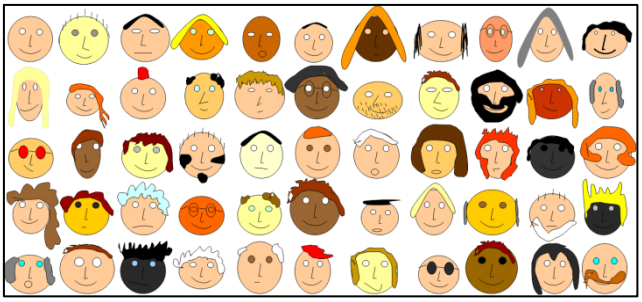
Registration & Shipment Manual

INFORM

INdividualized Therapy FOr Relapsed Malignancies in Childhood



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Website: http://www.dkfz.de/de/inform

Registry Code: NCT-2013-0220

German Clinical Trial Register ID: DRKS00007623

Version and date: Version 10, dated 14.10.2016

Important Notice

Please ensure that all cases are discussed with the respective GPOH entity specific study group for eligibility for INFORM.
After receiving informed consent it is mandatory to register every patient in the central MARVIN database before tissue shipment.
INFORM shipment forms, provided with an INFORM patient ID will be automatically generated upon registration of a patient in MARVIN. Only after registration and with these forms, tissue can be shipped to the Central Pathology Laboratory in Heidelberg. Tissue shipped without INFORM patient ID and no previous registration in MARVIN cannot be processed. A free of charge shipment can be ordered via GO! Express (chapter 2.8).

For all patients, two types of material are required:

I) Malignant material of the current disease episode (fresh frozen)

II) Non-malignant material (germline, e.g. blood)

Please read this manual carefully while incomplete submissions will, without exception, significantly delay the process!
For information regarding sample shipment, please read chapter 2 and contact the Central Pathology Laboratory in Heidelberg in case of further questions:

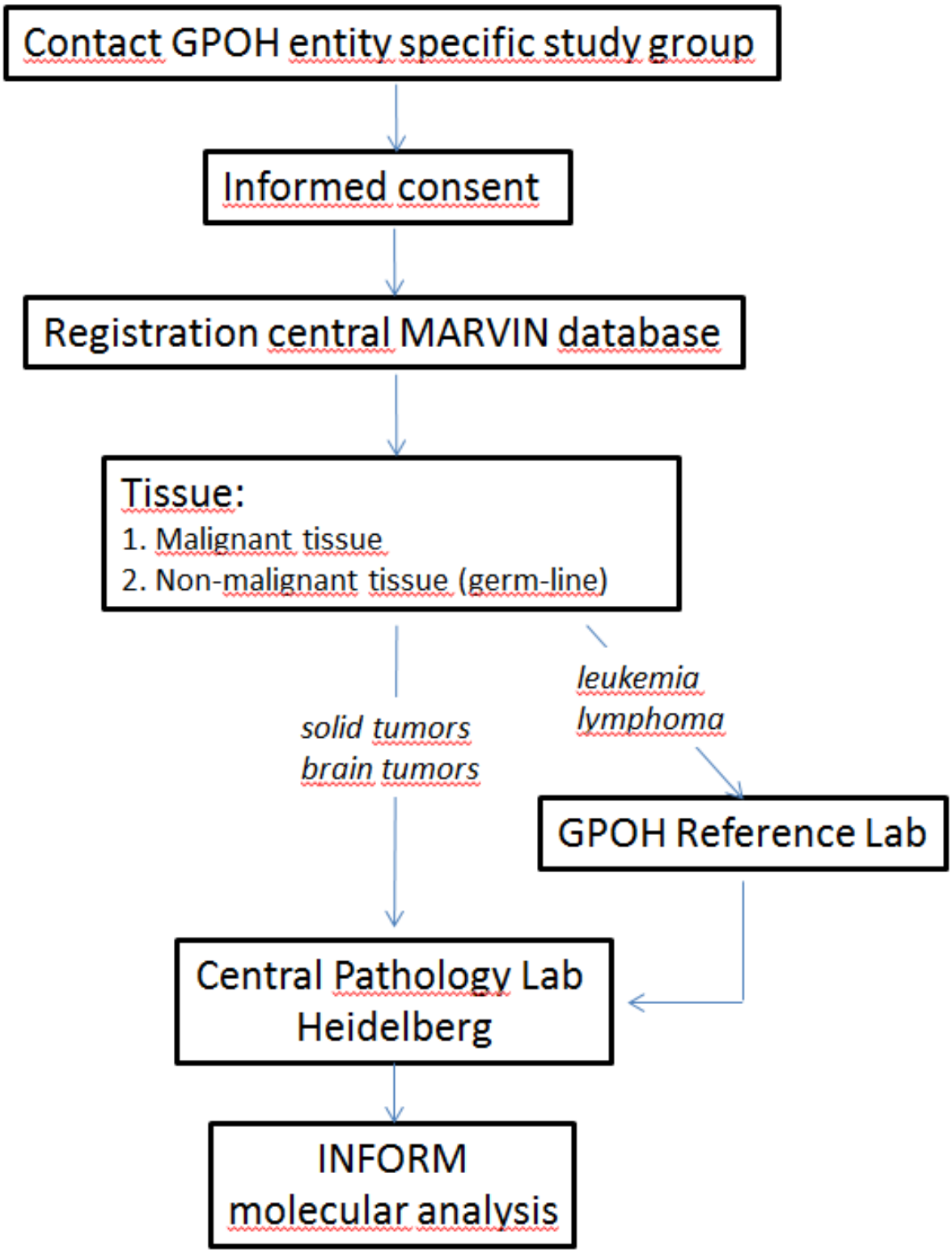
Petra Fiesel / David Capper
Tel.: 06221 56-4650
INFORM_samples@DKFZ.de

