EUnetHTA 21

Guidance Document

D7.1.3 – Process for handling commercially confidential data

Part of D7.1 – Guidance for the interaction between HTA and HTD

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Document history and contributors

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The work in EUnetHTA 21 is a collaborative effort. While the agencies in the Hands-on Group actively wrote the deliverable, the entire EUnetHTA 21 consortium was involved in its production throughout various stages. This means that the Committee for Scientific Consistency and Quality (CSCQ) reviewed and discussed several drafts of the deliverable prior to validation. Afterwards the Consortium Executive Board (CEB) endorsed the final deliverable prior to publication.

Associated HTAb & Stakeholders participating in public consultation

The draft deliverables of D7.1 were reviewed by associated HTAb and was open for public consultation between 20.07.2022 and 19.08.2022.

Associated HTA bodies who reviewed	Dachverband der Österreichischen Sozialversicherung, [DVSV], Austria Norwegian Institute of Public Health, [NIPH], Norway Evaluation and Planning Unit – Directorate of the Canary Islands Health Service, [SESCS], Spain Regione Emilia-Romagna, [RER], Italy Health Information and Quality Authority [HIQA], Ireland Finnish Medicines Agency [FIMEA], Finland
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List of abbreviations

ATMP	Advanced Therapy Medicinal Products
CEB	Consortium Executive Board
CHMP	Committee for Medicinal Products for Human Use
COI	Conflict of Interest
CSCQ	Committee for Scientific Consistency and Quality
ECA	EUnetHTA 21 confidentiality agreement
EUnetHTA 21	European Network of Health Technology Assessment 21
HaDEA	European Health and Digital Executive Agency
HOG	Hands on group
HTA	Health Technology Assessment
HTAb	Health Technology Assessment bodies
HTAR	EU HTA-Regulation
HTD	Health Technology Developer
INN	International Nonproprietary Name
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
MA	Marketing authorisation
SOP	Standard Operating Procedure

1 GENERAL PRINCIPLES AND PURPOSE

1.1 General principles

EUnetHTA 21 is committed to open, fair and transparent engagement with all stakeholders. This includes, on the one hand, making the widest possible range of information available to all stakeholders to support decision-making and, on the other hand, balancing the public interest against the commercial interests of individuals or companies. However, high degree of transparency is in the public interest on having access to the information on which reports and decisions are based.

EUnetHTA 21 assumes that only comprehensive unbiased information on the potential benefits and risks of specific interventions leads consequently to unbiased decisions in public health. This is one of the most important principles of medical ethics and respects the needs and right to information of patients and their doctors, research participants, clinical practice guideline development panels and health technology assessment bodies (HTAbs), research ethics committees and clinical researchers. This is supported by the definition of HTA in the HTAR Article 2 (5): "Health technology assessment' or 'HTA' means a multidisciplinary process that summarises information about the medical, patient and social aspects and the economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased and robust manner."

1.2 Purpose and Scope

This guidance addresses the procedure and principles for access to various information in the documents of the HTA processes and the handling of confidential information.

It relates primarily to information published in HTA documents. Any person involved in the preparation of HTA documents or having access to the information must sign a EUnetHTA 21 confidentiality agreement (ECA)[1]. This applies to staff of the HTAbs , regulatory authorities, involved clinical experts, patients or other experts. A separate confidentiality agreement between the HTD and HTAb is therefore redundant and not necessary. It should be noted that the institutions involved must comply with their national/European legislation regarding access to documents and protection of personal data[2]. This document only covers the part of confidentiality that deals with the publication of documents (such as the submission dossier, the JCA – report or comments received in a public consultation).

Although the project plan was to cover the handling of academic-in-confidence data in the deliverable, this type of confidential data was left out of this guideline. Apart from the fact that are not explicitly mentioned in the HTAR, we note that in May 2022 the International Committee of Medical Journal Editors (ICMJE) has extended their recommendations stating that:

[1] The EUnetHTA 21 Confidentiality Agreement (ECA) form can be found on the EUnetHTA 21 webpages: https://www.eunethta.eu/coic/.

