

HARTWIG MEDICAL FOUNDATION - GUIDING PRINCIPLES

Version 3.0

These 'Guiding Principles' were most recently updated as per 1 April 2020. Hartwig Medical Foundation may amend these Guiding Principles at any time by publishing an amended version on its website.

1 MISSION

1.1 Hartwig Medical Foundation has the clear mission to promote advances in cancer research and the treatment of cancer, with the ultimate aim of improving the healthcare for current and future cancer patients. Specifically, Hartwig Medical Foundation strives to ensure that every cancer patient receives the most effective treatment for that specific patient, including the correct medication, at the correct time, in the correct period and at the correct dosage. There is still a great deal of progress to be made in this field, for instance through better use of information and data that are already available in this respect.

How does Hartwig Medical Foundation aim to achieve this?

1.2 Hartwig Medical Foundation aims to achieve its mission by collecting and collating genetic and clinical data (including treatment data) from cancer patients in a single database. Data are always stored in encoded form (only with a patient code but without a name) so that the data cannot directly be related to an individual by Hartwig Medical Foundation. Hartwig Medical Foundation is provided with this encoded genetic and clinical data by several hospitals, treatment centers and research institutes with whom Hartwig Medical Foundation collaborates.

1.3 Hartwig Medical Foundation has available state of the art sequencing equipment, bio-informatics, software and IT, which is used by Hartwig Medical Foundation to sequence biological material from cancer patients in order to generate genetic data. This process is always carried out on behalf of hospitals, treatment centers and research institutes with whom Hartwig Medical Foundation collaborates and who use the genetic data generated by Hartwig Medical Foundation in the context of research, clinical research or the treatment of the patient. In certain situations, Hartwig Medical Foundation and these hospitals, treatment centers and research institutes may agree that Hartwig Medical Foundation stores the generated encoded genetic data as well as clinical data in its database (of course in accordance with applicable laws and regulations).

1.4 The extensive, centralized information in the database offers many options and opportunities in the cancer research field. That is why Hartwig Medical Foundation makes data from the database available — under strict conditions — to certain parties, such as researchers and scientists. They can use the information from the database to conduct further research on the relation between a specific genetic deviation and the responsiveness of a patient to a certain treatment. In this document, the term 'treatment' should be read as including medication.

2 CORE VALUES

2.1 Hartwig Medical Foundation applies the following core values:

- Development. Hartwig Medical Foundation aims at contributing to scientific research, in order to promote the development of new treatment methods and, thus, to contribute to the development of safe, effective and affordable treatment.
- Integrity. Hartwig Medical Foundation handles data, including patients' personal data, in a reliable, careful, secure and transparent manner.
- Reliability. Hartwig Medical Foundation seeks to be a reliable partner for patients, hospitals, treatment centers, research institutions, academic institutions and experts, in order to promote scientific and social advances in the field of cancer.
- Fairness. Hartwig Medical Foundation values and operates in accordance with the FAIR principles. This means that the data stored in Hartwig Medical Foundation's database are findable, accessible, interoperable and reusable.

3 SAFEGUARDING THE CORE VALUES

3.1 The aforementioned core values are essential for Hartwig Medical Foundation. They are non-negotiable and underlie all of Hartwig Medical Foundation's decisions. Hartwig Medical Foundation translates the core values into specific arrangements and goals as far as possible, and safeguards them from a variety of perspectives, namely (i) social, (ii) ethical, (iii) legal, and (iv) contractual. Below, each of these perspectives will be further elaborated.

Social sphere

3.2 Society needs new, more efficient methods of research into cancer and cancer treatment and development. The collection and exchange of data plays a central role here. A great deal is already possible in terms of technology — including the use of electronic patient records and eHealth applications — and a tremendous amount of information is available. Applying the available technology to the available information — in the right way — can lead to a huge step forward in the field of healthcare innovation.

3.3 For quite some time, there has been a trend within the healthcare sector towards sharing more information, improving the quality of available information and fostering increased and better collaboration. Parties such as Health-RI play an important role in this respect. For example, Health-RI has observed that many research results fail to reach patients, that data become lost or cannot be used or reused and that money is wasted as a consequence. It has also identified fragmentation of data, of organizations, and of the way in which resources and samples are handled. Health-RI's goal is thus to develop an efficient, high-quality research infrastructure, with sufficient attention being paid to procedure and regulations, alongside high-quality local facilities.

