients should be able to sign informed consent on paper or electronically. ICs should be modularized. Modules are needed at least for care, trial, research, biobanking, data storage and data transfer. Patients should be able to withdraw IC by any way he/she wishes. Re-consent should be made available automatically.

Appendix 1 - Abbreviations and acronyms

BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte Federal Institute for Drugs and Medical Devices
COG	Children's Oncology Group
CTMS	Clinical Trial Management System
DBA	Data Protection Authority
EC	European Commission
EMA	European Medicines Agency (former: EMEA)
ERC	Ethics Review Committee
GBA	Gemeinsamer Bundesausschuss
GCP	Good Clinical Practice
GPOH	Gesellschaft für Pädiatrische Onkologie und Hämatologie
HIS	Hospital Information System
IC	Informed Consent
ICF	Informed Consent Forms
IEC	Independent Ethics Committee
IRB	Institutional Review Board also known as IEC
IT	Information Technology