EUnetHTA 21

Procedure Guidance

HANDLING DECLARATION OF INTEREST (DOI) AND EUNETHTA 21 CONFIDENTIALITY AGREEMENT (ECA) FORMS

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DOCUMENT HISTORY AND CONTRIBUTORS

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Disclaimer

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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 is 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.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF ABBREVIATIONS

CA	Collaborative Assessment
CHMP	Committee for Medicinal Products for Human Use
COI	Conflict of Interest
COIC	Conflict of Interest Committee
CSCQ	Committee for Scientific Consistency and Quality
DOI	Declaration of Interest
ECA	EUnetHTA Confidentiality Agreement
EUnetHTA 21	European Network of Health Technology Assessment
GDPR	General Data Protection Regulation
HCP	Health Care Professional
HTA	Health Technology Assessment
HTAR	HTA Regulation (EU) 2021/2282
HTD	Health Technology Developer
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
PM	Project Manager
SAWP	Scientific Advice Working Party

1 OBJECTIVE

A procedure guidance has been developed during *EUnetHTA Joint Action 3 (JA3)* for transparent description of *EUnetHTA's* processes in handling conflict of interest *(COI)* declared in the EUnetHTA Declaration of Interest (*DOI*) form. The earlier guidance was used throughout the production of assessment reports and Early Dialogues under JA3, although authoring teams experienced that it was challenging to identify clinical experts without a major conflict of interest, especially for (ultra-)rare diseases. Under EUnetHTA 21, its aim is to assist in decision-making on the involvement of individuals in the joint production of Joint Clinical Assessments (JCA), Collaborative Assessments (CA) and Joint Scientific Consultations (JSC) in terms of presence of conflicts based on the assessment of interests declared. This guidance has taken inspiration from the one developed and used in JA3 for JCA/CA and Early Dialogues with the addition of addressing the issue of the involvement of experts with COI in the framework of the evaluation of a technology indicated in rare disease.

This procedure equally applies for individuals representing HTA bodies participating in joint work (internal) and experts (external).

2 DEFINITIONS

Assessment team (JCA/CA) JSC team (JSC)	The individuals representing an HTA body participating in JCA/CA and JSC production. • For JCA/CA production, the Assessment team consists of Assessors and Co-assessors; • For JSC production, Assessor and Co-assessors and Participants are assigned to each JSC.
Conflict of Interest (COI)	A situation in which the interests of a participant to joint production are likely or be perceived, by their nature or intensity, to bring into question their independence or impartiality.
Conflict of Interest Committee (COIC)	The COIC is a neutral independent committee that reviews the DOI of all participants of JCA/CA and JSC to assess whether they have any conflict of interest. The COIC consists of minimum three members and has one Chair.
Declaration of Interest (DOI) form	DOI form for individuals engaging in EUnetHTA 21 activities to provide details on their affiliations, family members, financial interests for review by the COIC.
EUnetHTA Confidentiality Agreement (ECA) form	ECA form for individuals engaging in EUnetHTA 21 activities on agreeing on handling confidential information when carrying out joint production.
EUnetHTA 21 Secretariat	The EUnetHTA 21 Secretariat consists of the ZIN Secretariat as consortium lead, the ZIN JCA Secretariat and the G-BA JSC Secretariat.
Expert (external)	An individual who is not technical staff of an HTA body involved in the joint production, e.g. including but not limited to the following: health care professional (HCP), academics, epidemiologist, economist, patient, patient representative, consumers, citizens etc. Individuals involved on behalf of HTDs for the specific JCA/CA or JSC in these lines of expertise do not qualify as external experts.
JCA/CA Assessor / JSC Assessor	An individual representing an HTA body participating in a JCA/CA or JSC production and responsible for undertaking a single (or set of) task(s), and for the quality and timing of the task(s);
JCA Project Manager / JSC Project Manager	A JCA project manager is a person at the JCA Secretariat responsible for coordinating JCA or CA. A JSC Project Manager is a person at the JSC Secretariat responsible for coordinating JSC.
Joint production	Jointly produced JCA/CA, JSC, or other joint production, which require management of COI.

