CUBE GUIDELINES

SIE Guidelines Methodology Manual

Version 1.1 – January 2015

Sommario

1 – Mission and core principles

1.1.Premise

The development and updating of high-quality practice guidelines require substantial resources, and most organisations are under pressure to produce more guidelines in a shorter time with increasingly limited resources.
Moreover, despite evidence that routine application of clinical practice guidelines effectively improves the quality of health-care, utilization of guidelines is scarce due to several reasons such as the format (length and textual versus graphical/interactive presentation, portability), clearity, ambiguity, comprehensiveness, regular updating, inconsistency with other guidelines, availability of tools (checklists, calculators, patient information material) for the clinical practice.

1.2 Objectives

The new SIE guideline project has a doublefold aim:

- to provide regularly updated high-quality guidelines taking advantage of existing high quality international guidelines
- to enhance the efficient use of high-quality guidelines through innovative dissemination tools

1.3 Core principles

The core methodologies on which the new guidelines project will be based are ADAPTE and GRADE.
Both the methods are based on the PICOT paradigm. PICOT stays for *Patient, Intervention, Comparator, Outcome, and Time*. PICOT is the format a clinical question needs to have in order to make it answerable with evidence-based methods
More specifically according to ADAPTE, the harmonization process of existing guidelines will be based on the following core principles:

- Respect for the evidence-based principles of guideline development
- Reliable and consistent methods to ensure the quality of the adapted guideline
- Participative approach, involving all key stakeholders, to foster acceptance and ownership of the adapted guideline
- Explicit consideration of context during adaptation to ensure relevance for local practice
- Transparent reporting to promote confidence in the recommendations of the adapted guideline
- Accountability to the primary guideline sources

As endorsed by the international GRADE working group, the classification of practice recommendations is defined as strong (Grade 1) or weak (Grade 2), according to the balance between benefits, risks, burden, and cost, and the degree of confidence in estimates of benefits, risks, and burden. The system classifies quality of evidence (as reflected in confidence in estimates

of effects) as high (Grade A), moderate (Grade B), or low (Grade C) according to factors that include the risk of bias, precision of estimates, the consistency of the results, and the directness of the evidence.

In order to enhance the implementation of the best available clinical evidence SIE aims at providing Italian hematologists with “portable”, “ interactive” and comprehensive high quality guidelines. Since guidelines retain a relevant legal and economic value, SIE also aims at providing stakeholders and judges with appropriate tools for judging appropriate vs inappropriate practice and for approval/funding priorization.
The project has been named “CUBE”, just to remind the multiple facets of the planned guidelines.

2 – Actors

2-1 General organization

The Task Force devoted to Guidelines includes a Strategic Committee, a Methodology Committee and a Scientific Committee. An Extended Committee provide the Task Force feedback and allows validation of guidelines.

2-2 Strategic Committee

2-2-1 Members

It includes SIE President plus four members selected by the President himself among past-presidents and senior leaders of national and international research networks.

2-2-2 Duties

The strategic committee is responsible for:

a) Selecting members of the area-specific Scientific Committee

b) Selecting the leaders of the Methodology Committee

c) Supervising on Conflict of Interest

d) Keeping relationships with SIE

e) Planning guidelines updates

2-3 Methodology Committee

2-3-1 Members

The Methodology Committee is composed by experts in the field of clinical methodology. The committee may comprise up to 10 members and is organized into two Methodology Working Groups (MWG), each with a leader and members selected by the leader: West MWG and East MWG.

2-3-2 Duties

The Methodology Committee is in charge of:

a) Educating members of the Scientific Committees

b) Coordinating topic/issue selection

c) Conducting guidelines retrieval and critical appraisal

d) Elaborating tabular and algorithmic representation of guideline content

e) Coordinating guideline harmonization

f) Formulating PICOTs for orphan areas

g) Revise literature GRADE

h) Yearly literature scan

2-4 Working Groups

2-4-1 Members

The Area-Specific Working Groups comprises experts in specific areas of the hematology. Each Area-specific Working Group is coordinated by a member designed by the Steering Committee and is committed to:

a) Selecting of domains of each guidelines

b) Priorizing of issues

c) Identifying the aims of each guidelines

d) Selecting the Critical Outcomes for each PICOT

e) Validating PICOT-based recommendations

f) Validating recommendation algorithm derived from harmonization of guidelines

g) Driving national peer-review (Extended Committee)

h) Implementing legal and economic aspects of the guidelines

i) Writing textual items for Web and paper editing

j) Annual updating based on peer-review

2-4 Extended Committee

The Extended Committee is composed by 5 SIE members elected by the Working group members of each Area.

