Charter for the Ethics Board of U-BIOPRED
version 11 March 2010 - PdB

Introduction

The U-BIOPRED project Ethics Board (EB) identifies, examines and provides advice on ethical aspects of research as well as good scientific conduct taking place in the context of U-BIOPRED.

Mission Statement

The EB will work in a collegiate, collaborative and inclusive manner according to the human equivalence principle to provide ethical guidance and balanced opinion in order to enhance the excellence U-BIOPRED aspires to. The EB will elevate the awareness of and disseminate information on ethics issues.

Terms of Reference

- The EB is a voluntary, multidisciplinary group comprised of members of the patient representation, paediatric and non-paediatric clinical and non-clinical scientists, an ethicist, a lawyer and an industry representative.
- All members of the EB need to provide a disclosure statement regarding their relationship(s) to any of the participating organizations in U-BIOPRED. The EB is a high-level advisory group for evaluation, advice and guidance on all ethics and scientific conduct issues arising within U-BIOPRED. It will be the responsibility of the EB to ensure that ethical practices are adhered to within U-BIOPRED by monitoring the activities of all work packages. The EB assures that ethical standards on the conduct of the scientific (clinical and laboratory) studies are implemented completely as necessary or appropriate to prevent a conflict of interest or the appearance of an ethics conflict. The EB has specific responsibility on ethics in relation to (studies with) children. The EB is not responsible for gaining ethical approval by local or national authorities. This remains the responsibility of the study applicants.
- The EB sets standards on the conduct of good scientific practices which include at least the topics in line with the activities promoted by the Office for Research Integrity of the US Department of Health and Human Services (http://ori.dhhs.gov). The conduct of good clinical science by CROs and the standards made by the EB should be in line with each other.
- The EB will receive necessary documents and protocols in order to evaluate these according to criteria outlined in the standard operating procedure (SOP) of the EB prior to submission of the documents to legal, local ethics committees. The EB provides advice to the applicants. The EB will also monitor study progress according to its SOP and provides advice for modification if applicable to the study leaders.
- In case the advice provided by the EB is not being taken into account, the EB will inform the Scientific Board (SB) for further steps to be taken.
- Any violation of the ethics code (“ethics Standard Operating Procedure”) or any scientific misconduct will be reported to the SB. In case of enduring conflict with the SB the EB will provide its advice to the highest decision level within the project, i.e. the General Assembly.
- Where appropriate the EB, in conjunction with project partners, and any relevant external agencies will contribute to maintaining researchers’ awareness of ethical issues.
Although it will be the responsibility of individual partners to keep well informed about the legal and local ethical regulations relevant to their own area of expertise within U-BIOPRED, the EB will be responsive to specific requests for advice, clarification and information from U-BIOPRED partners.

The EB will contribute towards a project ethics and governance policy and advise on, and where appropriate contribute to, the ethics training of project partners.

The EB shall have the authority to conduct or authorize investigations into any matters within the scope of its responsibilities as it shall deem appropriate, including the authority to request any scientist, employee or advisor of the project to meet with the EB.

Communication will be maintained between EB members by a members’ only distribution list. Communication with the wider U-BIOPRED community will be via common e-mail distribution list and via the U-BIOPRED website.

Training for EB members will be initiated from expertise within the EB membership. The training involves general ethical aspects, good scientific conduct and patient involvement.

Reporting responsibilities are to the Management Board in the form of minutes of each EB meeting and the minimum of one annual report.

Annual self-evaluation: the EB shall evaluate its own performance annually. Criteria include time (for responding and finalizing issues), quality and adequacy of response.

Privacy and confidentiality – it is agreed that in the interests of openness the business of the EB may be openly discussed outside of the EB group unless explicit agreement has been reached that an item or issue is confidential. Minutes of the meetings will be copied to the Scientific Board and the Management Board, and are available for wider disclosure via the U-BIOPRED website.

Public statements, oral and written presentations on behalf of the EB – it should be presumed that public statements regarding EB activities are made in the spirit of corporate representation. Such statements must be clearly distinguished from any statements made in a personal capacity.

The EB is willing to add terms of reference points concerning ethics that are raised by official organizations.