[2] Directive 95/46/EC

- "The ICMJE does not consider results or data contained in assessment reports published by health technology assessment agencies, medical regulators, medical device regulators, or other regulatory agencies to be duplicate publication."

Therefore, it is no longer necessary to describe the handling of academic-in-confidence data for HTA production.

1.3 Relevant articles in Regulation (EU) 2021/2282

Articles from Regulation (EU) 2021/2282 directly relevant to the content of this practical guideline are:

- Recital 29: Transparency and public awareness of the process is essential. Where there is confidential data for commercial reasons, the reasons for confidentiality need to be clearly set out and justified and the confidential data well delimitated and protected.

- Recital 41: Joint clinical assessments and joint scientific consultations necessitate the sharing of confidential information between health technology developers and HTA authorities and bodies. In order to ensure the protection of such information, information provided to the Coordination Group in the framework of joint clinical assessments and joint scientific consultations should only be disclosed to a third party after a confidentiality agreement has been concluded.

- Article 11 (5) Assessment process for joint clinical assessments: *"The health technology developer shall also signal any information it considers to be confidential and justify its commercially sensitive nature."*

- Article 19 (3) Approval of joint scientific consultation outcome documents: "*The Coordination Group shall include anonymised, aggregated, non-confidential summary information on the joint scientific consultations, including on comments received during their preparation, in its annual reports and on the publicly accessible webpage of the IT platform referred to in Article 30(1), point (a)."*

- Article 28 (h, i) Commission support for the Coordination Group: "[…] the Commission shall: […]

  (h) facilitate the cooperation, in particular through the exchange of information, with the European Medicines Agency on the joint work referred to in this Regulation related to medicinal products, including the sharing of confidential information;

  (i) facilitate the cooperation, in particular through the exchange of information, with expert panels and the Medical Device Coordination Group on the joint work referred to in this Regulation related to medical devices and in vitro diagnostic medical devices, including the sharing of confidential information.

2 DEFINITION OF CONFIDENTIAL INFORMATION

Currently, there is no legal interpretation of the concept of "commercially confidential information" that has been universally adopted by all member states and stakeholders.

2.1 Commercial confidential information

Within the framework of the service contract, EUnetHTA 21 defines Commercial confidential information as follows[3]:
Commercial confidential information' shall mean any information submitted by the HTD which is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the HTD.

The following aspects will be considered as commercially confidential information:

- trade secrets[4] (including e.g. formulas, programs, process or information contained or embodied in a product, unpublished aspects of trade marks, patents etc)
- structures, chemical analytics
- development plans of a company for a medical product or device Contracting details
- pricing details (market share and coverage, volume projections, sales forecasts)

Transparent information and sharing data on methodology and on clinical data is in the public interest. Therefore, these data will be generally considered as non-confidential, with exceptions possible if they are identified in the procedure as confidential information (for example, information that - if made public- would prevent the unbiased conduct of clinical trials.).

2.2 Personal data

The present document does not provide any information on the handling of personal data[5]. This will be laid down elsewhere [LINK to GDPR guidance to be added later]. However, personal data must be protected and treated as confidential. As a general rule, "Personal data" will not be released and will be redacted before a document is made available. EUnetHTA 21's data policy will follow the rules the EMA outlined in their 0070 policy[6], regarding individual patient data. Neither individual patient level data, nor any information which may possibly result in the identification of individual patients will be provided by EUnetHTA 21. Only aggregated data will be presented in the reports. In conclusion, HTDs are advised that personal data (i.e.

[3] Definition on the basis of the EMA definition according to Policy/0070 EMA/144064/2019
[4] 2016/943/EU Directive on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure
[5] Reg EU 2016/679: means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person
[6] European Medicines Agency policy on publication of clinical data for medicinal products for human use, EMA 2019, online https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf

patient ID number, names, address) or person identifiable aspects are not included n. . EUnetHTA 21 citations will be GDPR compliant.

3 PRINCIPLES OF HANDLING CONFIDENTIAL DATA

In principle, confidential documents can occur in the different HTA procedures or at different steps within a procedure.

