



EUROPEAN
HEMATOLOGY
ASSOCIATION



EHA GUIDELINES METHODOLOGY FOR DIAGNOSIS AND THERAPY OF BLOOD DISORDERS

Formats for EHA guidance documents:

- ⊙ Evidence based guidelines
- ⊙ Consensus based recommendations

EVIDENCE BASED GUIDELINES

Aim of the project

The aim of this project is to develop evidence-based guidelines providing clinical practice recommendations that can support the appropriate choice of diagnostic procedures and/or therapeutic interventions in the field of hematology.

Design and Methods

The development of the guidelines is a multistep process, consisting in:

1. **Appointment of the Chair(s) and selection of a Steering Committee;**
2. **Selection of an Expert Panel;**
3. **Handling of Conflicts of Interest**
4. **Generation of key questions and list of indications;**
5. **Systematic review of the literature and synthesis of evidence;**
6. **Consensus phase;**
7. **Formulation of recommendations.**

1. Appointment of the Chair(s) and selection of a Steering Committee

The Chair(s) of the project will be appointed by the EHA Guidelines Committee (EHA-GC) and jointly with partner Scientific Societies / Networks in cooperative initiatives. Then, the Chair(s) of the Project will select a Steering Committee (3-4 members), which will be responsible for development of guidelines. Disclosure of potential conflicts of interest will be required and reviewed by the Guidelines Committee before these will be officially appointed.

In cooperative initiatives, the Chairs will agree on the general objective(s) of the project, the methodology and the conflict of interest policy to adopt. The selected methodology is expected to adhere in its principles to the operational procedures included in this working document.

2. Selection of an Expert Panel

An Expert Panel will be selected by the Steering Committee, comprising members experienced in the area under consideration and active in both clinical care and research, taking into account geographical representation and specific areas of expertise. Disclosure of potential conflicts of interest will be required to the Members of the Panel and reviewed by the EHA-GC. The Expert Panel will be responsible for the detailed definition of the aim of the project and generation of the key clinical questions, the synthesis of the scientific evidence, and the formulation of recommendations. For definition of objectives and final review, the Expert Panel will incorporate whenever possible, patient representatives of the corresponding disease area.

3. Handling of Conflict-of-Interest

The Steering Committee and the Expert Panel and all potential experts involved are required to identify any financial interests or affiliations with mentioned institutions, organizations, or companies and also any competing interest that could be perceived as a bias in the work. A conflict of interest can be financial or be a personal competing interest.

Before the official appointment, the Chair(s), the Steering Committee, the Expert Panel and all potential experts involved are obliged to disclose an actual, potential or perceived conflict of interest regarding their relations with pharmaceutical industry and medical professional organizations, as well as their involvement in developing guidelines in other projects.

If there is a reasonable perception of a conflict of interest during the execution of the project, the member involved will provide information about the interest and how it may conflict with his/her member role: if the member, the Steering Committee or the Guidelines committee consider it impossible to resolve the conflict, the member will resign. The EHA Good Governance Committee will resolve any dispute regarding the exclusion of members in relation to conflict of interest.

4. Definition of the objective of the project and generation of the key clinical questions

A first panel meeting/teleconference will be organized with the aim of defining the objectives of the project and to formulate a list of key clinical questions addressing appropriate diagnostic procedures and therapeutic strategies, candidate patient sub-groups and risks deriving from the therapy. Questions will be rank-ordered and selected using the criterion of clinical relevance, and the set of questions of the project will be defined.

5. Systematic review of the literature and synthesis of evidence

Each member of the Expert Panel will be assigned a specific issue, based on the previously defined set of key clinical questions and according to the member's specific field of interest. Each member will be invited to perform a review of the literature on the assigned issue and to compile a summary of the available evidence relevant to the key clinical question under consideration. A dedicated staff with access to literature sources and expertise in the appraisal of scientific evidence will support the panelists in the selection, collection and review of the articles of interest.

The search of the literature will be performed according to the following criteria (plus additional criteria specific to the topic under consideration):

- English language;
- Year of publication: cover the past 20 years- longer periods may be warranted in certain fields;
- Studies including 10 target patients or more; in the setting of (ultra-) rare diseases important studies with fewer patients can be included;
- Source: PubMed, proceedings of EHA, ASH meetings;
An evidence table will then be compiled presenting summaries of the studies relevant to each of the key clinical questions addressed by the guideline, and the level of evidence will be rated according to the GRADE (Grades of Recommendation Assessment, Development and Evaluation) (www.gradeworkinggroup.org/) or SIGN (Scottish Intercollegiate Guidelines Network) (www.sign.ac.uk) or equivalent system. Briefly, the quality of evidence for each main outcome is determined according to study design, study quality, consistency, and directness, and ranked accordingly.

6. Consensus phase

The members of the Expert Panel will formulate in an independent manner evidence-based statements that address the key questions. One/two consensus meetings will be held to achieve a consensus for all of the statements produced. Delphi questionnaire and nominal group techniques can be used for exploiting this phase of the process.