Structure of the Ethics Board
The EB consists of approx. 10 members (chair and co-chair non-inclusive) comprised of one adult and one paediatric clinician, one non-clinical scientist, one animal expert, one ethicist, one lawyer, one methodologist.statistician and 3 patients/parents of patients and/or representatives of patient organisations. Each member will be appointed for two years and may be reappointed for another 3 years. The chair and co-chair will serve a two-year term, but he/she can be appointed to serve an additional three-year term. The first chair will be the scientific leader of WP10, the co-chair will be a representative of an EFPIA member. Except as otherwise permitted by the steering committee of WP10, each member of the EB shall not be directly involved in the studies performed in U-BIOPRED.
# Patient’s Perspective Criteria List

*Criteria for evaluation of research protocols, study designs and other documents from the patient’s perspective*

## 1. Relevance.

<table>
<thead>
<tr>
<th>Score</th>
<th>1.1</th>
<th>health related quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.2</td>
<td>Improvement of health</td>
</tr>
<tr>
<td></td>
<td>1.3</td>
<td>Applicable to more diseases</td>
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<tr>
<td></td>
<td>1.4</td>
<td>Improvement of care for patients</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>Improvement of societal participation</td>
</tr>
<tr>
<td></td>
<td>1.6</td>
<td>Exploitable result</td>
</tr>
<tr>
<td></td>
<td>1.7</td>
<td>Applicability of project result in practice</td>
</tr>
</tbody>
</table>

## 2. Right of Say.

<table>
<thead>
<tr>
<th>Score</th>
<th>2.1</th>
<th>Patients are a source of knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.2</td>
<td>Patients are equal discussion partners</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
<td>Patients are full citizens</td>
</tr>
</tbody>
</table>

## 3. Ethics and Safety.

<table>
<thead>
<tr>
<th>Score</th>
<th>3.1</th>
<th>The method is the least aggravating in relation to the goal</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>3.2</td>
<td>Safety of participants in the study</td>
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<td></td>
<td>3.3</td>
<td>Freedom of Choice</td>
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<td></td>
<td>3.4</td>
<td>Rules, codes, social norms and values</td>
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<tr>
<td></td>
<td>3.5</td>
<td>Human dignity</td>
</tr>
<tr>
<td></td>
<td>3.6</td>
<td>Responsibility and Carefulness</td>
</tr>
<tr>
<td></td>
<td>3.7</td>
<td>Information about the project results</td>
</tr>
</tbody>
</table>
Total scores of:
1   relevance                 (max. 70 points)
2   right of say              (max. 30 points)
3   ethics and safety        (max. 70 points)
To each aspect 10 points (highest and best appreciated) can be given maximally.
Neutral score of 5 points : aspect is not described and should not be described in the protocol.
Score 0 – 5 points        : aspect is not described, but should be described in the protocol.
                          Protocol must be improved!
Score 5 – 10 points      : aspect is described in the protocol.

Your comments to each of the 3 paragraphs:
Please provide both positive and negative aspects

1.  Relevance

2.  Right of Say

3.  Ethics and Safety

Your advice to the project leaders:
Endorse without comment  : yes / no
Modify according to your comments : yes / no

Your name:

Date:

# criteria based on:
Clarification of the criteria.

Relevance

1.1 **Health related quality of life**
The expected project results improve the quality of life of the patient group (physically, mentally or socially). Less physical limitations during daily activities caused by health-related problems like climbing stairs, body washing, clothing and shopping. Less mental limitations due to feelings of anxiety or depression. Less social limitations due to the way the disease affects the possibilities to act in a family, participate at work or spare time activities, or to visit family or friends.

1.2 **Improvement of health**
This is important for improvement of health of the patient group.

1.3 **Applicable to more diseases**
The description pays attention to comorbidities and/or complications, is there any relevance to other diseases. There is no need for unnecessary replication in other diseases.

1.4 **Improvement of care for patients**
The expected project result leads indeed to an improved health care as experienced by patients.

1.5 **Improvement of societal participation**
Improved possibilities to participate in the society: e.g. being volunteer at school or elsewhere, being member of a society, or being employed.

1.6 **Expansible result**
The expected project results are utilisable for the patient group.

1.7 **Applicability of project result in practice**
The project plan also contains an implementation plan how results can be brought into practice – if not then the patient group will not profit.

Right to say

2.1 **Patients are a source of knowledge**
The project is also based on wishes and needs of the patient group. Acknowledgement of the value of patient’s disease experiences is given next to professional knowledge.

2.2 **Patients are equal discussion partners**
The patient group is one of the parties in the project, and involved in e.g. negotiations on study design, study execution, evaluation, dissemination and implementation. The project information is available in lay terms and understandable by 95% of the population. Feedback of the project results will also be done in lay terms.

2.3 **Patients are full citizens**
Within the project patients are being regarded as full, self-conscious and emancipated citizens, and are not being regarded as unemancipated and dependent citizens.

Ethics and Safety

3.1 **The method is the least aggravating in relation to the goal**
If the project result seems relevant for other diseases then the project leaders should inform the research and care field about this (principle of universality). Are the benefits from the project higher than the burden (e.g. a better drug for asthma versus patients undergoing an intervention to see whether the drug makes them better or sicker). What is the risk of failing to work, go to school or participate in social activities? This is the only way to reach the goals. There are no alternatives less burdening for patients available based on the informed consent.