For all other additional information regarding the INFORM registry, please contact the NCT Clinical Trial Center in Heidelberg:

Dr. Janna Kirchhof / Dr. Kristian Pajtler / Ruth Witt / Dr. Martina Nesper-Brock
Tel.: 06221 56-6913/ -7255 / -7294 / -7439
INFORM_info@DKFZ.de

For some entities (leukemias, NHL and neuroblast-infiltrated bone marrow) the material has to be shipped via an entity specific reference laboratory (after consultation with the entity specific study group). There, DNA and RNA will be extracted and should be forwarded to the Central Pathology Laboratory in Heidelberg with INFORM shipment forms, provided with INFORM patient ID.

Flow Chart


Contact GPOH entity specific study group
Informed consent
Registration central MARVIN database
Tissue:
1. Malignant tissue
2. Non-malignant tissue (germ-line)
solid tumors
brain tumors
leukemia
lymphoma
GPOH Reference Lab
Central Pathology Lab
Heidelberg
INFORM
molecular analysis

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1. Registration

1.1 Central MARVIN database

In the INFORM registry, patient data is captured and stored via remote data entry system in the central MARVIN database of the GPOH. Before registration, all cases should be discussed for eligibility with the respective GPOH entity specific study group as there may be open Phase I/II trials available for certain patient subpopulations (i.e. neuroblastoma).
After receiving informed consent it is mandatory to register every patient in the central MARVIN database before tissue shipment. INFORM shipment forms, provided with an INFORM patient ID will be automatically generated upon registration of a patient in MARVIN. Only after registration and with these forms, tissue can be shipped to the Central Pathology Laboratory in Heidelberg.

1.2 Access to the central MARVIN database

Every GPOH approved pediatric oncology center can request for an INFORM registry MARVIN access via the NCT Clinical Trial Center in Heidelberg. Name and email address of staff members, who should be entitled to have access to the INFORM Registry in MARVIN and the name of the requesting center have to be sent to the INFORM study center by email (**INFORM_info@DKFZ.de**). MARVIN training is mandatory, before access can be provided as it is routine practice with all GPOH trials that use the MARVIN platform. If the person has already been trained, access will be granted within short time. For questions regarding MARVIN and access please contact the NCT Clinical Trial Center Data Management group (Christine Grasy / Angelika Freitag / Marlene Diewald, Tel. 06221 56-7457/ -6237).