- 3.4 Hartwig Medical Foundation supports this goal and is contributing to this development. It does so by collecting genetic and clinical data, including treatment data, from cancer patients in a single database, and making those data available for scientific research (under strict conditions).
- 3.5 An important difference with existing initiatives is that Hartwig Medical Foundation only stores results from DNA/RNA analysis of biological human materials and corresponding clinical data, rather than the biological human materials itself. This makes Hartwig Medical Foundation's activities essentially different from those of biobanks. Hartwig Medical Foundation is the first party in the Netherlands to facilitate advances in research into (the correct treatment of) cancer in this way.

Hartwig Medical Foundation is aware that it is thus venturing into – partly – unknown territory, and therefore regularly monitors the results and permissibility of its activities. Hartwig Medical Foundation engages (legal) assistance where necessary or desirable.

Nature of the data

- 3.6 Naturally, Hartwig Medical Foundation is aware that it has personal, sensitive and confidential data at its disposal. In a society where technology is widely available and information is shared to an increasing extent, patients, hospitals, treatment centers and research institutes must be able to rely that Hartwig Medical Foundation handles this data carefully and securely.

In Hartwig Medical Foundation's view, it goes without saying that data are to be collected and stored as securely as possible, taking account of the state of the art and the latest insights in the field of data security.

- 3.7 Hartwig Medical Foundation only has available encoded data. As a result, Hartwig Medical Foundation is not able to directly relate or link the genetic and clinical data to a specific patient. The same applies for researchers and scientists to whom data in the database of Hartwig Medical Foundation is made available.
- 3.8 Furthermore, Hartwig Medical Foundation only stores patient data in its database if and to the extent that this is possible pursuant to the applicable legislation and regulations. In addition, Hartwig Medical foundation ensures that no superfluous data are stored in the database. Hartwig Medical Foundation outsources its data processing and storage to a reputable IT company whose extensive expertise includes the data security field, whereby Hartwig Medical Foundation itself retains control of the database at all times. In this respect, Hartwig Medical Foundation agrees upon strict arrangements with the IT company.

Data access requests

- 3.9 Hartwig Medical Foundation also handles the assessment of requests for access to data in its database with due care. Each request is tested and assessed by independent bodies of Hartwig Medical Foundation (the Scientific Council and the Data Access Board) using a clear, publicly accessible protocol (as laid down in the Rules of Procedure Data Access Requests which can be found on <https://www.hartwigmedicalfoundation.nl/en/applying-for-data>).
- 3.10 Hartwig Medical Foundation is aware that publishing scientific articles is an important way to advance research into cancer treatment. However, with a view to careful data handling, not every research plan automatically qualifies for access to data from the database.
- 3.11 The involved research plan must relate to innovative scientific and/or healthcare-economic research aimed at improving the collective healthcare system, improving/developing new treatment methods, the effective and efficient use and off-label use of existing cancer medication, and/or improving/developing safe, effective and affordable cancer medication. The research must be relevant, new, feasible, and of social and/or scientific value. Moreover, the purpose of the research must align with Hartwig Medical Foundation's core values.
- 3.12 If Hartwig Medical Foundation decides that data can be made available to a researcher, scientist or other party, it always makes available only a specific set of data (not the whole database) that, furthermore, may only be used for the approved, relevant and specific research purpose. In the license agreement that is entered into by and between Hartwig Medical Foundation and the researcher, scientist or other recipient of data, such parties commit to comply with strict requirements governing the use and protection of the data made available by Hartwig Medical Foundation.
- 3.13 As Hartwig Medical Foundation is aware that supply chain responsibility is highly important, Hartwig Medical Foundation's contracting parties are also required to apply the above guiding principles, such as the purpose limitation requirement.
- 3.14 If Hartwig Medical Foundation itself wishes to make use of the data from its database – other than in the context of internal management and processes – or engages third parties for the use of data from its database, the same rules and protocols apply to Hartwig Medical Foundation as to external parties. One of the implications of this is that Hartwig Medical Foundation, too, must submit its request to the Scientific Council and Data Access Board for assessment.
- 3.15 Hartwig Medical Foundation also makes available statistical information based on the data in its database. Aforementioned Rules of Procedure Data Access Requests do not apply to requests for statistical and aggregated information based on the data from Hartwig Medical Foundation's database.

