APPLICATION FOR EVALUATION OF A RESEARCH PROJECT TO THE MEDICAL ETHICS COMMITTEE II

of the

RUPRECHT KARL UNIVERSITY OF HEIDELBERG

MEDICAL FACULTY MANNHEIM

MANNHEIM UNIVERSITY HOSPITAL

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This application is suitable for independent studies, epidemiological studies, and MPG studies in accordance with MPG §23b.

The application is **not** suitable for drug research and MPG studies in accordance with §20 ff.

Please note the information on the individually drafted patient information and consent form in the appendix to the application, the sample text on the subject of "data protection," and the final check at the end of the application form. The application can only be reviewed by the ethics committee if it contains at least the standard information.

Ethik-Kommission IIIn accordance with §15 of the Professional Code of Conduct for Physicians in Baden-Württemberg, I request that the Medical Ethics Committee of Heidelberg University review my study proposal described below.

I. GENERAL INFORMATION

Reception stamp

1. Date of application: **July 31, 2011**

2. Project name (English title): **TARGIT-BQR (TARGeted Intraoperative RadioTherapy – Boost Quality Control Registry)**

3. Is this a multicenter study? Yes: X No:

4. Specify type of study: **Quality assurance according to radiation protection guidelines**

Pilot study? Comparative? Placebo? Open? Randomized? Single-blind? Double-blind?

5. Name and address of the responsible study director in the field of medical EK II:
Prof. Dr. F. Wenz, Clinic for Radiation Therapy & Radiooncology, UMM
A clinical study should only be conducted by a qualified person in order to clearly define responsibility.

5.1 Name and address of the responsible project manager (LKP) in Germany, see 5.1
(applies to multicenter studies whose principal investigator is not based in the area of Medical Ethics Committee II):

5.2 Responsible investigator: Prof. Dr. F. Wenz

5. Names and roles of other investigators:

Dr. Elena Blank, Dipl Psych Grit Welzel, Anke Keller (study nurse), data collection, statistical analysis

6.0 Medical clinic/clinics or departments or institutes where the project is to be carried out:

Clinic for Radiation Therapy & Radio-Oncology, UMM

7. Head of clinic or institute: Prof. Dr. F. Wenz

8.0 Who is covering the costs of the study (please also indicate partial funding)? Not applicable

The expense allowance for the Medical Ethics Committee II for the assessment of the project will be covered by (provide billing address): (only studies without any financial support are free of charge; see also the official fee schedule of the Ethics Committees of Heidelberg University)

9.0 Has an application with the same content already been submitted to another ethics committee ?

No

a) If yes, when and where:

b) Has a vote already been cast (please enclose a copy):

10. For multicenter study applications:
Has a positive vote been obtained from the project manager/study director (LKP) responsible for Germany?
For multicenter studies, **the vote of the responsible project manager/study director (LKP) must be available before** the application can be assessed by the local ethics committee.

Mannheim Medical Ethics Committee as the leading EC

II. DESCRIPTION OF THE PROJECT

11. Aim of the study (brief outline with the main objectives):

As part of quality assurance in accordance with radiation protection guidelines and X-ray regulations, radiation therapists are required to provide regular follow-up care after therapeutic radiation application. As a rule, annual follow-up examinations with structured documentation of local control and side effects take place for up to 5 years after the end of therapy.

Intraoperative radiotherapy has been performed for breast cancer as an early tumor bed boost for several years in accordance with national guidelines (Sautter-Bihl et al: DEGRO practical guidelines for radiotherapy of breast cancer. Strahlenther Onkol 2007; 183:661-666). We have already published several articles on the safety and toxicity of the procedure (e.g., Wenz F, Welzel G, Blank E, Hermann B, Steil V, Suetterlin M, Kraus-Tiefenbacher U: Intraoperative radiotherapy (IORT) as a boost during breast conserving surgery (BCS) using low kV X-rays – the first five years of experience with a novel approach. Int J Radiat Oncol Biol Phys 77:1309-1314, 2010).

As part of the project, a multicenter study will now be conducted to determine whether the results we have achieved can also be achieved in regional healthcare settings. To this end, patients who receive IORT as an early tumor bed boost and are treated and followed up in accordance with the guidelines will be prospectively registered and documented. For this purpose, pseudonymized data from the other centers will be faxed to the registry center in Mannheim and evaluated by us.