3 RESPONSIBILITIES

3.1 Responsibilities of any individual participating in JCA/CA or JSC production, including individuals representing HTA bodies participating in EUnetHTA 21 activities or experts (external)

- Filling out, signing and returning the DOI/ECA form to reflect his/her actual or past situation to the best of his/her knowledge and belief in its full completeness. The completed and digitally signed or a signed and scanned DOI/ECA form must be sent to the Project Manager within the timeline given (two weeks prior to the commencement of any specific task). Any individual not returning his/her DOI/ECA form on time cannot be involved in the task, until the DOI/ECA form has been subsequently submitted and evaluated. The DOI/ECA form should be completed in sufficient detail to enable the evaluation and the decision upon the inclusion or exclusion of the individual for the task. In case of clarifying questions from the Project Manager, the individual is required to provide requested information in the given timeframe if they would like to participate in the given task;
- Promptly notifying the Project Manager about any additional interests he/she acquires during the period of the joint production by completing a new DOI form detailing the changes;
- Update their DOI form at least once every 12 months as long as JCA/CA or JSC production is ongoing.

3.2 Responsibilities of the JCA / JSC Project Manager

- The JCA Project Manager responsible for coordinating JCA or CA. The JSC Project Manager is responsible for coordinating JSC;
- Defining the context of the task: the sources of the actual conflicts, based on the technology under assessment, potential comparator(s), or a relevant technology under development and indication(s) considered within a task. For joint work, the JCA / JSC Project Manager defines the context of the task based on the information provided by the applicant;
- Consulting EUnetHTA 21 Secretariat and the DOI database about the existence and/or status (valid (i.e. updated within the last 12 months) or not) of DOI forms, prior to requesting the individual to complete them (to avoid requesting individuals to complete the forms repeatedly);
- Providing the DOI/ECA forms to any individual invited to be involved in the task prior to commencement of any work in specific projects. The completed forms should be returned two weeks prior to the commencement of any specific task to the JCA/ JSC Project Manager, otherwise the individual cannot be involved in the task;
- Reviewing the DOI forms to evaluate if the information provided is complete (formal evaluation);

  Note: DOI form should be filled in with sufficient detail. At the Project Manager's discretion or upon request from the COIC, the individual may be contacted via the dedicated Project Manager in order to clarify missing or incorrect information. Clarifying information should be focused on the nature of the information provided to enable further evaluation of the presence of conflict of interest.
- Securing the collection of expert's background based on the information asked in the DOI form (i.e. expertise in the field related to the task, potential involvement in trials, any membership in associations, etc.). The Project Manager can perform complementary research on data provided by the expert in order to support the COIC in its interpretation of the expert's declared interests. Should the Project Manager find additional relevant information to that declared on the DOI form, this information may be used in the evaluation of the COIC;

  Note: The Project Manager does not have any responsibility if a potential COI is identified following the complementary research.
- Uploading the DOI/ECA forms (including related annex(es) and supporting documents if applicable) to the DOI database;

- Sharing the DOI forms (including related annex(es) and supporting documents if applicable) with the COIC for review, in case an interest is declared;
- Contacting the individual upon the COIC having follow up questions or an identified COI;
- Sharing the decision of the COIC with the JCA/CA Assessment Team, JSC Team member or expert in question.
- Deletion of DOI forms after the completion of one's involvement at the request of the person who does not wish to further participate in EUnetHTA 21 activities in the future . Although DOI forms are to be kept for the full duration of EUnetHTA 21, the timing of the deletion under the HTA R is to be decided.

3.3 Responsibilities of the COIC

- Evaluation of the presence of potential COI according to the procedure described in section "4. Evaluation" within 10 working days of receiving the DOI form in its full completeness. Based on the DOI form (including related annex and supporting documents if applicable) the COIC takes a decision on the inclusion or exclusion of an individual;

  Note: The evaluations will be conducted specifically for the task for which the individual has been requested to be involved. Thus, the decision of the COIC concerning the involvement of an individual is valid solely for the requested task.

- Sharing the decision together with a short summary of the analysis in writing with the dedicated Project Manager. In case of follow up questions or identified COI, the individual is then being contacted by the Project Manager.

3.4 Responsibilities of the EUnetHTA 21 Secretariat

- Creating and maintaining a database for the completed DOI/ECA forms including an overview of the interest that has been declared and a summary of the COIC analysis for the individual. This database is only accessible to a limited number of individuals within EUnetHTA 21 (see https://eunethta.eu/doi/);
- Informing the relevant individual one month prior to the expiration date of the DOI form to update his/her DOI form, in case the replace assessment by production is still ongoing. The DOI form is valid for 1 year based on the signature date of the individual.

4 EVALUATION

In order to reduce the administrative workload of engaging in EUnetHTA activities at the start of EUnetHTA 21 operations, consortium partners will only be required to provide DOI/ECA forms prior to any engagement in a JCA/CA or JSC production activities. The COIC will evaluate these forms taking into account the rules necessary for all. For other activities than JCA/CA or JSC production, it is assumed that all individuals engaged on a specific dossier have explicitly declared any potential COI to the respective consortium partner employing them, regardless of the actual employment status (i.e. full-time employee or subcontractor).