1.3 INFORM patient ID

The patients' name and all confidential information are subject to medical confidentiality and to the regulations of the Bundesdatenschutzgesetz (BDSG). Only the treating physician/hospital will be able to link the registry data to personal information like name and address. The registry does not keep record on patients' name or address.
An INFORM patient ID will be automatically generated after registration of a new patient in MARVIN. Only after registration and accompanied by a shipment form, tissue can be shipped. Tissue from patients without INFORM patient ID and no previous registration in MARVIN cannot be processed.

1.4 Patient registration step 1: In- and Exclusion criteria

Please check whether a patient is eligible before starting the registration procedure in MARVIN. This includes discussion of the case with the respective GPOH entity specific study group. Patient registration in the central MARVIN database takes place via a two-step process. In the first step, general and entity specific in- and exclusion criteria are screened. When eligible for INFORM, the patient will be registered. After this first registration step, an INFORM patient ID and INFORM shipment forms will be automatically generated. From this moment on, tissue can be shipped to the Central Pathology Laboratory in Heidelberg. For in- and exclusion criteria, please see our website.

1.5 Patient registration step 2: Baseline assessment

To speed up the process, it is not necessary to enter the full baseline characteristics into the database to obtain an INFORM patient ID, which enables sample shipment within a relatively short time span. It is however mandatory, to finish the second registration step (baseline characteristics) within 14 days after sample submission in order to allow the INFORM registry to report potential targets. In case of an incomplete baseline characteristics registration, no targets can be reported.

1.6 Additional information

For further information concerning the INFORM registry, please see the registry protocol, or contact the NCT Clinical Trial Center in Heidelberg:

Dr. Janna Kirchhof / Dr. Kristian Pajtler / Ruth Witt / Dr. Martina Nesper-Brock
Tel: 06221 56-6913/ -7255 / -7294 / -7439
Email: INFORM_info@DKFZ.de
Website: http://www.dkfz.de/de/inform

2. Shipment of patient material

2.1 General information

It is mandatory to register every patient in the central MARVIN database before tissue shipment. For detailed registration information, please see chapter 1.

Only samples accompanied by shipment forms, and provided with the INFORM patient ID, will be processed (please do not send patients' names).

- ➔ **Please fill all required sample and contact information in the MARVIN form "Shipment of Material".**
- ➔ **After completing the form click on: "Transform: Print Shipment Sheet" and send it together with the material to the address stated on the sheet.**

Mandatory material requirements (see also Table 1 - 4):

I) Malignant material of the current disease episode (fresh frozen)

II) Non-malignant material (germline, e.g. blood)

The INFORM analyses cannot be performed with Formalin fixed paraffin embedded (FFPE) material.

Additionally to the fresh frozen tumor material of the current refractory/relapsed/progressive disease episode, non-malignant (germline) material is required. If possible, ship non-malignant tissue together with malignant material. The analysis only starts when both samples have arrived in the Central Pathology Laboratory in Heidelberg.

Please note that fresh frozen and non-malignant material should be sent as soon as possible. The time between biopsy/puncture of the current disease and receipt of all required samples and information in the Central Pathology Laboratory in Heidelberg may not exceed 8 weeks.

For some entities (leukemias, NHL and neuroblast-infiltrated bone marrow) the material has to be shipped via an entity specific reference laboratory (after consultation with the entity specific study group). There, DNA and RNA will be extracted and should be forwarded to the Central Pathology Laboratory in Heidelberg with INFORM shipment forms, provided with INFORM patient ID. See chapter 2.3 for further details.

A free of charge overnight shipment service via GO! Express can be ordered following the instructions in chapter 2.8.

Requested material for research purposes:

Please also provide **tumor material of the primary diagnosis or a previous relapse** whenever possible.

For brain tumors, please send **frozen cell free plasma** for circulating tumor DNA analysis.

