Administrative

1. Project title

2. Project acronym

3. Investigators

4. Affiliation of investigators
   Department and institute

5. Contact person
   Primary contact for this proposal

6. Contact email
   Email address of the contact person

7. Funding source
   Name of (external) funding party, if applicable

Project overview and approvals

8. Is this proposal part of a broader research project (e.g., a consortium, infrastructure initiative, international multicenter study or PhD project) in which Hebon data are or will be used?

☐ No
☐ Yes

If yes, please briefly describe the overarching project and explain how this HOP request fits within it. Also indicate what is expected from Hebon in terms of contributions, such as data access, infrastructure use, (co-)work package leadership, or other roles. (max 200 words)

9. Short project description (max 250 words)
   Provide a brief background and clearly outline the study aims

10. Project or protocol attachment (if applicable)
    If available, send a project proposal or study protocol to hebon@nki.nl (e.g., submitted as part of a broader study or funding application). This is not required for all HOP applications.

11. Existing relevant approvals
    If the project is part of a multicenter or linked study, please also indicate whether central or site-specific approvals have been obtained.

    Grant approval: N ☐ Y ☐
    Medical ethical committee approval: N ☐ Y ☐
    Non-WMO (non-Medical Research Involving Human Subjects act): N ☐ Y ☐
    Other:

12. Expected relevance (max 250 words)
    Describe the scientific and/or societal relevance of the project.

13. Incidental findings
    Describe whether there is a risk of incidental findings and if so, which and how they will be dealt with. Follow the Hebon policy on incidental findings and the COREON code of conduct.

14. Tumor field

☐ Breast	☐ Melanoma	☐ Lymphoma	☐ Stomach, colon, liver
☐ Gynecology	☐ Pancreas	☐ Thyroid	☐ Dermatology
☐ Hematology	☐ Neuro-endocrine	☐ Soft tissue	
☐ Head & Neck	☐ Sarcoma	☐ Pancancer	
☐ Lung	☐ Urology	☐ Neurological	

15. Timeline of the project
    Start date:

    End date:

Study population

16. Indicate whether the project can begin immediately upon if the Hebon Steering Committee approves the proposal? (max 100 words)

17. Definition of the study population (max 200 words)
    Clearly define the study population by stating the age range, sex, mutation status (e.g., *BRCA1*, *BRCA2*, *CHEK2*), and vital status (alive, deceased). Where applicable, include relevant ICD-10 codes and the period during which diagnoses were made. Clearly list inclusion and exclusion criteria separately.

18. Participant types
    Please select from which type of participants you request data.
    Hebon participants fall into different categories, including those who signed an informed consent, non-responders, and individuals who were deceased before invitation.*

    **Non-responders are defined as individuals who received both an invitation and a reminder letter but did not respond within six months. For these individuals, as well as those who were already deceased prior to the invitation, only limited information is available, particularly in relation to DNA test results and linkage with the Netherlands Cancer Registry (NCR) and Palga. Access to these data requires approval by the Hebon Steering Committee and subsequent evaluation by the Institutional Review Board of the Netherlands Cancer Institute Antoni van Leeuwenhoek.*

☐ Informed consent
☐ Non-responder
☐ Deceased prior to Hebon invitation

Data types

Data sources and requested variables

Please specify which variables you request per Hebon dataset in the codebooks provided on www.hebon.nl/hop-aanvraag, and send this to hebon@nki.nl. Please ensure that the accompanying codebook clearly indicates which variables are needed for this project and from which source.

Due to the dynamic nature of the database, not all information is immediately available for the entire cohort. In particular, lab-confirmed data (e.g., genetic test results or pathology-confirmed diagnoses) may be incomplete. In such cases, self-reported information may be available instead, but only for individuals who completed a Hebon questionnaire. When lab-confirmed data become available at a later stage, these can be requested as an update.

19. **Mutation status**

- ☐ Only include lab-confirmed data
- ☐ Prefer lab-confirmed data; only self-reported data if lab-confirmed data are not available
- ☐ Not applicable to this request

20. **Treatment data**

- ☐ Only NCR and/or Palga confrmed
- ☐ Preferably NCR and/or Palga confirmed, only self-reported if not available
- ☐ Not applicable.