Publications further to a data access request

- 3.16 Hartwig Medical Foundation is not involved in the research performed by a researcher, scientist

or other party to whom data is made available by Hartwig Medical Foundation pursuant to a data access request. The publication of research results based on the data made available by Hartwig Medical Foundation is important for scientific advances and, as such, is supported by Hartwig Medical Foundation. However, in the event of such publication, Hartwig Medical Foundation is not involved in the content of any publication.

- 3.17 In addition, Hartwig Medical Foundation will not, for example, claim intellectual property rights in third party discoveries resulting from data provided to those third parties. Hartwig Medical Foundation, however, applies a certain publication policy (which can be found on <https://www.hartwigmedicalfoundation.nl/en/data-policy>), acknowledging the sources of the data that have contributed to the published results.
- 3.18 The above may, obviously, be different in the event that Hartwig Medical Foundation collaborates with third parties in a specific research project.

Collaboration

- 3.19 Hartwig Medical Foundation is aware that social and scientific advances cannot be made without collaboration. That is why Hartwig Medical Foundation seeks to collaborate with patients, hospitals, treatment centers, academic institutions, interest groups and experts, where possible. The basic principle here is that each party does what it is good at. Hartwig Medical Foundation brings parties together and facilitates the appropriate and efficient use of medical and research data. Supply chain responsibility plays a central role here. Each link in the chain must handle the other parties' data and interests in an ethical manner.
- 3.20 Where possible, Hartwig Medical Foundation also promotes collaboration in scientific research. If the same research plan emerges from various centers or research institutes, Hartwig Medical Foundation may advise the respective parties to join forces in a single research project.

Ethical sphere

- 3.21 There is a growing awareness in society on the value of personal data, including medical data. This means that there is a greater need for openness and participation regarding the use of personal data. Hartwig Medical Foundation is aware of this, and considers transparency about the use of data to be of great importance.
- 3.22 Hartwig Medical Foundation is, for example, fully open about what it does with personal data and why. Hartwig Medical Foundation describes this inter alia in its Privacy Policy, which is available here: <https://www.hartwigmedicalfoundation.nl/en/data-policy>. Furthermore, ethical aspects are taken into account when Hartwig Medical Foundation assesses requests for access to data in its database.

Informed consent

- 3.23 In principle, Hartwig Medical Foundation only works with 'informed consent' from patients and

strives to offer patients options for controlling the use of their data. Under the applicable legislation and regulations and particularly, the General Data Protection Regulation, the genetic data and clinical data that are processed by Hartwig Medical Foundation qualify as 'special categories of personal data'. Hartwig Medical Foundation has designed its processing activities and policies in such way that these comply with the strict requirements that apply to this type of data.

- 3.24 However, in extraordinary cases Hartwig Medical Foundation works with data from patients whose biological human material was taken quite some time ago (for instance in case of retrospective studies). In those cases, the informed consent pursuant to which the biological human material was obtained is inadequate to serve as a sufficient legal basis for Hartwig Medical Foundation's activities (which, after all, were not known about when the relevant biological human material was taken, as Hartwig Medical Foundation did not yet exist at that time).
- 3.25 In so far as possible, in such cases Hartwig Medical Foundation will proceed to attempt to obtain adequate informed consent or to arrange for it to be obtained. However, that is not always possible or practically feasible, for example where the patient in question has died in the interim, and may even be undesirable, for example when the patient is very ill. Under certain circumstances, the public interest that Hartwig Medical Foundation seeks to serve, justifies Hartwig Medical Foundation working with personal data in these situations as well in so far as the patient did not object to that at the time. Obviously, an important condition in this respect is that the privacy and medical interests of any patients concerned are sufficiently safeguarded in accordance with these Guiding Principles. In these situations Hartwig Medical Foundation only acts after the interests involved have been carefully balanced.
- 3.26 In addition, Hartwig Medical Foundation is aware that processing of personal data could be hampered or obstructed in the event that patient data are not or insufficiently pseudonymised, or if sufficient or sufficiently clear informed consent has not been obtained. In such cases, Hartwig Medical Foundation can imagine that a socially compelling research interest may justify overriding possible privacy objections. The nature and objectives of the research play an important role in this regard. Research into a ground-breaking method of treatment at an advanced stage may more readily provide such justification than research with a less direct social benefit/interest. Obviously, this is subject to the condition that legal limits are respected and that the invasion of privacy is so minor that that patient can still trust that his or her data will be handled with due care. Hartwig Medical Foundation is aware that continuous vigilance is required to safeguard the privacy of patients. The patient and the hospitals, treatment centers and research institutes are entitled to this, and must be able to trust that data will be handled with due care.
- 3.27 The Data Protection Officer of Hartwig Medical Foundation assists in this respect. Where possible, Hartwig Medical Foundation also seeks to collaborate with interest groups. For example, Hartwig Medical Foundation believes that patients' associations have a role to play in sharing their thoughts about participation and control options for patients, particularly with