12. Planned start and expected duration of the study: September 1, 2011

13. a) Examination of patients

Number/inpatient: 1000
Number/outpatients: 0
Patients capable of giving consent 100
Patients unable to give consent 0

b) Examination of test subjects: Not applicable

Number:

14 Expected duration of the study phase for each patient/subject: 5 years

15. Age of patients/subjects:

Lower limit: 18 years
Upper limit: 85 years

16. What exactly will be done with the patient/subject?

Detailed description requested. Additional measures that are purely study-related must be clearly indicated.
What is the ratio of the expected benefits of the study to the risks associated with it?

The patient receives standard therapy and follow-up care in accordance with guidelines. No additional imaging examinations or blood samples are taken. The standard documentation is faxed to us and evaluated by us.

16.1 Purely study-related measures on patients/subjects that would not otherwise be necessary, e.g.:

Inpatient stay	No				
Blood samples: quantity, number of samples, timing		No			
Bladder catheter			No		
Endoscopy			No		
Biopsies, other tissue sampling			No		
Lumbar puncture, amount of cerebrospinal fluid					No
X-ray diagnostics			No		
Computed tomography				No	
Magnetic resonance imaging				No	
Positron emission tomography			No		
Radioactive substances/tracers			No		
Other invasive measures		No			

17 a) Inclusion criteria for patients/subjects:

I. Are women of childbearing age included? Yes
II. How is conception protection ensured, if applicable: Yes, standard under RT
III. Are study participants who are incapable of giving consent included? No
IV. Are underage study participants included? No

b) Exclusion criteria for patients/subjects:

I. Are women of childbearing age excluded? No
II. Is drug abuse checked and how? No
III. Are study participants who are incapable of giving consent excluded? Yes

18. Is this a

- trial under the Medical Devices Act (MPG)? No
  If "yes," then the application must be submitted via DIMBI.
  If there is a CE mark, the intended purpose is identical, and no invasive or stressful examinations are carried out for the purposes of the study, § 23b MPG applies and you can proceed with this application.
- Trial to which the X-ray Ordinance applies: No
- Experiment to which the Radiation Protection Ordinance applies: No
- **Experiment in which genetic information is determined: No**

19. Does the research involve human tissue? No
Has consent been obtained regarding the origin of the tissue?
Is it possible to trace the tissue back to the donor?

20. Is this research involving human genetic material? No

20.1 Does the data protection concept for this study meet the requirements of the European research project "Advanced Clinico Genomic Trials on Cancer (ACGT; www.eu.acgt.org or www.privacypeople.org)?**"** Yes

21 If the general requirements for clinical trials pursuant to Section 23b MPG are met, proof of the CE mark must be provided.

Not applicable

22 If the study

- directly in the interests of patients: No
- a purely scientific purpose without direct diagnostic and therapeutic value for patients: yes
- the future development of diagnostic and therapeutic procedures: yes
- the acquisition of knowledge about the causes and prognosis of diseases: no
- Gaining insights into specific issues relating to the health status of the population: No
- Other objectives: Yes, comprehensive quality assurance

23. What typical side effects or complications can be expected?

No study-related measures

24. Are there any risks for the subjects/patients? No

If yes, which ones:

25. To what extent does the study place an additional burden on subjects/patients?

Not applicable, as only additional documentation is required.

26. Are those involved proficient in the techniques to be used? Yes

27. How can complications be recognized and treated? Not applicable

27. Type and frequency of planned monitoring measures before, during, and after the examination period? According to guideline

28. Is there insurance coverage and for whom (study participants or investigator)?

Not applicable

Type of insurance:

28.1 Where study participants are insured

Subject insurance analogous to the insurance required by law in the German Medicines Act (AMG) and Medical Devices Act (MPG) for high-risk projects
Coverage must be confirmed and the insurance provider must be based in the Federal Republic of Germany.

Accident/travel insurance for test subjects/patients; additional or standalone
The German Medical Association (Ethik-Kommission II) recommends such insurance for test subjects and patients who are examined at other locations or who have to travel for study purposes, provided that no other insurance cover exists for this.