In case of further questions regarding sample shipment:

Petra Fiesel / David Capper
Tel: 06221 56-4650
Fax: 06221 56-4566
Email: INFORM_samples@DKFZ.de

2.2 Minimal material requirements solid tumors and brain tumors

In case of solid tumors and brain tumors, samples will be shipped directly to the Central Pathology Laboratory in Heidelberg. It is mandatory to send malignant tissue of the current disease (fresh frozen) and non-malignant material (germline) within 8 weeks after biopsy. **For the minimal tissue requirements see Table 1.**

Please also provide **fresh frozen tumor tissue of the primary diagnosis or a previous relapse whenever possible**.
If only Formalin fixed paraffin embedded material is available, please provide 10 unstained sections of 2µm and 10 unstained sections of 10µm, or the FFPE block, of the primary tumor or a previous relapse (accompanied by shipment forms, and provided with the INFORM patient ID, please do not send patients' names).

For brain tumors, please also send frozen cell free plasma (derived from 10ml EDTA blood (5ml EDTA blood in small children)) on dry ice. See chapter 2.10 for plasma collection instructions.

Solid tumors and brain tumors	**Preferred**	**Alternative**
Malignant tissue	**Fresh frozen tumor tissue*:** • **at least one pea-sized snap frozen piece of tissue** (in case of resection) • one large core biopsy (in case of needle biopsy) • 5 stereotactic biopsies (e.g. in case of brain tumor biopsy) * Snap freeze in liquid nitrogen A.S.A.P. according to GPOH guidelines (chapter 2.9)	Tumor DNA (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) & Tumor RNA (optimally >3µg) minimum concentration of 45ng/µl (in 35 - 75µl) extracted from fresh frozen tumor tissue, tumor cell content >40%
Non-malignant material (germline)	**Blood** (5ml EDTA) and for brain tumors: frozen cell free plasma	Saliva (2ml)
only if post allogeneic SCT I) patient germline & II) donor germline	I) Blood / DNA from blood of the patient before SCT & II) Blood of the donor	I) Saliva (2ml) & II) Blood / DNA from blood of the patient post SCT (with complete donor chimerism)

Table 1: Minimal material requirements solid tumors and brain tumors. Additional material will increase the chance of successful analysis. Please send on dry ice, optimally in the GPOH tumor box. Store and ship EDTA-blood frozen (or cooled within 4 days, for details see chapter 2.8).

If the patient ever **received allogeneic stem cell transplantation**, the following germline controls are needed:
I) patient germline: blood / DNA from blood of the patient before SCT or saliva **AND**
II) donor germline: blood of the donor or blood / DNA from blood of the patient post SCT (with complete donor chimerism).

Please send **saliva only in exceptional cases**, as low DNA yield and bad quality is expected. Rinse mouth with water and collect saliva in sterile tube after 10min. Freeze saliva immediately after collection and ship on dry ice. Shipment on room temperature is possible with Oragene Collection Kits OG-500 / OG-575 (available on request at INFORM_samples@dkfz.de).

If extraction of nucleic acids will be performed at your side, please make sure that the used malignant tissue is suitable:
Tumor DNA and tumor RNA must derive from fresh frozen tumor tissue (do not use FFPE material). Extract from vital tumor material with as little necrosis as possible. Select areas with highest tumor cell content (aim for >80% of total cells). Tumor cell content has to be at least 40%.
It is recommended to always use nuclease free H_2O for elution of DNA and RNA. The concentration should be measured with Qubit (not e.g. nano drop). If possible, please send a higher amount and a higher concentration as indicated in Table 1.

For neuroblastoma (if biopsy tissue is not available) bone marrow with neuroblast infiltration has to be shipped via the neuroblastoma reference laboratory. Please see chapter 2.6 for further details.

2.3 Routing leukemia, lymphoma and Neuroblast-infiltrated bone marrow

For leukemia, NHL and neuroblastoma (if solid tissue is not available) the material has to be shipped via the entity specific reference laboratory (after consultation with the entity specific study group).

The reference laboratories will check the samples for blast content. Bone marrow with low blast content may be enriched or sorted (tumor cell content has to be >40% for INFORM analyses). Extraction of high-quality DNA and RNA will be conducted in the reference laboratories.
Suitable samples will be forwarded to the Central Pathology Laboratory in Heidelberg. The time between sample taking/puncture of the current disease and receipt of all required

samples and information in Heidelberg should not exceed 8 weeks; otherwise the analyses will not be performed.