The COIC evaluates the presence of any potential COI declared in the DOI form to decide upon the inclusion or exclusion of an individual with regard to the task. The COIC takes responsibility for ensuring that the DOI procedure is properly followed and implemented. In case of potential interests that were not declared by the individual, but become visible during the evaluation process, the respective individual cannot participate in the given task. When there is a later identified COI, in case there is a participant with the same role, this participant could review the contribution from the individual with the COI and check its validity. For transparency, the contribution of the expert with COI should be stated clearly in the final joint production with detailed information on their input to ensure that those who later read the evaluation are able to do so in light of this information.

To ensure that the data collected through DOI and ECA forms are handled in a lawful manner, compliance to General Data Protection Regulation (GDPR) (1) is essential. Data providers are informed upon their rights and asked to express their explicit consent to that the data holder, Zorginstituut Nederland as part of EUnetHTA 21 handling their data throughout the COI assessment according to the

terms of use (see https://www.eunethta.eu/terms-of-use/). The data provided by filling out these forms are therefore handled under Article 6 (1) (a) and has the rights under Articles 15-21 of the GDPR (1). Individuals need to express their explicit consent to Zorginstituut Nederland as part of EUnetHTA 21 handling their data for the purposes of COI assessment; otherwise, the individual cannot be involved in the task.

Upon uploading the data collected through DOI forms to the DOI Database, the provided data will also be made available for all members of EUnetHTA 21 consortium, in order to enable partners that have HTA implementing authority, for the purpose of reviewing the provided information against national provisions that need to be taken into consideration additionally to the guidelines and assessment of the EUnetHTA 21 COIC. Findings by these partners must be shared with the EUnetHTA 21 COIC by a fixed deadline to be included in the deliberations of the EUnetHTA 21 COIC.

The decision on the inclusion or exclusion of an individual for the task is taken by the COIC following the evaluation. The COIC consists of the EUnetHTA 21 Secretariat, one representative of the JCA/CA Secretariat, one representative of the JSC Secretariat, and the chair of the COIC. COIC members themselves should not be directly involved in the specific task, but a member can assess other individual participants even in activities where their own organisation participates. The representatives of the JCA/CA Secretariat or JSC Secretariat may consult the assessment team prior to the decision.

In total, there are three votes (JCA/CA Secretariat, JSC Secretariat and the chair of the COIC) and a decision is made by a majority vote.

A potential COI occurs when an individual provides at least one statement other than ‘no’ as an answer to the questions from 2.1-3. (Employment with a company/institution; Consultancy; Strategic Advisory Role) in the DOI form. Also the section 1.1. (Current activities) is critically checked as this might give rise to potential conflicts of interest.

Once a potential COI is found, the COIC has to assess whether this is considered a major COI and could lead to exclusion of the individual from the task.

4.1 Major conflict

The following actual or past situations lead to the exclusion of the individual from the task (there may be exceptions):

1. Principal investigator of a study, or contributing considerably to the design of a study (industry-sponsored) which is aimed at evaluating the technology under assessment, a comparator, or a relevant technology under development;

   Note: For JCA/CA production, this relates to studies that are included, especially in either the effectiveness or safety domain of the assessment.

2. Provision of paid or unpaid advisory or consultancy services within the last 3 years (e.g., participation on an industry-sponsored board (i.e. advisory or other)) related to the technology under assessment, a comparator, or a relevant technology under development;

3. Employment at a company producing the technology under assessment, a comparator, or a relevant technology under development within the last 3 years; employment at a consultancy or contract research organisation providing services related to the technology under assessment, a comparator, or a relevant technology under development; or employment by relevant lobby group within the last 3 years;

4. Being current member of an association (patient or HCP or technological/ methodological organization (i.e., association)) funded mainly by the industry (>40 % of association budget);

5. Currently receiving funds for research activities related specifically to the technology under assessment, a comparator, or a relevant technology under development;

   Note: Funds may come from companies or from relevant lobby groups and can include research group/laboratories funded by industry or relevant lobby groups.

6. Having a current financial interest, or had a financial interest within the last 3 years (e.g. ownership by holding shares, stocks or the like) in the company producing the technology under assessment, a potential comparator, or a relevant technology under development or a financial interest in industrial sector funds;

7. Covering/subsidising travel costs including feewaivers or paying a honorarium (two or more by the same company within the last 3 years), for delivering a presentation on a topic specific to the technology under assessment, a comparator, a relevant technology under development (e.g. targeting same indication) or for attending conferences/meetings sponsored by only one company producing either the technology under assessment, a comparator, or a relevant technology under development;
8. Being an active participant (e.g. clinical expert, rapporteur or co-rapporteur) in Scientific Advice Working Party (SAWP); or Committee for Medicinal Products for Human Use (CHMP) or other committees of the European Medicines Agency and in the Assessment teams at the same time for the same product in the same indication.