regard to retrospective studies.

- 3.28 When access to data in the database is requested, a careful assessment is made as to whether the intended use of the data falls within the scope of the patient's informed consent. Hartwig Medical Foundation exercises restraint, where the informed consent is insufficiently clear.
- 3.29 On the other hand, Hartwig Medical Foundation strives to avoid scientific research being unnecessarily obstructed by an overly strict interpretation of open standards and grey areas in the applicable legislation and regulations. Without scientific research, the development of new, better or more efficient treatment methods would be impossible. To conduct such scientific research, patient data are necessary.

Commercial use

- 3.30 In accordance with the legal requirements for processing personal data, Hartwig Medical Foundation works in the public interest, without a profit motive. This means, for example, that Hartwig Medical Foundation ensures that data from its database are only used in accordance with its objectives (i.e. scientific research in the public interest).
- 3.31 If commercial parties, such as pharmaceutical companies, can contribute to Hartwig Medical Foundation's mission, Hartwig Medical Foundation will wish to facilitate this.
- 3.32 However, this would only be possible in the event that the research of commercial parties predominantly serves a public interest.
- 3.33 Hartwig Medical Foundation will assess whether this requirement is met in each specific case. Naturally, requests from such parties for the provision of data must also pass the same test via the Data Access Board and the Scientific Council on the basis of the Rules of Procedure Data Access Requests. Hartwig Medical Foundation will never permit the use of data for marketing or other purely commercial purposes.

Fees

- 3.34 Hartwig Medical Foundation makes data in its the database available to researchers or scientists for free.
- 3.35 If, however, Hartwig Medical Foundation decides to provide data to a commercial party in a case as referred to in 3.30 above, Hartwig Medical Foundation may request a fee. In addition, Hartwig Medical Foundation may also request a fee if a request for data requires disproportionate effort on the part of Hartwig Medical Foundation. These fees are directly fed back to the Foundation and are thus fully applied in furtherance of Hartwig Medical Foundation's objectives and mission: the advancement of scientific research into cancer and cancer treatment.
- 3.36 Data will never be 'sold'. All that is provided is a contractual right to use specific data from the database for a specific research question.

Patients' control options

- 3.37 The basic principle is that, at all times, the patient retains control of the data relating to him or her.
- 3.38 Specifically, this means that a patient always has the option of accessing his or her data, having it deleted from the database, withdraw consent previously given and object to the further use of the data. When a patient decides to withdraw his/her consent or to have deleted his/her data from the database, this only has future effect. This means that Hartwig Medical Foundation will delete the patient's data from the database and will no longer use it. However, it is not possible for Hartwig Medical Foundation to undue previous use of this patients data by Hartwig Medical Foundation and/or researchers to whom the data of this patient have been made available further to a data access request.
- 3.39 As Hartwig Medical Foundation itself has no direct contact with the patient (Hartwig Medical Foundation does not know from which patients it stores personal data in the database, as all these data is encoded), the hospitals, treatment centers and research institutions that provide Hartwig Medical Foundation with the data have an essential role in offering and implementing the control options to the patients. In this respect, Hartwig Medical foundation makes arrangements with the involved hospitals, treatment centers and research institutions.