Only samples accompanied by shipment forms, and provided with the INFORM patient ID, will be processed in Heidelberg (please do not send patients' names).

- ➔ **Please fill all required sample and contact information in the MARVIN form "Shipment of Material".**
- ➔ **After completing the form click on: "Transform: Print Shipment Sheet".**
- ➔ **Safe the PDF file and send it to the reference laboratory via email or fax.**

If you do not have all required information, please ask the reference laboratory to generate shipment forms for registered patients in MARVIN.

2.4 Minimal material requirements acute leukemia

In case of acute leukemia, samples have to be shipped to the corresponding leukemia reference laboratories:
ALL-relapse to Dr. Arend von Stackelberg in Berlin
AML to Prof. Dr. Dirk Reinhardt in Essen

Extracted tumor DNA and tumor RNA of the current disease episode as well as non-malignant DNA should be forwarded to the Central Pathology Laboratory in Heidelberg within 8 weeks after sample taking/puncture. **For minimal material requirements see Table 2.**

Please also provide tumor DNA and tumor RNA of the primary diagnosis or a previous relapse whenever possible.

Furthermore, in case of **post allogeneic stem cell transplantation patients**, it is obligatory to send:

I) patient germline: extracted DNA from remission bone marrow before SCT or saliva **AND II) donor germline:** blood of the donor or DNA from remission bone marrow of the patient post SCT (with complete donor chimerism, MRD negative).

Please send **saliva only in exceptional cases**, as low DNA yield and bad quality is expected. Rinse mouth with water and collect saliva in sterile tube after 10min. Freeze saliva immediately after collection and ship on dry ice. Shipment on room temperature is possible

with Oragene Collection Kits OG-500 / OG-575 (available on request at INFORM_samples@dkfz.de).

Acute leukemia	**Preferred**	**Alternative**
Malignant material	**Tumor DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) & **Tumor RNA** (optimally >3µg) minimum concentration of 45ng/µl (in 35 - 75µl) extracted from leukemic blasts, tumor cell content >40%	enriched or sorted leukemic blasts (as frozen cell pellets, without buffer, optimally divided in two tubes), tumor cell content >40%
Non-malignant material (germline)	**Non-malignant DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) extracted from complete remission bone marrow	Saliva (2ml)
only if post allogeneic SCT I) patient germline & II) donor germline	I) DNA from remission before SCT & II) Blood (5ml EDTA) of the donor	I) Saliva (2ml) & II) DNA from remission post SCT (with complete donor chimerism, MRD negative)

Table 2: Minimal material requirements leukemia. If possible, send a higher amount and a higher concentration. Please send on dry ice, optimally in the GPOH tumor box.

2.5 Minimal material requirements lymphoma

In case of NHL, samples have to be shipped to the lymphoma reference laboratory in Gießen (Prof. Dr. Wilhelm Wößmann, Dr. Birgit Burkhardt).

Extracted tumor DNA and tumor RNA of the current disease episode as well as non-malignant DNA should be forwarded to the Central Pathology Laboratory in Heidelberg within 8 weeks after sample taking/puncture. **For minimal material requirements see Table 3.**

Please also provide tumor DNA and tumor RNA of the primary diagnosis or a previous relapse whenever possible.

If the patient ever **received allogeneic stem cell transplantation**, the following germline controls are needed:
I) patient germline: DNA extracted from blood (without blasts) / DNA from complete remission bone marrow of the patient before SCT or saliva **AND**
II) donor germline: blood of the donor or DNA extracted from blood (without blasts) / DNA from complete remission bone marrow of the patient post SCT (with complete donor chimerism, MRD negative).

Please send **saliva only in exceptional cases**, as low DNA yield and bad quality is expected. Rinse mouth with water and collect saliva in sterile tube after 10min. Freeze saliva immediately after collection and ship on dry ice. Shipment on room temperature is possible with Oragene Collection Kits OG-500 / OG-575 (available on request at INFORM_samples@dkfz.de).