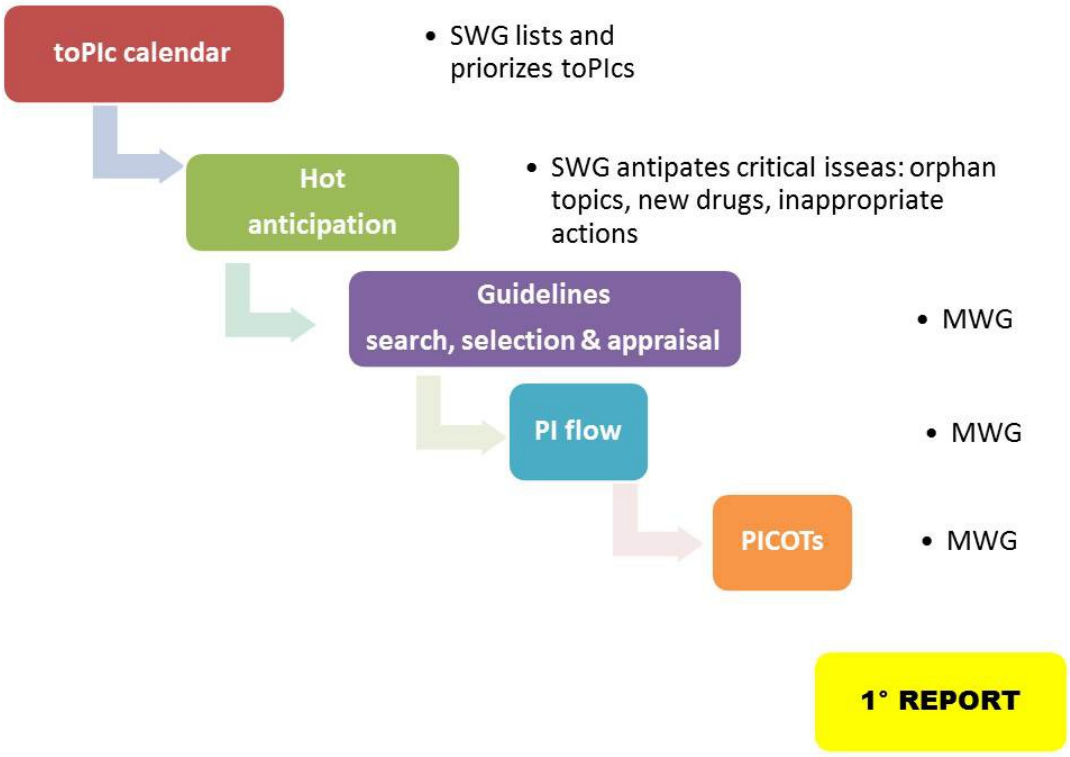
They are in charge of:

- Validation of the whole guideline
- Final approval in case of lack of concordance in the Working group members

3 – The Process

The whole guideline elaboration process was designed according to GRADE and ADAPTE standards.

The starting phase for the preparation of each guideline follows the flow chart depicted below:.



Where:
SWG = Scientific Working Group.
MWG stays for Methodology Working Group.
toPIc = each topic identifies a population (i.e. naïve patients with FCL) and a class of interventions (i.e. treatment)

The detailed process that will be adopted will implies the following steps:

- Identification and development of each single PI (Population and class of intervention)
-