3.2 **Safety of participants in the study**
In case of patient-bound research the project leaders take care of providing a suitable insurance for participants related to disease burden, failure to work, study or participate in social activities. Side effects, discomfort, aftermath, and after care are being taken care of by the project, and this is known to participants.

3.3 **Freedom of Choice**
Participants will be provided (written) information in lay terms about the project, and more than 24h to think about their participation. The information is given as a patient informed consent form, which includes the freedom to make their own choice to participate (yes or no). It should be stated explicitly that their choice will not affect the quality of health care provided by their caregivers. Participants will also get written information on the complaint procedure.
3.4 **Rules, codes, social norms and values**
The project leaders have follow the legal (local and national) regulations and laws, and rules regarding behavioural and professional codes.

3.5 **Human dignity**
The project leaders have a holistic view about the participants – hence they not only view the patient part but also an individual with a family, friends, education or being employed, and with spare time. The project leaders avoid that participants feel helpless or ashamed.

3.6 **Responsibility and Carefulness**
The project leaders and scientists take care of the participants in the best possible way. The project leaders should provide information to the patient’s physician about participation and potential consequences of the research (i.e. side effects, discomfort etc.).

3.7 **Information about the project results**
Project results should be provided to the patient group and participants in lay terms.
Criteria for Good Scientific Conduct - outline.

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Good Scientific Practice represents a set of recommendations and commitments governing scientific activities within U-BIOPRED project. The aim is to create an environment conducive to quality research and prevent problems from arising in relation to the integrity of scientists in their work. Criteria for good scientific conduct constitute a framework for self-regulation that complement (never substitutes) laws in the involved countries. Good scientific conduct includes honesty, accuracy, efficiency and objectivity.

The following practices are regarded as misconduct in science and should be avoided:

- Violation of official rules and regulations;
- Abuse of confidentiality;
- Violations of authorship and publication;
- Inappropriate/insufficient supervision of researchers in training;
- Lack of appropriate preparation of protocols before the start of the research;
- Fragmented or duplicated publications;
- Failure in fulfilling the International Criteria for Authorship;
- Failure to report misconduct;
- Obstruction of investigations and retaliation;
- Not getting appropriate training (for all investigators) on the protection of human research participants;
- Unresolved or unreported conflicts of interest. Conflicts of Interests are important in case of financial gain, work commitments, or intellectual and personal matters;
- Conflict of commitment:
  - not honoring time commitments as specified in the grant agreement;
  - charging multiple sources of funding for the same time;
  - not providing enough time for training of students or researchers as a mentor;
  - inappropriate use of the institutional (research) affiliation for private interest.

For the good conduct of science the following actions should be taken:

- Obtain permission and authorization for data collection (e.g. approval by ethics committees). This includes permission for use of: human subjects in studies, biological or hazardous agents, information from other databases or websites, published copyrighted or patented processes or materials or photographs;
- Accepting continuing responsibility for compliance (to the rules) through all study stages. The continuing responsibility includes:
  - enrolling only those study participants (“subjects”) that meet the approved inclusion and exclusion criteria;
  - properly obtaining and documenting informed consent;
  - obtaining prior approval for any deviation from the approved protocol;
  - keeping accurate records;
  - promptly report to the U-BIOPRED Ethics Board and the local authorities any unanticipated problems involving risks to study participants or others.
- Clarify the ownership of the data (see Project Agreement for details):
  - who owns the collected data?
  - what rights does one have to publish data?
  - does collecting data impose obligations to the investigator?
- Use appropriate methods: reliable techniques and methods, appropriate statistical methods, no bias in results by choice of method.
- If animal studies are involved in whichever country in Europe, work according to or in line with the UK¹, Dutch² or German³ Animal Welfare Act. Correct working according to these Acts implies:
  - knowing what activities are subject to regulation (according to either of the these Acts);
  - understanding and following the rules for project approval;
  - obtaining appropriate training;

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² http://www.vet.uu.nl/nca/userfiles/other/The_Dutch_Experiments_on_Animals_Act.pdf
- accepting continuing responsibility for compliance through all study stages;
- striving for the three "R" principles: reduction, replacement and refinement.

- Identify and resolve Conflicts of Interest as soon as possible. Conflicts of interest should not be interfering with the responsible practice of work. For this, the Conflict of Interest form has been developed and needs to be filled in by every project participant (see Conflict of Interest form and accompanying description).

The good scientific conduct criteria also include those mentioned specifically in the Project Agreement (PA; see below). These criteria include handling and dealing with biomaterials according to legal rules and laws, obtaining informed consent from donors and approvals from legal institutions (like local or national ethics committees), and performing the study according to human rights as described in the Helsinki Declaration (2008) (http://www.wma.net/en/30publications/10policies/b3/index.html).

