



The future of cancer therapy

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Reporting of genetic results and incidental findings

POL022
Version 1.0

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Table of Contents

1	PURPOSE	3
2	DEFINITIONS	3
3	POLICY	4
3.1	Hereditary cancer mutations or incidental findings	4
3.2	Genetic finding from a biomarker-driven trial or from a prospective research project	4
3.3	Genetic finding in the scope of future/further research.....	4
4	REFERENCES.....	5
5	DOCUMENT HISTORY	5

1 PURPOSE

Genetic testing is becoming an integral part of modern medicine, especially in oncology. While genetic testing holds great promise for personalizing treatment, much of the data produced by particularly large-scale genetic sequencing is of unknown or uncertain medical value. Moreover, it can reveal information about not only the current disease, but also other diseases with a genetic component. Disclosing individual results, beyond the primary purpose, is fraught with ethical and practical complexity. Policies and legislations differ between countries regarding disclosure of results, emphasis on respecting individual choices, and threshold for utility/validity of findings.

In accordance with the Declaration of Helsinki (1), UNESCO Universal Declaration on Bioethics and Human Rights (2), the WMA Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks (3), the CIOMS International Ethical Guidelines for Health-related Research Involving Humans (4), the Council of Europe's Convention on Human Rights and Biomedicine (the 'Oviedo Convention') (5) and Article 15 of the EU General Data Protection Regulation (GDPR) (6) a subject has the right to obtain access to any personal data, including genetic data, from the controller (EORTC). However, the "Right to respect for private life", according to the Article 10.1 of the Oviedo Convention need also to be respected. Finally, all communication should occur in the context of genetic counselling or at least explaining significance of results.

This document defines the policy of EORTC in regard to reporting genetic findings to the treating clinicians. The clinician will decide if and how to report those findings to the patient.

2 DEFINITIONS

- **Genetic testing:** Collective term for any analysis performed on human genetic material (DNA/RNA), including epigenetics.
- **Genetic data:** Personal data relating to the inherited or acquired genetic characteristics of a natural person which give unique information about the physiology or the health of that natural person and which result, in particular, from an analysis of a biological sample.
- **Genetic raw data:** Sequencing or molecular data that have not been processed to generate a comprehensive molecular report
- **Somatic:** Any molecular finding acquired during the life of a person or only discovered in cells of non-germline origin or which is not confirmed to be present in the germline, e.g. molecular features in tumor DNA.
- **Germline:** Any molecular finding confirmed to be present in the germline, i.e. hereditary.
- **Hereditary cancer mutations:** A germline mutation in a causative gene for a familial cancer syndrome, as defined by the American College of Medical Genetics and Genomics (ACMG) consortium (7, 8).
- **Genetic incidental finding:** A finding discovered in the course of research beyond the primary aim. This is an unanticipated, unsolicited finding. This refers here only to non-cancer related germline molecular features, as defined by the ACMG consortium (7, 8).
- **Biomarker-driven clinical trial:** A clinical trial where prospective determination of a molecular feature of the cancer is an integral part of the clinical trial. The molecular feature determines patient randomization or cohort allocation or serves as a stratification factor.

3 POLICY

The principles developed in this policy apply to all EORTC clinical studies and research projects, as well as intergroup studies, for which EORTC is the coordinating group. Patients enrolled in EORTC trials can at any point request to receive all molecular data arising from their samples, via their treating physician. This can be a comprehensive molecular report (and raw data if requested), if such report was generated in the scope of the study, or the genetic raw data only, in case no analysis was performed at the patient level.

The scope of this policy is limited to the communication between EORTC and the clinicians. EORTC does not communicate directly to patients nor interfere in the communication between clinicians and patients.

3.1 Hereditary cancer mutations or incidental findings

Hereditary cancer mutations or incidental findings (7, 8), if identified during the molecular analysis, will be communicated to the treating physician.

The physician should follow the applicable legislation and policy of their country (9, 10) for communication of genetic findings to patients. The treating physician shall decide whether to inform the patient (or his/her family, when applicable) taking into account the status of the patient (death, alive, life expectancy, health status), the scientific validity of the finding and the patient wish. Communication of these findings to patients should preferentially occur by/with presence of a genetic counsellor.

3.2 Genetic finding from a biomarker-driven trial or from a prospective research project

Prospective genetic testing as part of a biomarker-driven clinical trial is performed using validated assays (CE-IVD labelled where possible) by a central lab working with the required quality standards. All genetic results arising from such analysis will be returned to the treating physician, as given the prospective nature of the genetic testing, the genetic data produced may have medical relevance for the individual patients beyond the primary use (e.g. in case several actionable mutations are identified). If there is a risk of introducing bias in a study (assessed by the study team), those results may only be shared when the patient is no longer in the study (e.g. upon progression).

If the molecular analysis is not performed using a validated assay, the reporting of the molecular findings will be flagged as Research Use Only and should be validated by an orthogonal test by the treating physician, prior to patient treatment.

When possible, molecular tumor board (MTB) should be organized with expert clinicians to discuss the molecular findings and a possible impact on the patient treatment.

3.3 Genetic finding in the scope of future/further research

Retrospective genetic testing in the context of defined translational research or further (as not defined in the study protocol) research often occurs several years after the study start, and is often exploratory

and for research use only. Moreover, analyses are performed on aggregated data and can reveal new insights at a population level, but the usefulness at the patient level is difficult to predict.

Therefore, reporting of somatic genetic finding may not be performed based on data generated in the scope of future/further research.

4 REFERENCES

- 1- WMA Declaration of Helsinki - [https://www.who.int/bulletin/archives/79\(4\)373.pdf](https://www.who.int/bulletin/archives/79(4)373.pdf)
- 2- [Records of the General Conference, 33rd session, Paris, 3-21 October 2005, v. 1: Resolutions - UNESCO Digital Library](#) (page 80)
- 3- [WMA Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks – WMA – The World Medical Association](#)
- 4- [WEB-CIOMS-EthicalGuidelines.pdf](#)
- 5- [CETS 164 - Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine \(coe.int\)](#)
- 6- [Art. 15 GDPR – Right of access by the data subject | General Data Protection Regulation \(GDPR\) \(gdpr-info.eu\)](#)
- 7- Marilyn M. Li, Elizabeth Chao, Edward D. Esplin, David T. Miller, Katherine L. Nathanson, Sharon E. Plon, Maren T. Scheuner, and Douglas R. Stewart; ACMG Professional Practice and Guidelines Committee (2020). Points to consider for reporting of germline variation in patients undergoing tumor testing: a statement of the American College of Medical Genetics and Genomics (ACMG). <https://doi.org/10.1038/s41436-020-0783-8>
- 8- Kalia, S. S., Adelman, K., Bale, S. J., Chung, W. K., Eng, C., Evans, J. P., ... Miller, D. T. (2017). Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): A policy statement of the American College of Medical Genetics and Genomics. *Genetics in Medicine*, 19(2), 249–255. <https://doi.org/10.1038/gim.2016.190>
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5 DOCUMENT HISTORY

Version N°	Brief description of change	Author	Effective date
1.0	Initial release	Marie Morfouace	30 Jun 2021