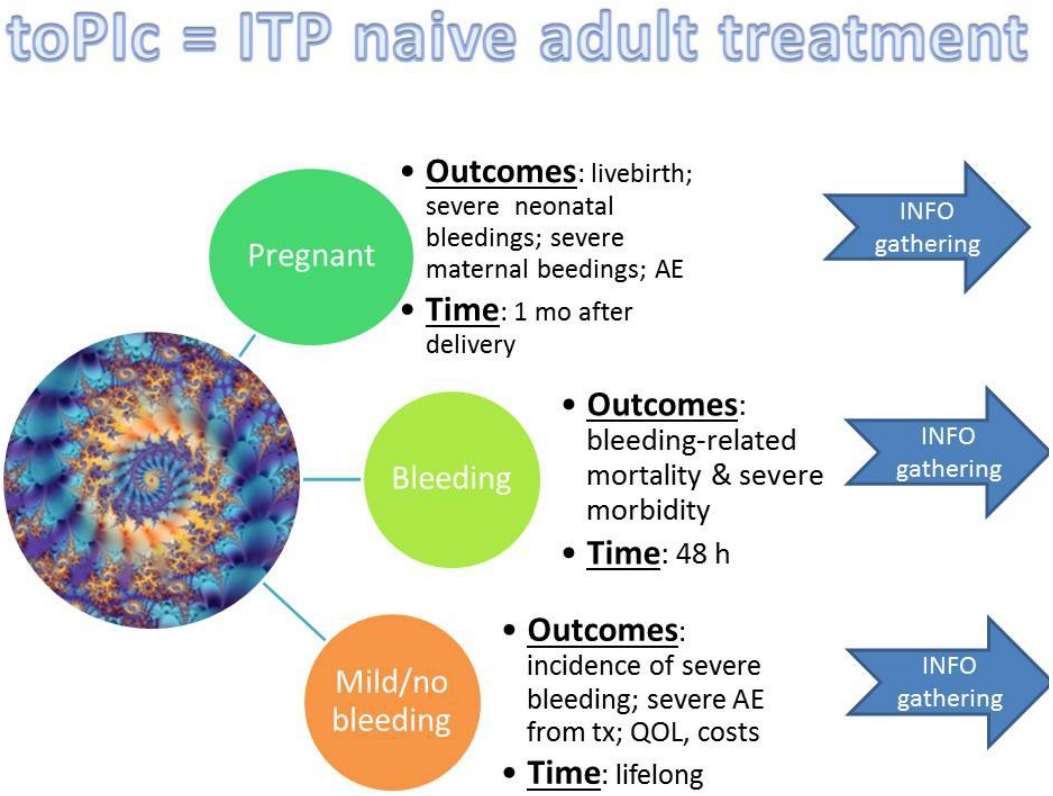


Figure 3 – Details of the process from PI flow to PICOT elaboration.

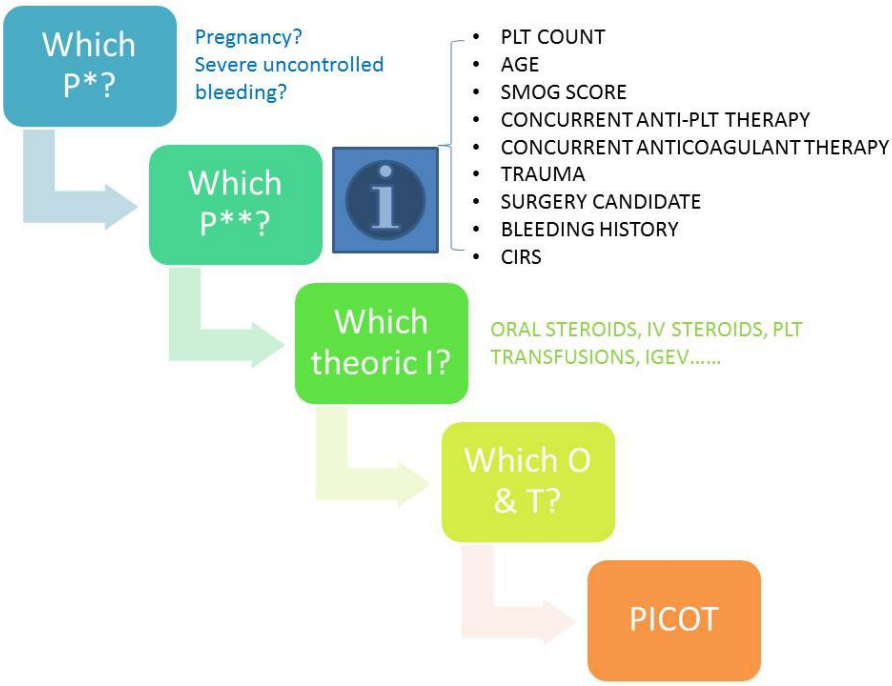


Figure 4 – Final results of guideline retrieval. Recommendations derived from selected guidelines are compared for each PICOT.,