NHL	Preferred	Alternative
Malignant material	**Tumor DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) & **Tumor RNA** (optimally >3µg) minimum concentration of 45ng/µl (in 35 - 75µl) extracted from blasts or fresh frozen biopsy tissue, tumor cell content >40%	Fresh frozen tumor tissue: at least one pea-sized snap frozen piece of tissue
Non-malignant material (germline)	**Non-malignant DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) extracted from blood (without blasts) or complete remission bone marrow	Blood (5ml EDTA, if without blasts) or Saliva (2ml)
only if post allogeneic SCT I) patient germline & II) donor germline	I) DNA from blood (without blasts) / DNA from complete remission bone marrow of the patient before SCT & II) Blood of the donor	I) Saliva (2ml) & II) DNA from blood (without blasts) / DNA from complete remission bone marrow of the patient post SCT (with complete donor chimerism, MRD negative)

Table 3: Minimal material requirements lymphoma. Additional material will increase the chance of successful analysis. Please send on dry ice, optimally in the GPOH tumor box. Store and ship EDTA-blood frozen (or cooled within 4 days), for details see chapter 2.8.

2.6 Minimal material requirements Neuroblast-infiltrated bone marrow

In case of bone marrow with neuroblast infiltration, samples have to be shipped to the neuroblastoma reference laboratory in Köln (Prof. Dr. Matthias Fischer).

Extracted tumor DNA and tumor RNA of the current disease episode as well as non-malignant DNA should be forwarded to the Central Pathology Laboratory in Heidelberg within 8 weeks after sample taking/puncture. **For minimal material requirements see Table 4.**

Please also provide tumor DNA and tumor RNA of the primary diagnosis or a previous relapse whenever possible.

If the patient ever **received allogeneic stem cell transplantation**, the following germline controls are needed:
I) patient germline: blood / DNA from blood of the patient before SCT or saliva **AND**
II) donor germline: blood of the donor or blood / DNA from blood of the patient post SCT (with complete donor chimerism).

Please send **saliva only in exceptional cases**, as low DNA yield and bad quality is expected. Rinse mouth with water and collect saliva in sterile tube after 10min. Freeze saliva immediately after collection and ship on dry ice. Shipment on room temperature is possible with Oragene Collection Kits OG-500 / OG-575 (available on request at INFORM_samples@dkfz.de).

bone marrow with neuroblast infiltration	**Preferred**	**Alternative**
Malignant material	**Tumor DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) & **Tumor RNA** (optimally >3µg) minimum concentration of 45ng/µl (in 35 - 75µl) extracted from bone marrow aspirate containing >40% neuroblast infiltration (% after cytospin, not in bone marrow smear) or extracted from fresh frozen biopsy tissue	Fresh frozen tumor tissue: at least one pea-sized snap frozen piece of tissue (if available) or enriched or sorted neuroblasts (as frozen cell pellets, without buffer, optimally divided in two tubes), tumor cell content >40%
Non-malignant material (germline)	**Blood** (5ml EDTA) or **Non-malignant DNA** (optimally >4µg) minimum concentration of 25ng/µl (in 50 - 160µl) extracted from blood or complete remission bone marrow	Saliva (2ml)
only if post allogeneic SCT I) patient germline & II) donor germline	I) Blood / DNA from blood of the patient before SCT & II) Blood of the donor	I) Saliva (2ml) & II) Blood / DNA from blood of the patient post SCT (with complete donor chimerism)

Table 4: Minimal material requirements neuroblastoma. If possible, send a higher amount and a higher concentration. Please send on dry ice, optimally in the GPOH tumor box. Store and ship EDTA-blood frozen (or cooled within 4 days), for details see chapter 2.8.

2.7 Requested material overview

Indication	Malignant material		Non-malignant material*	
	Preferred	Alternative	Preferred	Alternative
ALL-HR	1	2	6	7
ALL post-SCT	1	2	8 + 9	7 + 9
AML	1	2	6	7
Non-hodgkin lymphoma	1	3	6	4 or 7
Soft tissue sarcoma	3	1	4	7
DSRCT	3	1	4	7
Osteosarcoma	3	1	4	7
Rhabdoid tumors	3	1	4 + 5	7
Ependymoma	3	1	4 + 5	7
Medulloblastoma	3	1	4 + 5	7
Ewing sarcoma	3	1	4	7
High grade glioma	3	1	4 + 5	7
Neuroblastoma (solid)	3	1	4	7
Neuroblastoma (neuroblasts)	1	2	4	6 or 7
Other	3	1	4 + 5	7

Table 5: Requested material overview

* If the patient ever received allogeneic stem cell transplantation, germline controls of the patient before SCT and of the donor are necessary (for details see Table 1 - 4).