3.1 Joint Scientific Consultation (JSC)

All documents related to JSCs shall be generally treated as confidential in their entirety. In particular, this is mandatory prior to marketing authorisation. However, the documents will be shared with those involved in the specific JSC within EUnetHTA 21 and with the experts (e.g. HCP, patients) involved, as appropriate. All participants with access to the documents have signed an ECA.

Not to be released externally:

- The letter of intent and the application form (including dates, company, active substance, claimed indication and details of application).
- Briefing Book
- final recommendations*

* The Final recommendations from the JSC must be submitted in the underlying documentation of the subsequent JCA submission dossier by the HTD and will therefore be shared with the JCA assessor and co-assessor. Information from the recommendations that relate to methodological aspects of study design may be included in the final JCA report, if required. Joint Scientific consultations can be a source for updating or developing scientific guidelines on HTA evidence requirements, in particular, disease-specific guidelines. Therefore, information with no reference to a specific product may also be used in the development of guidelines.

Can be released externally:

In the EUnetHTA 21 monthly newsletter or at information events an overview on basic information on JSCs in general will be provided without reference to the individual application or specific JSCs. For example: the number of final JSC scheduled, number of applicants, the intended therapeutic areas (such as oncology, metabolic diseases etc.) or type of medicinal products (Orphan drugs, ATMP etc) or medical devices (MD) or in vitro diagnostics (IVDs).

3.1.1 Joint clinical assessments (JCA)

Information that is already in the public domain is not considered as commercially confidential.

Thus, for medicinal products a distinction must be made between pre-authorisation and post-authorisation confidentiality. Especially the wording of the indication or other information that is in the summary of product characteristics can only be released after marketing authorisation (MA).
In EUnetHTA 21, the project plan and timeline with definite dates for the final report will be published after the CHMP opinion.

For medical devices or in vitro diagnostics, the JCA process shall be in accordance with the timelines of the deliverable D4.7.2 - Framework for assessment of high risk MD and in vitro diagnostics" and considers the timelines and procedural steps of the MDR[7] and IVDR[8].

For medicinal products, MD and IVD

To support the production and transparency of the JCA, the assessor and co-assessor can cite and transcribeinformation on methods and clinical results from the entire submission dossier, including information from the Clinical Study Reports (including study protocols and statistical analysis plans), safety data or statistical analysis plan.

Transparent information, public awareness of the process and sharing data on methodology and on clinical data is in the public interest. Therefore, these data will be generally considered as non-confidential, with exceptions possible if they are identified in the procedure as confidential information (for example, clinical information that - if made public- would prevent the unbiased conduct of an ongoing clinical trial).

The Submission Dossier, excluding the underlying documentation, will be published (without redaction) on the EUnetHTA 21 website. Information on methodology and clinical data from the entire Submission Dossier (including underlying documentation) may be cited and transcribed for the JCA report and thus enter the public domain.

Where there is confidential data for commercial reasons, the reasons for confidentiality need to be clearly set out and justified. If the information needs to be redacted, EUnetHTA21 will state in its report that the HTD has stipulated that relevant data should be held in confidence for commercial reasons. (See section 4)

In case this information is submitted with the dossier of medicinal products, the following

a) will not be released externally:

- Information on the Quality and Manufacturing of medicinal product (except general information).
- Composition and product development (including detailed data concerning active substance, formulation, manufacturing, test procedures, assay information and validation)
- detailed descriptions of the manufacturing and control processes for the finished product, types of test methods used and the appropriateness of the specification, details of the validation of the manufacturing, degradation products, qualitative and quantitative information.
- Any confidentiality issue regarding novel packaging or aspects of the medical device that is used directly with the medicinal product) should be justified by the applicant, and will be assessed according to the above principles.