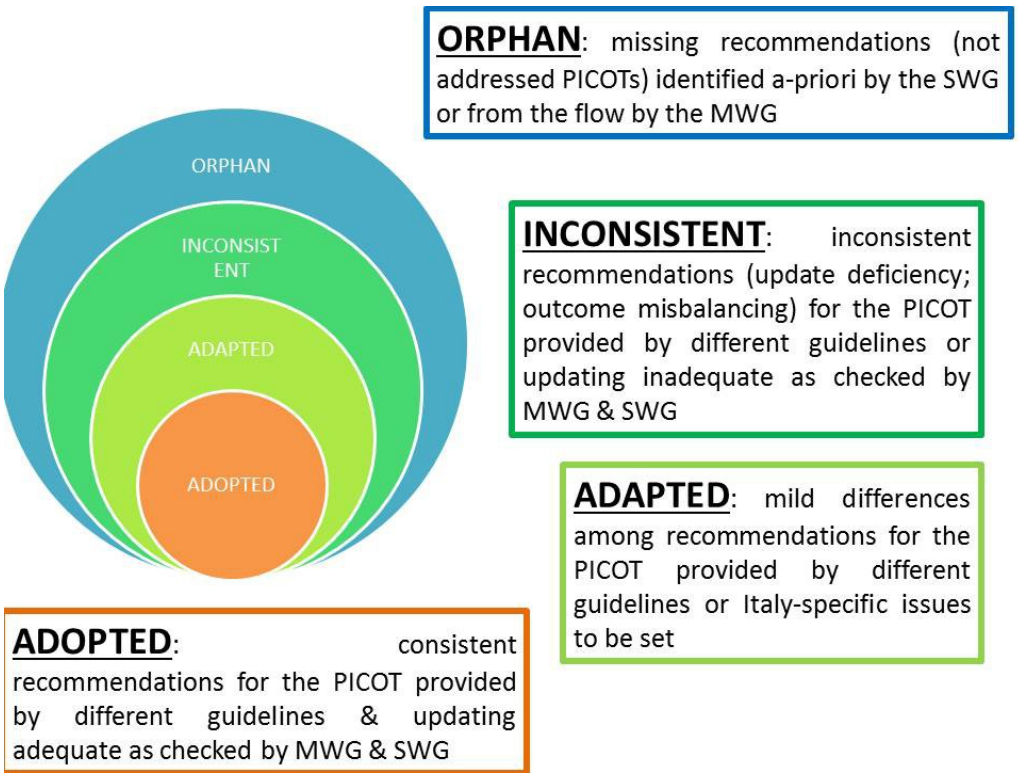


Figure 5 – Harmonization final phase : management of AAIO recommendations derived from retrieved guidelines.

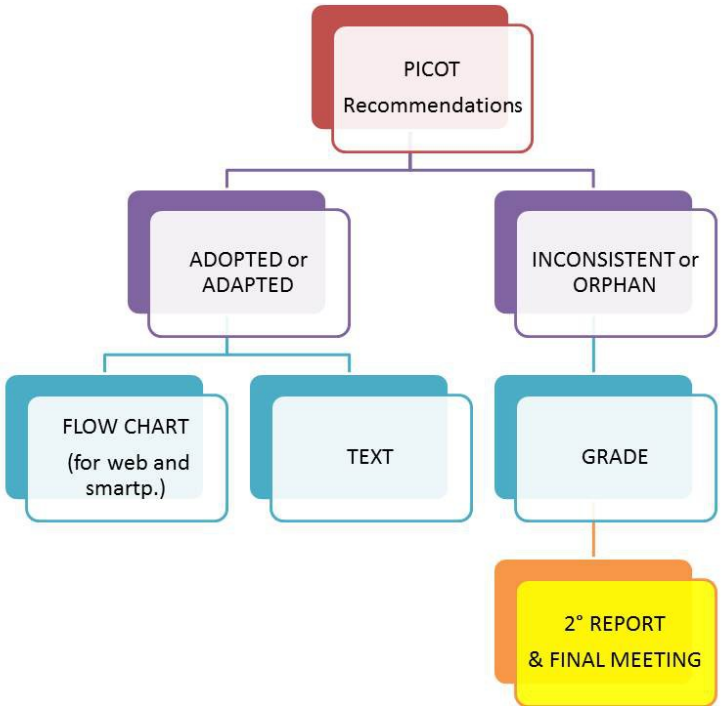
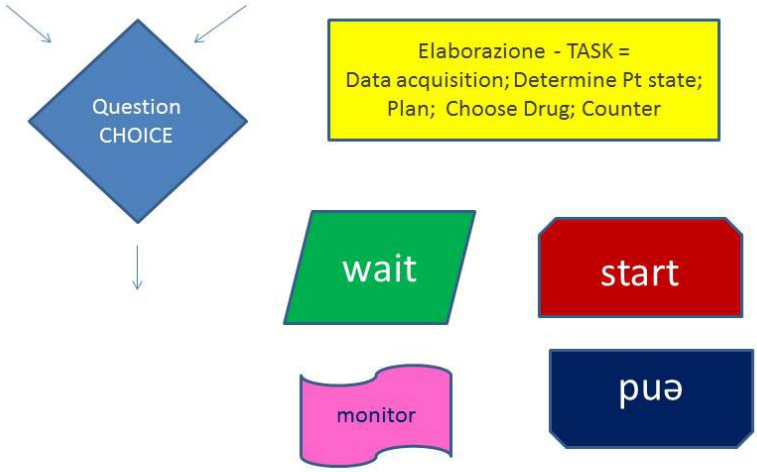