A scenario analysis might be performed if needed to reach a consensus on the indication of a certain treatment or procedure in selected cases (i.e. clinical scenario). To address this, a series of clinical scenarios may be defined based on the parameters relevant to therapy choice. For each clinical scenario the members of the Expert Panel will be asked to grade the appropriateness of performing a certain procedure or providing a certain treatment. Then, an analysis of the panelists' scores may be carried out (median, dispersion of ratings) with the aim of defining level of agreement (agreement, indeterminate, disagreement), and appropriateness rating (appropriate, uncertain, inappropriate).

7. Formulation and grading of recommendations

Final recommendations will be formulated and graded according to GRADE criteria (or equivalent) for rating strength of recommendations.

CONSENSUS-BASED RECOMMENDATIONS

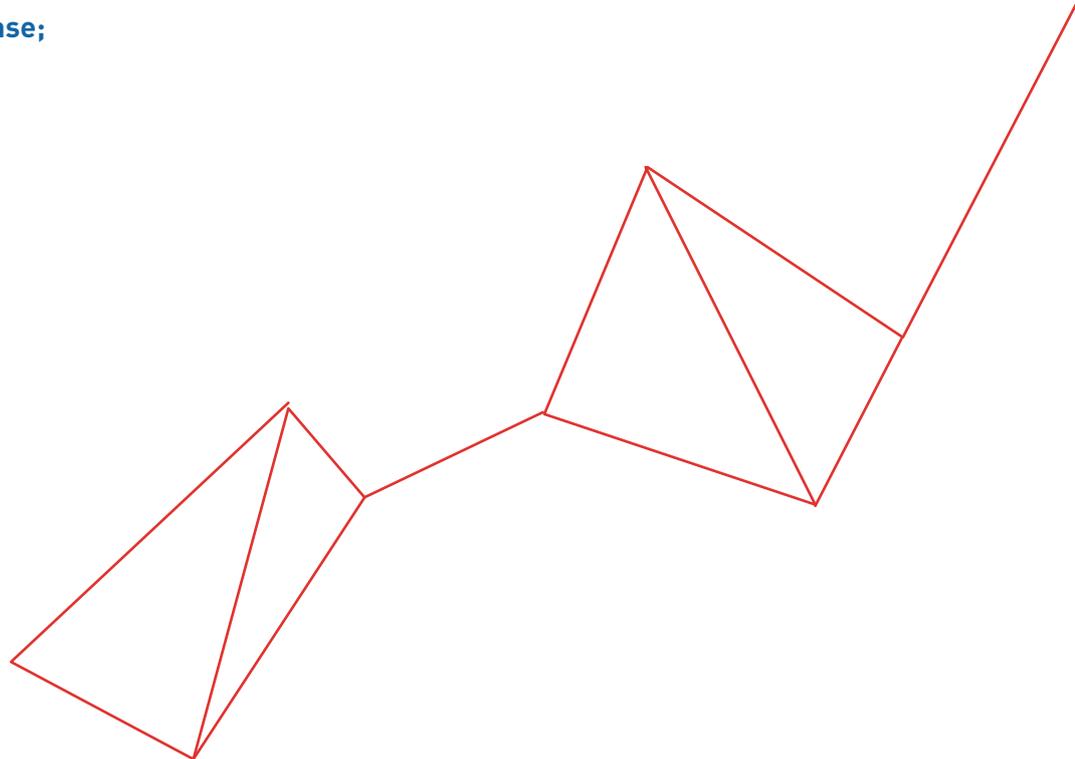
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Design and Methods

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2. Selection of an Expert Panel
3. Handling Conflict-of-Interest
4. Generation of key questions and list of indications;
5. Consensus phase;



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The Expert Panel will be responsible for the detailed definition of the aim of the project, the generation of the key clinical questions and the formulation of recommendations. For definition of objectives and final review, the Expert Panel will incorporate whenever possible, patient representatives of the corresponding disease area.