28.2 In which the employees of the University Hospital GmbH (UMM), the Central Institute for Mental Health, or the Medical Faculty involved in the study are insured against liability claims by study participants (hospital liability insurance – research and teaching sector)

28.3 Other type of insurance, which?

Details of the insurance provider:
Name of the insurance provider, full address including telephone and fax number,
Policy number: (Please enclose a copy of the contract)

28.4 Were the study participants informed of the insurance obligations in the patient/subject information, or is a copy of the obligations provided?

Not applicable

29 Is the clinical trial investigator informed about the results of the technical safety assessment of the investigational products and the anticipated risks associated with the clinical trial? Yes

30 Have similar or comparable projects already been carried out or are they currently being carried out?

If so, with what results? Yes, single-center, see publication, high safety and low toxicity rate

31. For other studies:
Are there any doubts as to whether the project complies with the Declaration of Helsinki 1964, as revised in 1996? No

III. Information, explanation, consent, Federal Data Protection Act

The Ethics Committee II of the Medical Faculty of Heidelberg University is of the opinion that the processing of the initials and/or full date of birth of a trial participant does not constitute pseudonymization of health data within the meaning of Section 2a (2) sentence 2 no. 1 b)-d) AMG in conjunction with § 3 (6a) Federal Data Protection Act (BSOS) and is therefore unauthorized within the meaning of § 43 (2) No. 1, possibly in conjunction with § 44 (1) BDSG.

32. **Does the written subject/patient information presented here correspond to the final version** (in the case of multicenter studies, the latest and approved version of the ethics committee responsible for the LKP)**? Yes**

33. **Patient or subject information and the declaration of consent should be written in a single document with consecutive page numbers and must be signed by the person providing the information and the study participant at the end of the document.**

34. **Is the patient information and consent form marked with a current version number and date in the footnote? Yes**

35. **Has an information sheet appropriate for the age group been created for the participation of minors? Not applicable**

36. **Has the patient/subject information sufficiently addressed and clearly indicated other, alternative treatment methods?**

    Not applicable

37. **Has the privacy policy been adapted to the individual study conditions? Yes**

38. **Is the section on data protection integrated into the patient/subject information and highlighted by a frame or bold print? Yes**

39. **Has the method of pseudonymization been described in an understandable manner and does it ensure data protection in accordance with legal requirements** (Federal Data Protection Act §3, para. 6)**? Is the section on data protection sufficiently detailed and understandable to laypersons? Yes**

40. **Who provides clarification? Treating physicians**

41. **If the patient's capacity to make decisions could be called into question, who objectively assess the patient's capacity to make decisions? Not applicable**

42. **Has consideration been given to the possibility that a legal guardian for the patient may be required? Not applicable**

IV. Final Check

Does the patient information and consent form meet the standard criteria?

- Does the patient information and consent form have a version number?
- Have the latest proposed changes been implemented and marked (bold, italics, etc., is this the final version)?
- Is it headed with the name of the investigating clinic and the responsible investigator?
- Is the insurance provider named, including the policy number and full address?
- Are all topics covered in the patient information? (see sample texts)
- Does the declaration on confidentiality, data processing, and data protection comply with legal requirements?
- Are all medical terms translated in a way that is understandable to laypeople?
- Is a contact person for the study participant named and contact details provided in the patient information?
- Has the study participant been expressly made aware of the insurance obligations, if applicable?
- Are the required signatures present?
- Is the phrase "the patient/subject has received a copy of the patient information and consent form" mentioned?
- Is there a reference to voluntariness, the possibility of withdrawal, etc.?

- Have the special circumstances of patients who are unable to give consent been taken into account?
- Have the currently valid X-ray regulations and radiation protection regulations been observed?

V. Application formalities

This completed application (1 copy in paper form) must also be accompanied by an electronic form (CD-ROM) of the application.

Overview of the required documents:

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1. **Application form**
2. **Test plan – possibly a summary in the application form**
3. **A sample of the written, layman-friendly patient/subject information/data protection/consent form.**
4. **Proof of patient/test subject insurance, if required.**
5. **CE certification and material description (only for research projects in accordance with Section 23b of the German Medical Devices Act (MPG)).**
6. **Organized electronic form of the application with all documents (CD-ROM).**

I agree to the research project being carried out at my clinic/institute:

Signature of the responsible study director and name in block letters

Signature of the head of the clinic/institute and name in block letters

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Send these documents to:

Medical Ethik-Kommission II
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of Heidelberg University
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...and this is how you can reach us:

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