Hebon maintains a dynamic database, and data availability may change over time. The most recent complete linkage with the Netherlands Cancer Registry (NCR) was performed in 2023. The next linkage with Palga is scheduled for 2025. Participants enrolled after these dates may not yet be linked to the respective registries.

21. If additional or more specific data from NCR and/or Palga is required for your project, a separate data request must be submitted to the relevant registry. For non-responders and individuals who were deceased prior to the Hebon invitation, linkage with NCR must be requested via ZorgTTP. The costs associated with these linkage requests are the responsibility of the project applicants. Please consult the codebooks and contact Hebon prior to submission if you are unsure whether such a request is needed.

- ☐ No extra data from NCR and/or Palga is requested
- ☐ Yes, please specify what data is required (max 150 words)

22. **Risk factor questionnaire data**

Please indicate which version(s) of the Hebon questionnaire you require for your study. A baseline questionnaire was administered in 2012–2013 and updated in 2019, with some questions modified, removed, or added. Follow-up questionnaires are also available, typically 5 to 10 years after baseline, with more frequent follow-up among mutation carriers.

The phrasing of questions has evolved over time. Notes on the availability of specific variables can be found in the codebooks. If anything remains unclear, you can contact Hebon for further information.

- ☐ Female Baseline questionnaire 2012-2013
- ☐ Female Baseline questionnaire 2019
- ☐ Female Baseline questionnaire 2026
- ☐ Male Baseline questionnaire 2012-2013
- ☐ Male Baseline questionnaire 2025
- ☐ Female Follow-up questionnaire 2012-2013
- ☐ Female Follow-up questionnaire 2021

23. **Mammography data**
    Mammography data are only available for individuals who have provided informed consent for this purpose. Please note that data collection is ongoing and currently incomplete across the Hebon network. At this stage, data have been collected from approximately one quarter of hospitals. In addition, not all participants undergo mammography at the hospital from which they received their Hebon invitation. In many cases, screening may take place at a regional hospital or independent screening center, which limits data availability.

    If your study requires access to mammography data, please contact Hebon in advance to discuss current availability and feasibility.

- [ ] No mammography data is requested
- [ ] Yes

New participant inclusion and additional data collection

Some studies may require the inclusion of new Hebon participants (e.g., individuals with a specific mutation not yet invited), or the re-contact of existing participants for additional data collection (e.g., questionnaires or measurements).

Applicants are responsible for preparing and conducting these activities. Hebon can provide contact details and limited support, but practical tasks (e.g., printing and mailing) must be handled by the applicants.

24. Does your study require the inclusion of new participants in the Hebon study?
- [ ] No
- [ ] Yes. If so, please specify who should be invited, the rationale, and provide an estimate of the number of individuals required (max 150 words).

25. Does your study require the re-contact of existing Hebon participants for additional data collection (e.g., through questionnaires, interviews, or measurements)?
- [ ] No
- [ ] Yes. If so, please describe which subgroup you intend to approach, what data will be collected, how this will be done, the participant burden, and the planned timeline (max 300 words).

Analysis

26. Analysis plan (max 500 words)
    Please include clear outlines of the methods of analysis and refer back to your research questions and/or aims.

27. Please indicate whether a formal power analysis has been conducted for this project. If so, summarize the assumptions and outcome of the calculation. If not, provide a rationale for the estimated number of participants needed to achieve the study aims.

Authorships

I confirm that I will follow the Hebon author guidelines, in line with article 8.8c of the Hebon collaboration agreement. This includes:

- *Inclusion of one co-author per Hebon center (8 in total)*
- *Inclusion of 'Hebon' as co-author (the Steering Committee members at the time of submission, as listed on the Hebon website), with appropriate acknowledgements for funders*
- *Inclusion of a representative responsible for the collection of a substantial part of the data used*
- *For international publications: if only one author is allowed, it will be 'Hebon'; if two, 'Hebon' and the project PI, provided this PI is also a member of the Hebon Steering Committee; and if three or more, 'Hebon', the PI, and center representatives proportionally based on data contribution.*

☐ Yes, I confirm
☐ No, not fully. Please specify how and why the approach will differ (max 300 words):