Legend Table 5:

1) **Tumor DNA** (optimally >4000ng, with a minimum concentration of 25ng/µl, in a volume of 50 - 160µl) AND **Tumor RNA** (optimally 3000ng, with a minimum concentration of 45ng/µl, in a volume of 35 - 75µl). If possible, send a higher amount and a higher concentration.

   Extracted from enriched or sorted leukemic blasts (tumor cell content at least 40%) or from bone marrow aspirate containing >40% neuroblast infiltration (% after cytospin, not in bone marrow smear).

   Or extracted from fresh frozen tumor tissue (tumor cell content at least 40%; aim for >80% of total cells; extract from vital tumor material with as little necrosis as possible; use nuclease free H_2O for elution; measure concentration with Qubit.

   Please also provide Tumor DNA and Tumor RNA of the primary diagnosis or a previous relapse whenever possible.

2) Enriched or sorted leukemic blasts or neuroblasts (as frozen cell pellets, without buffer, optimally divided in two tubes). Tumor cell content at least 40%.

3) **Fresh frozen tumor tissue**, if possible also of the primary diagnosis or a previous relapse. At least one pea-sized snap frozen piece of tissue (in case of resection), one large core biopsy (in case of

needle biopsy) or 5 stereotactic biopsies (e.g. in case of brain tumor biopsy). Additional material will increase the chance of successful analysis.

4) **Blood** (5ml EDTA), store and ship EDTA-blood frozen (or cooled within 4 days).

5) For brain tumors only, send **frozen cell free plasma** (derived from 10ml EDTA blood (5ml EDTA blood in small children)). See chapter 2.10 for plasma collection instructions.

6) **Non-malignant DNA** (optimally >4000ng, with a minimum concentration of 25ng/µl, in a volume of 50 - 160µl). If possible, send a higher amount and a higher concentration. Extracted from complete remission bone marrow (or in case of lymphoma extracted from blood without blasts).

7) Saliva (2ml). Only in exceptional cases, as low DNA yield and bad quality is expected. Rinse mouth with water and collect saliva in sterile tube after 10min. Freeze saliva immediately after collection and ship on dry ice. Shipment on room temperature is possible with Oragene Collection Kits OG-500 / OG-575 (available on request at INFORM_samples@dkfz.de).

8) In case of **post allogeneic stem cell transplantation leukemia patients**, it is obligatory to send **patient germline:** extracted DNA from remission bone marrow before SCT

9) **AND donor germline:** blood of the donor or DNA from remission bone marrow of the patient post SCT (with complete donor chimerism, MRD negative).

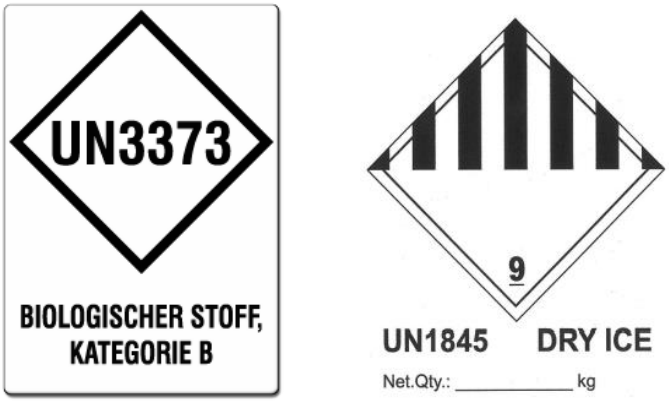
2.8 Transportation service and Shipment conditions

Send malignant material as soon as possible after surgery via GO! Express delivery. Do not wait for histopathological confirmation of diagnosis as this will cause significant delay in sample analysis. If possible, ship non-malignant material together with malignant material. The analysis only starts when both samples have arrived in the Central Pathology Laboratory in Heidelberg.