Figure 6 – Different type of clinical actions represented in the interactive flow-chart that graphically

represents the guideline (for web and smartphone).



4 – Topics

The clinical domains as selected by the Strategic Committee:

a) Acute leukemia
b) Chronic myeloid leukemia
c) Ph-negative chronic myeloproliferative disorders
d) Chronic lymphocythic leukemia
e) Lymphomas
f) Multiple myeloma and related-disorders
g) Myelodysplastic syndromes
h) Thrombosis and haemostasis
i) Support therapy
j) Infections
k) Red blood cell disorders

The Scientific Committee of each area selects the topic to be addressed during the current year by the following analythic hierarchy process:

- Listing of possible topics
- Listing of values for priorization
- Pairwise comparison of values (scores -9 to +9)
- Geometric means allow to calculate a rank
- Identification of three major values
- Calculation of percent weight of the three major values

- Pairwise comparison of topics according to each value (scores -9 to +9)
- Geometric means are calculated and weighted against the values relative weights
- Ranking of topics and selection
- Domain refinement of the selected topic

Domain refinement includes consensus on the definition of disease and the clinical setting (i.e. primary idiopathic thrombocythopenia in adults). Refinement might also restrict the domain to the sole therapeutic or the sole diagnostic process.

5 – Harmonization

According to the ADAPTE methodology, for each selected topic, a search for existing guidelines should be conducted in a standard list of repositories (see table xx – ADAPTE Manual).

5-1 Systematic search for guidelines

The 46 databases listed in Appendix 2 will be systematically searched with progressive and explicit keyword refinement.

5-2 Critical selection of retrieved guidelines

Clinical Practice Guidelines will be identified by three criteria, all of which need to be fulfilled: 1) list of prescriptive recommendations for health-care workers; 2) association of recommendations with scored quality of evidence and/or strength of the recommendation; 3) endorsement by an institution/scientific society/agency.

Each retrieved guideline will be described by a checklist including:

- Title
- Authors (experts)
    - Multidisciplinary panel?
- Institution
    - Network
    - International (or “gold-standard”) Scientific Society
    - National Scientific Society
    - Health-care Agency
    - Hospital
- National or international?
    - Country
    - International
- Language(s)

- Publication date
    - Updates
- Systematic review of evidence performed?
    - End of literature search date
- Peer review performed?
- Population
- Setting
- Intervention

The selection process starts by publication date: no guideline published before the year 2000 without subsequent revision will be selected; guidelines based on literature review ended before 2010 (without subsequent updates) will be selected only if international or peer-reviewed.

Next selection step regards adequacy of population, setting and intervention to the profile defined by the Scientific Committee.

Finally, English language is required for the guideline selection.

5-3 Critical appraisal of guideline quality

AGREE items are checked for each selected guidelines by two independent reviewers (Appendix 1). Inconsistent score are discussed face-to-face.

5-2 Tabular representation of guideline content

According to ADAPTE methodology manual, the content of guideline recommendations is reported in a synopsis table (matrix) indexed with one PICOT per row and one guideline per column.

The guidelines achieving highest AGREE scores will be used a referral backbone: clinical questions will be formerly extracted from it and subsequently integrated with those present in other guidelines.