[7] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance)
https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745&from=FR

[8] Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (Text with EEA relevance)
https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0746&from=FR

- Contractual agreements.
- Formal advice documents (e.g., official meeting minutes, final written recommendation)

The underlying documentation included in the Submission Dossier will not be published as such, however, information on clinical or methodological aspects may be cited or transcribed in the JCA report.

b) Could be released externally (after MA is granted):

- Submission dossier (except the underlying documentation)
- Comment forms from the factual accuracy check by HTD including the answers from assessor/co-assessor and the completed checklist
- Information on the structure of the active substance (will be published at the time of allocating the INN).
- Non-Clinical and Clinical Information
    - Information encompassing non-clinical and clinical development of the medicinal product and the subsequent assessment (after authorisation, including information related to environmental risk assessments and risk management plans)
    - data included in clinical trial study reports (personal data should be protected).
    - Information on study designs, analytical methods, statistical analysis plan
    - the outcome of discussion at CSCQ JCA or other scientific groups (divergent opinions expressed within the CSCQ or CEB)
- Data inputs and outputs from any evidence synthesis process.
- List of references.
- Information on pre-clinical studies.

4 INFORMATION FOR THE HTD

The HTD shall signal any information it considers to be confidential and justify its commercially sensitive nature when they submit the submission dossier and during the factual accuracy check of the JCA report. The HTD must submit a written objection to the publication prior to the publication of the JCA within the deadline of the factual accuracy check . The comments will be discussed within EUnetHTA 21 (CSCQ - JCA, assessor and co- assessor). Although generally the information on methodological and clinical aspects should not be considered confidential, EUnetHTA 21 recognises that in exceptional circumstances this information could be subject to redaction prior to publication. Following scrutiny of the proposed redaction a decision is made by the relevant committee (CSCQ or CEB in EUnetHTA21, and under the HTAR it could be a Subgroup or the Coordination Group) as to whether the report should be published with redactions or whether the HTD should be contacted again by the Secretariat. In case of a differing opinion to the HTD's opinion, the HTD will be informed prior to publication for further justification and exchange, as to whether the definition of commercially confidential information applies.

Data on methodology or clinical trial results (including safety data) that are considered relevant to the evaluation are generally not considered commercially confidential; however, there are exceptional cases that trigger the process mentioned above.

5 CONSIDERATIONS FOR THE HTA REGULATION

The HTAR serves as the basis for this deliverable. Due to the general framework of EUnetHTA 21, the Guideline deviates in some steps from the processes defined in the HTAR or does not cover some aspects, in particular:

- the HTAR foresees different timelines for JCA than EUnetHTA 21 JCA (e.g. publication of a project plan after CHMP Opinion or expert opinion for MDs only in EUnetHTA 21). Therefore, the status of confidential information can change before and after Marketing authorisation.
- The MD – framework is not finalized in its details. More specifications can be considered for MD for JCA under the HTAR.
- A body or committee at the level of the JCA subgroup could be responsible for performing the distinction if a comment is factual accuracy check related or not and they could be involved in any issues related to confidentiality that are highlighted by the HTD during the factual accuracy check. Answers will be provided by the assessor/co-assessor on the relevant comments.

6 APPENDIX 1 – PUBLICALLY AVAILABLE INFORMATION FOR A JCA

Process step	Product		Shared with	Free to cite?	Redaction possible	Published by EUnetHTA 21
Topic selection	Letter of Intent (HTD) (EUnetHTA 21)		All EUnetHTA 21 partners.	Yes	No	No
Scoping phase	Project Plan; detailing the consolidated PICO and JCA publication timelines (EUnetHTA 21)		Draft version is shared with HOG, CSCQ and CEB	N/A	No	Yes, final version is published after CHMP opinion for MD, the timeline for publication of the project plan still needs to be defined.
Assessment phase	Submission dossier (HTD)	Submission Dossier	HOG, CSCQ and CEB	Yes	No	Yes, at the time of publication of the final JCA report (for medicinal products: after MA, for MD/ IVD: after CE marking)
		Attachments to the Sub-mission Dossier	HOG, CSCQ and CEB	Yes, exceptions apply	No	No, unless explicitly requested by the HTD
	JCA report and summary (EUnetHTA 21)		Draft versions are shared with the HOG, CSCQ and CEB, clinical experts and medical editor. Also the HTD will receive the final draft version for factual accuracy check	N/A	No	Yes, published for medicinal products: after EPAR publication, for MD/ IVD: after CE marking