3. Handling of Conflict-of-Interest

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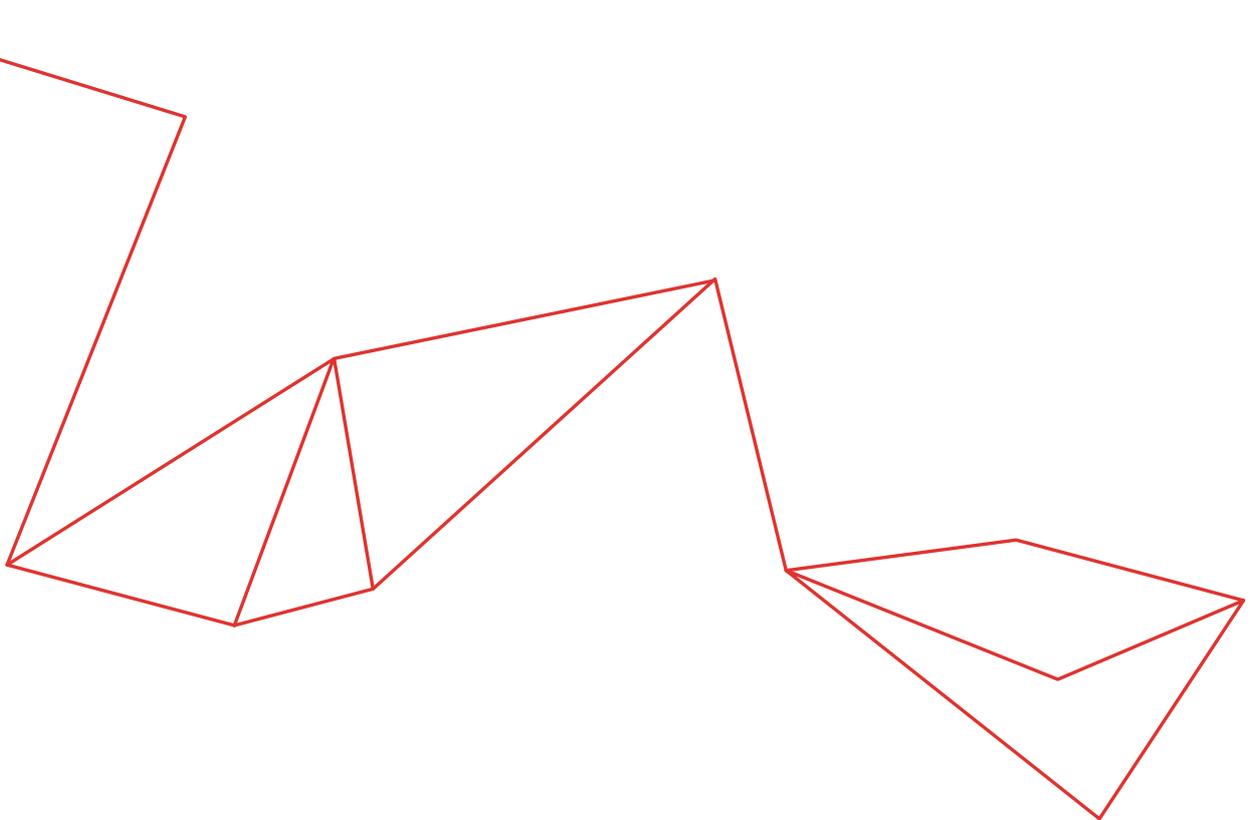
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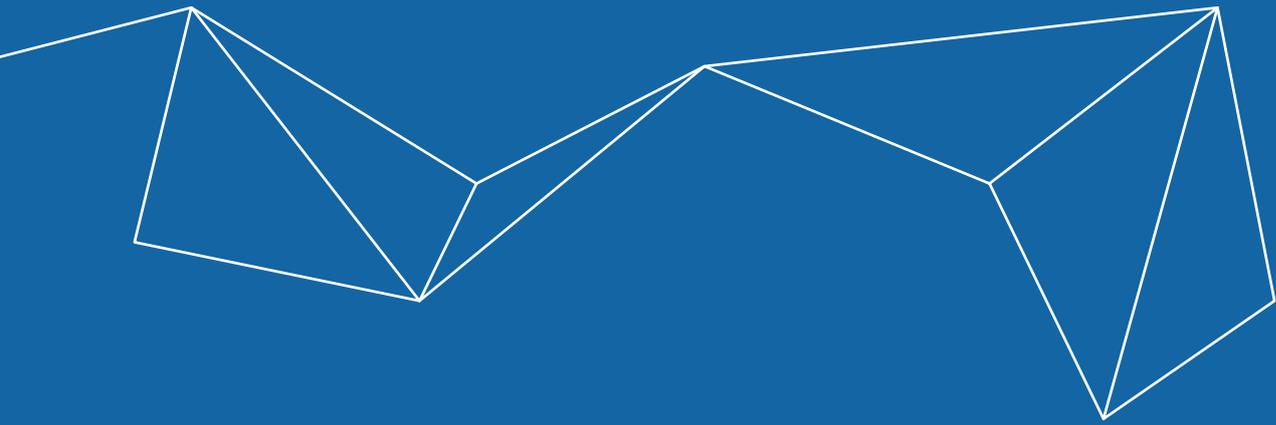
5. Consensus phase

The members of the Expert Panel will formulate independent statements that address the key questions based on their knowledge and experience. One/two consensus meetings may be held to achieve a consensus for all of the statements produced. Delphi questionnaire and nominal group techniques may be used for exploiting this phase of the process. A scenario analysis might be performed if needed to reach a consensus on the indication of a certain treatment or procedure in selected cases (i.e. clinical scenario). Then, an analysis of the panelists' scores may be carried out (median, dispersion of ratings) with the aim at defining level of agreement (agreement, indeterminate, disagreement), and appropriateness rating (appropriate, uncertain, inappropriate).





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