This list is not exhaustive and does not prevent consideration of other potential conflicts of interest. Interests related to family and household members will be assessed on a case-by-case basis using the same time frame as specified in the DOI form.

4.2 Exceptional circumstances

Under exceptional circumstances (e.g., lack of available experts without COI for a rare/ultra- rare disease), EUnetHTA 21 may still seek the expert opinion of an individual with an existing COI if this expert has unique skills and no other expert (with at least the same level of competency and without COI) can be identified, despite having contacted multiple experts. Although a COI either way, it should be evaluated if the COI is balanced between a number of companies/institutions and whether it is product-specific. The Assessment team should be informed that the expert involved in the procedure has links to the industry and that is within the framework of an exception to the COI rules. In cases where the COI is directly linked to a competitor, the expert shall not have access to any document requiring confidentiality and should only give advice on a predefined set of questions posed by the Assessment team.

The exceptional circumstances and the reasons for the decision should be well documented by COIC and communicated in detail to the Project Manager, HOG of the JCA or JSC, Committee for Scientific Consistency and Quality (CSCQ) and Consortium Executive Board (CEB). The exceptional circumstances and the reasons for decision should be also documented in the JCA/CA or JSC reports, with the respective individual agreeing to this information to be included. If the individual does not agree to the inclusion of this information, he/she will not be able to participate in JCA/CA or JSC production. For transparency, the contribution of the expert with COI should be stated clearly in the final joint production with detailed information on their input to ensure that those who later read the evaluation are able to do so in light of this information.

All decisions of involving a clinical expert in JCA/CA or JSC production are made on a case-by-case basis and depend on the exact context of the assessment.

4.3 Considerations related to the regulation on HTA

4.3.1 Publication of the DOI form

The HTA Regulation (HTAR) (2) generally states that information on COI need to be made publicly available. However, at this current stage and under the limitation of the service contract the Secretariat cannot publish the DOI forms on the EUnetHTA 21 consortium website. Notwithstanding and in order to enable consortium members to prepare for the implementation of the HTAR and carry out necessary legal updates to the contracts of experts engaging in JCA/CA or JSC production, this guidance, the common practice from the EMA (3) as well as the European Commission (4) will be taken into account to prepare the implementation of the HTAR at a later stage.

4.3.2 Selection of assessor and co-assessor

The HTAR also expects the assessor and co-assessor to be different to those who participated in the JSC on behalf of the Coordination Group. However, for JCA/CA production under EUnetHTA 21, if the necessary specific expertise is otherwise not available, the same assessor or co-assessor, or both, involved in the JSC may be appointed. The detailed criteria for selecting the assessor and co-assessor

will be described in a separate guidance titled Procedural Guidelines for appointing assessors and co-assessors.

Although this procedure aims to provide a comprehensive framework to COI assessment, the further development of the current guidance should enable capturing the relevant experience of agencies of the European Union. The possibility of updates to reflect the adaptation of procedure would also help ensuring the inclusiveness in the EUnetHTA 21 activities while increasing the quality of the guidance.

5 UNDERLYING DOCUMENTS

The preparation of this procedure involved the following main documents:

- EUnetHTA JA2 Declaration of Interest and Confidentiality Understating-FINAL - STATEMENT ON TERMS OF PARTICIPATION AND EXTERNAL ACTIVITIES OF EXPERTS (potential conflict of interest and confidentiality undertaking), 20140502 (as endorsed by Plenary Assembly, Madrid, 2014.04.10);
- EUnetHTA Standard Operating Procedures (SOP) Manual, EUnetHTA Joint Action2; 2012-15; Developed by the EUnetHTA Secretariat July 2013; Amended and approved April 2014;
- EUnetHTA Procedure Guidance for handling Declaration of Interest (DOI) and EUnetHTA Confidentiality Agreement (ECA) forms, version 1.2, EUnetHTA Joint Action 3. Amended and approved May 2021;
- Guidelines on the prevention and management of conflicts of interest in EU decentralised agencies, 10 December 2013;
- The European Medicines Agency Code of Conduct, EMA/385894/2012, 16 June 2016. Available at: https://www.ema.europa.eu/en/documents/other/european-medicines-agency-code-conduct_en.pdf

6 REFERENCES

1. Regulation (EU) 2016/679 (General Data Protection Regulation) [Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679.
2. Regulation (EU) 2021/2282 (Health Technology Assessment) [Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32021R2282.
3. Agency; EM. Policy on the handling of competing interests of scientific committees' members and experts. POLICY/0044. [Available from: https://www.ema.europa.eu/en/documents/other/policy-44-european-medicines-agency-policy-handling-competing-interests-scientific-committees_en-0.pdf
4. Commission Notice Guidance on the avoidance and management of conflicts of interest under the Financial Regulation 2021/C 121/01. [Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv%3AOJ.C_.2021.121.01.0001.01.ENG.