Please use a GPOH tumor box with dry ice to ship frozen samples.

Fresh frozen malignant tissue, DNA and RNA samples, saliva, plasma, effusions, leukemic blasts and neuroblasts should all be shipped on dry ice. Fill box completely with dry ice to ensure sufficient freezing of samples during shipment.

The box will be sent back to you. Since the box contains biological substances category B, the samples have to be packed according to “Verpackungsanweisung P 650”. The box has to be marked at the outside with:



EDTA-blood samples can be frozen or stored at 4°C for 1-4 days. Ship blood together with the fresh frozen tumor material (e.g. cooled in the lid of the tumor box or put on dry ice). If separate shipment is not avoidable send blood cooled, and consider that the samples do not stay longer than four days on 4°C including shipment duration.

Only samples accompanied by shipment forms, and provided with the INFORM patient ID, will be processed in Heidelberg.

- ➔ **Please fill in all required sample and contact information into the MARVIN form “Shipment of Material”.**
- ➔ **After completing the form click on: "Transform: Print Shipment Sheet" and send it together with the material to the address stated on the sheet.**

A free of charge overnight shipment service via GO! Express may be ordered.
Pickup service until 17:00, **only send on Monday-Thursday**, as sample receipt is not possible on weekends and public holidays.

You can find the "GO! Abholauftrag" in MARVIN, or on request from INFORM_samples@dkfz.de. Please fill out the marked zones (Abholadresse, Abholdatum, Zustelldatum, Abholzeit, Gewicht und INFORM-ID) and fax the Abholauftrag to GO! Express.

If you expect to send samples more frequently you can order "Frachtbriefe" via INFORM_info@DKFZ.de.

In case of further questions regarding sample shipment:

Petra Fiesel / David Capper
Tel: 06221 56-4650
Fax: 06221 56-4566
Email: INFORM_samples@DKFZ.de

2.9 Freezing guidelines

Short description of GPOH freezing guidelines for fresh tumor tissue:

- To avoid degradation of DNA and RNA snap freeze tissue as soon as possible **(optimally within 30 minutes)**.
- Always keep samples sterile.
- Please cut large tissue pieces into pea-sized fragments.
- **Label 1.8ml tubes with INFORM-ID, date of sample taken and localization.**
- Precool tubes in liquid nitrogen to avoid tissue sticking to the tubes.
- Snap freeze tumor tissue in liquid nitrogen.
- Transfer frozen tissue piece into precooled 1.8ml tubes.
- **Put at -80°C and ship on dry ice in a GPOH tumor box**

2.10 Instruction for plasma collection

- Only requested for brain tumors.
- Collect 10ml EDTA blood sample (5ml in small children).
- Place the tube in an ice/water bath and maintain chilled until centrifugation. Plasma separation should be carried out immediately after blood draw. If this is not possible, blood should be kept chilled and processed within a maximum of 2 hours to maintain sample integrity.

- Process collection tubes in a refrigerated centrifuge (set to 2°C to 8°C) at approximate 2000 x g for 15 minutes. Tubes may be centrifuged under ambient condition (room temperature) if a refrigerated centrifuge is not available.
- Taking care not to disturb the WBC layer (which forms a thin film between the upper plasma layer and the lower layer of packed RBCs), use the standard laboratory technique to transfer the plasma equally into fresh 15ml centrifuge tubes with conical bottom or 1,5 ml centrifuge tubes.
- Centrifuge plasma samples at 4°C for 10 min at 16,000 x g (in fixed-angle rotor).
  Note: If a centrifuge capable of this speed is not available, this step might be omitted and plasma should be frozen immediately (optimal -80°C).
- Carefully remove supernatant to a new tube with a pipette without disturbing the pellet.
- **Label tubes with INFORM-ID and date of sample taking.**
- Store plasma aliquot samples at -80°C until shipment. If a -80 °C freezer is not available, samples may be stored at -20 °C.
- **Ship on dry ice**, preferably together with the tumor sample.