Project Agreement point 4.5:
Each Participant represents and warrants that any human tissue or other biological samples (see PA-appendix 6 for definitions) required for use in the Project to be obtained, handled or used by it will be obtained, handled or used in accordance with all relevant laws and regulations (and where applicable local ethical guidelines) regarding the collection, use, transport and subsequent disposal of human tissue or biological samples and that any Ethics Committee approvals and donor informed consents required will be obtained prior to the commencement of the respective part of the Project work.

Project Agreement point 4.6:
Unless otherwise required or prohibited by law, each Participant undertakes that in relation to its performance of this Project Agreement:
(a) it will not employ, engage in or otherwise use any child labour in circumstances such that the tasks performed by any such child labour could reasonably be foreseen to cause either physical or emotional impairment to the development of such child;
(b) it will not use forced labour in any form (prison, indentured, bonded or otherwise) and its employees are not required to lodge papers or deposits on starting work;
(c) it will provide a safe and healthy workplace, presenting no immediate hazards to its employees. Any housing provided to its employees shall be safe for habitation. It will provide access to clean water, food, and emergency healthcare to its employees in the event of accidents or incidents in the workplace;
(d) it will not discriminate against any employees on any ground (including race, religion, disability or gender).
(e) it does not engage in or support the use of corporal punishment, mental, physical, sexual or verbal abuse and does not use cruel or abusive disciplinary practices in the workplace;
(f) it will comply with the laws on working hours and employment rights in the countries in which it [or any of its Affiliates] operates;
(g) it will be respectful of its employees’ right to join and form independent trade unions and of freedom of association.

The Participants agree that they are responsible for controlling their own supply chain and that they shall use reasonable efforts to encourage compliance with ethical standards and human rights by any subsequent supply of goods and services that are used by the Participants when performing their obligations under this Project Agreement.

Responsibility of the Ethics Board.
The U-BIOPRED Ethics Board acts independently in the service of the U-BIOPRED researchers with the objective of supporting research quality and contributing to the preservation of research integrity.

Specifically, it will
(i) monitor observance of the Good Scientific Criteria detailed above;
(ii) act as an arbitrating body in the case of uncertainties or conflicts that may arise in relation to research integrity;
(iii) inform and raise awareness among U-BIOPRED members of content of this document.
The EB will guarantee at all times the diligence of its activities, the independence of its decisions, the anonymity and confidentiality of personal information, the authority of the information generated, the impartiality of its deliberation, and the fairness of its resolutions, as well as the opportunity to appeal against those decisions. The EB can be contacted when needed through the chair or co-chair of the EB.
Criteria for good scientific conduct\(^4\)
(to be monitored throughout study).

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Permissions
- Is or will informed consent be obtained from donors and approvals from legal institutions (like local or national ethics committees).
  yes / no / not needed  if yes, date obtained:
- Is or will permission and authorization for data collection be obtained.
  yes / no / not needed  if yes, date obtained:
- If animal studies are involved, is or will approval be obtained from the (local) animal experimentation committee.
  yes / no  if yes, date obtained:

Conflicts
- Identify and resolve Conflicts of Interest of project partners or board members.
- Identify and resolve Conflicts of Commitment of project partners.

Techniques and methods
- The handling and dealing with biomaterials is according to legal rules and laws.
  yes / no
- Only those study participants ("subjects") are/will be enrolled that meet the approved inclusion and exclusion criteria.
  yes / no / not applicable
- Records are kept accurately: on paper, digitalized, if applicable secured.
  yes / no / not clarified
- Appropriate methods are/will be used: reliable techniques and methods, appropriate statistical methods, no bias in results by choice of method.
  yes / no
- If animal studies are involved, are these being performed according to or in line with the UK, Dutch or German animal welfare acts.
  yes / no  If no, why not and which measures will be taken?
- All investigators will be trained appropriately on the protection of human or animal research participants.
  yes / no

General issues
- The study is/will be performed according to human rights as described in the Helsinki Declaration (2008).
  yes / no
- Unanticipated problems involving risks to study participants or others are promptly reported to the U-BIOPRED Ethics Board and the local authorities.
  yes / no
  If patient safety issues arise, please add date and refer to safety SOP:
- Violations of authorship and publication.
  yes / no
  If yes:
   Nature of violation:
   Which follow-up actions are taken and when:
- Abuse of confidentiality.
  yes / no
  If yes:
   Nature of abuse:
   Which follow-up actions are taken and when:

\(^4\) The list of criteria for good scientific practices are in line with the activities promoted by the Office for Research Integrity of the US Department of Health and Human Services (http://ori.dhhs.gov).