Legal sphere

- 3.40 Hartwig Medical Foundation takes a great deal of care in setting up, using and providing access to the database. Hartwig Medical Foundation knows and respects its legal limits and what it can and cannot do under, inter alia, the General Data Protection Regulation (“**GDPR**”), the Dutch General Data Protection Regulation Implementation Act (*Uitvoeringswet Algemene verordening gegevensbescherming*) (“**UAVG**”) and the Medical Treatment Contracts Act (*Wet op de geneeskundige behandelingsovereenkomst*). Hartwig Medical Foundation has its methods legally assessed in collaboration with a designated team of attorneys.
- 3.41 In the event that Hartwig Medical Foundation encounters grey areas in the legislation and regulations, it carefully assesses the limits of what is permissible where that is necessary to advance cancer research and development. In doing so, Hartwig Medical Foundation applies the following principles in any event:
- patients' right to privacy is always respected. Personal data are processed in a careful and transparent manner;
 - the technical and organizational protection and security of data is essential;
 - data are processed in encoded form, so that Hartwig Medical Foundation will not independently be able to identify the patients whose data it is managing;
 - the data used are adequate, up to date, relevant and not excessive;

- Hartwig Medical Foundation uses and/or provides data from the database exclusively for the purposes for which Hartwig Medical Foundation received the data. Therefore, data are always used to foster advances in cancer treatment and research. The data provided or stored never exceed what is necessary for those purposes;
- in principle, Hartwig Medical Foundation only processes data on the basis of informed consent of the patient. Because Hartwig Medical Foundation has no direct contact with the patient, Hartwig Medical Foundation ensures that the parties providing the data, such as hospitals and treatment centers, have obtained such informed consent. The agreements concluded by Hartwig Medical Foundation contain various provisions in that respect – also to enable Hartwig Medical Foundation to comply with its obligations under the GDPR and the UAVG. If — as regards prospective studies — no valid consent has been obtained, Hartwig Medical Foundation cannot and will not proceed to store or provide patient data until the moment that sufficient informed consent that covers the processing has been obtained. Where retrospective studies are concerned, Hartwig Medical Foundation applies the principles described in paragraphs 3.24 above;
- Hartwig Medical Foundation ensures that data are processed within the European Union (**EU**) as far as possible. If it is necessary to take the data outside the EU (for example if it makes data available to foreign researchers), Hartwig Medical Foundation will guarantee a sufficient security level for the data. The receiving party must, at the very least, comply with all data protection principles that apply within the EU.

3.42 As well as complying with the applicable legislation and regulations, Hartwig Medical Foundation seeks alignment with codes of conduct drafted on a self-regulation basis, such as 'Human Tissue and Medical Research: Code of Conduct for Responsible Use' (*Code Verantwoord omgaan met lichaamsmateriaal ten behoeve van wetenschappelijk onderzoek*) drawn up by the Foundation Federation of Dutch Medical Scientific Societies. As long as it does not interfere with Hartwig Medical Foundation's mission, Hartwig Medical Foundation applies the 'best practice' principle when handling data, thus doing more rather than less where possible, even when less is permissible.

Contractual sphere

3.43 As long as it is in line with Hartwig Medical Foundation's mission and core values, Hartwig Medical Foundation applies the basic principle that data from the database should be accessible to everyone.

3.44 Partners must share and conform to Hartwig Medical Foundation's core values and must agree to the strict conditions that Hartwig Medical Foundation imposes with regard to patient privacy and data protection.

3.45 Hartwig Medical Foundation also safeguards its core values contractually, by, for example, making clear arrangements about matters as data use in its collaboration agreements and license agreements. In addition, the Rules of Procedure Data Access Requests are

contractually incorporated into relevant agreements, thus assuring compliance with the safeguards included therein. Consent and transparency obligations are, where relevant, contractually imposed on parties that receive data, and these parties are furthermore subject to contractual restrictions on what they can do with the data. Use for marketing purposes is excluded, for example, and it is not possible to sell data or make data available to others. Arrangements of a more practical nature are also made, for example regarding the transfer of clinical data, the supply of samples and the manner in which data are provided in encoded form.

- 3.46 Hartwig Medical Foundation also puts transparency first and foremost vis-a-vis its partners, for example regarding expectations, progress, costs and conditions in respect of the collaboration. In addition, Hartwig Medical Foundation is prepared to make template agreements available to interested parties, if so requested with a view to transparency or for other reasons.