7 APPENDIX

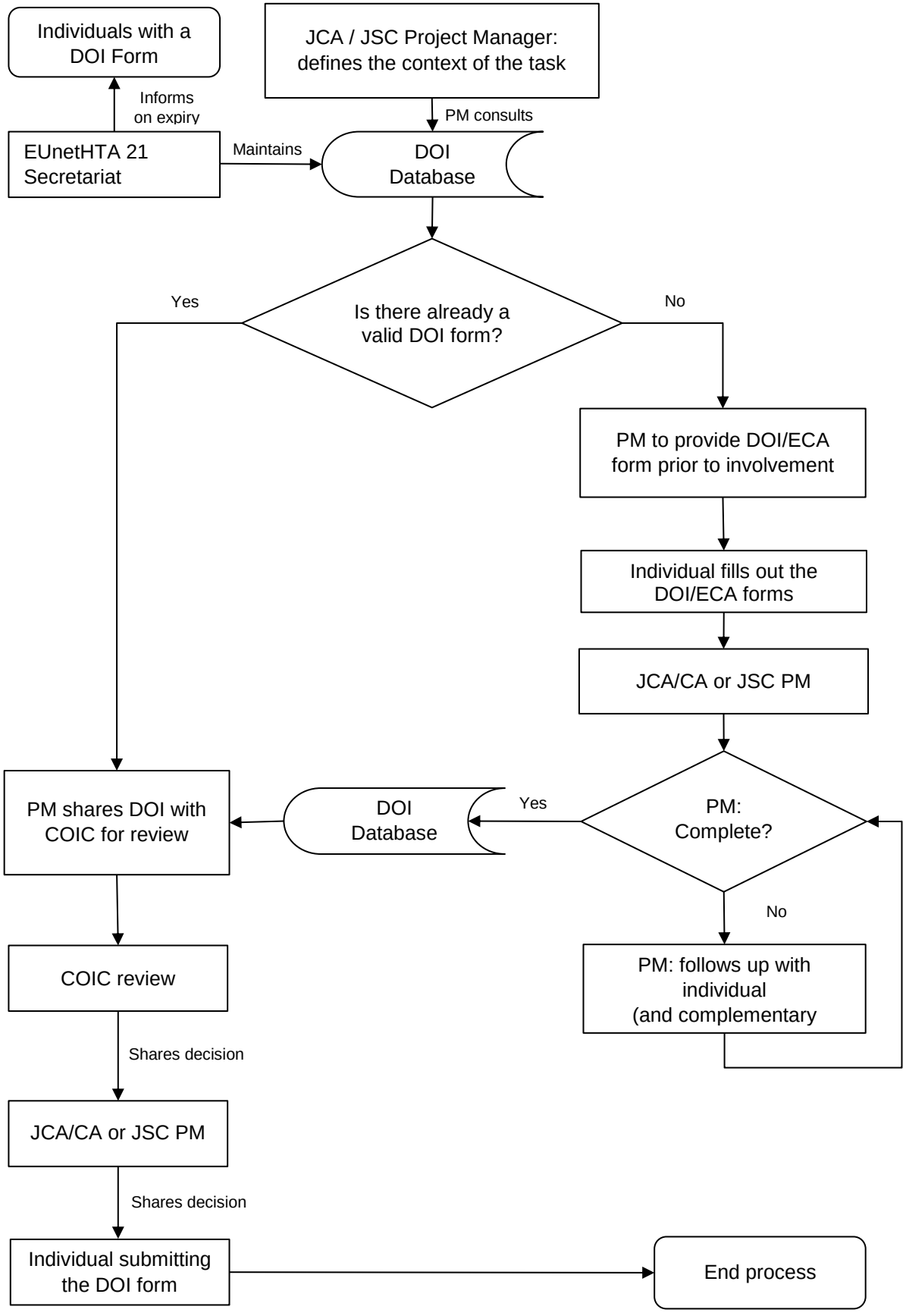

Figure A 1: Process for DOI collection and review