5-3 Algorithmic representation of guidelines content

A flow-chart of the recommended sequential actions is developed for each selected guideline. An algorithm is built through the guideline editor GUIDE, a JAVA-based tool developed by the Compute Sci Dpt of Pavia University. The editor allows for different representation of info-gathering actions, therapeutic decision actions, monitoring actions…… The editor also tacks the ontologies used by the guideline.

5-4 Identification of consistent recommendations

Consistency of recommendations is checked in synopsis tables. However, only consistent recommendations that the Scientific and Methodology WG judge to be adequately updated are ADOPTED.

The Methodology WG proposes the most adequate strength of recommendation and level of evidence to be associated with consistent recommendations, in case of consistent content but inconsistent weighting.

5-5 Identification of inconsistent recommendations

Recommendations for a single PICOT can be slightly different among guidelines or prove some difference due to the setting (i.e. country). These differences allow to ADAPTE the recommendations. On converse, huge inconsistencies due to different updating of guidelines or to different weighting of outcomes, in spite of the same evidence base, require to be addressed more carefully. If inconsistency derives from different updating, the recommendation provided by the most recently updated guideline can be chosen. Otherwise the PICOT needs to be fully exploited de novo.

5-6 Identification of orphan/CRITICAL topics

Orphan topics are identified based on the algorithmic representation of guidelines or a-priori by the Scientific WG.

6 – Original recommendations

6-1 Priorization of orphan-topics and inconsistent topics:

An analythic hierarchy process allows a transparent selection of topics to be addressed through the following steps:

a) Values, i.e. criteria for defining the relative importance of topics, are listed by the Scientific Committee
b) Values are compared pairwise and assigned a relative weight ranging from -9 to +9
c) Geometric means of relative weights are calculated
d) The top 3 ranked values are selected
e) Percent weight of the 3 values is calculated
f) Topics are judged pairwise according to each value (scores -9 to +9)
g) Geometric means of scores are weighted by the percent weight of each value
h) The top 3 ranked topics are selected

6-2 Formulation of PICOTs

Each selected topic is formulated in the Patient-Intervention-Comparator-Outcome-Time format in order to be addressed with the GRADE methodology. Critical Outcomes and Time Horizon relevant for the recommendation are selected by the Methodology WG and confirmed by the Scientific WG.

6-3 Systematic review of evidence

According to GRADE methodology, a search with specific keywords is conducted in COCHRANE LIBRARY, MEDLINE, EMBASE and the proceedings of ASH, EHA, ASCO meetings limited to the last 5 years. Selection rules are expected to vary between areas and PICOTS. Evidence tables are produced.

6-4 Elaboration of recommendations

Recommendations are proposed by the Methodology WG based on the evidence tables in the Second Report. Final discussion will be held at the final meeting.

7 – Dissemination

The flow-chart elaborated by the Scientific WG will be validated during the final meeting and will provide the graphic backbone for navigation through the guideline. Contents of the flow-chart boxes will be derived from PICOT-based recommendation. Adopted and adapted recommendations will be directly incorporated into the flow-chart, while orphan and inconsistent recommendations will need a subsequent elaboration of new recommendations. The flow-chart will have a color-code allowing the reader to distinguish robust / strong recommendations versus frail /mild ones and to distinguish between adopted or adapted recommendations and newly elaborated ones.

Those boxes of the flow-chart prompting calculation of scores, checking diagnostic criteria, checking response criteria or verifying therapy schedules will provide links to checklists and calculators in order to allow the user to integrate the guideline with his/her clinical practice by getting a full support.

A pocket guide is provided in Adobe Acrobat format to be downloadable from the web site.

8 – Updating

Each year the Methodology Committee will be in charge of reviewing newly published/presented evidence relevant to each developed guidelines. The Methodology Committee will select the evidence which potentially can trigger changes in the guideline content or structure and will elaborate a report for the Scientific Committee. The Scientific Committee parallel will revise current recommendations and lists recommendations deserving revision as well as new orphan topics to be addressed. The Scientific Committee will revise the evidence, will update the report submitted by the Methodology Committee and will confirm the requirement of modifications or new development of recommendations or guideline structure or content. A Consensus Process will select major and minor modifications. A GRADE process will be used to address major modifications.

9 – Conflict of interest policy

9.1 Introduction

The Società Italiana di Ematologia (SIE) is committed to the very highest ethical standards in all its activities, including the development of clinical policies for management and treatment of hematological diseases. The SIE has always taken a stringent approach to ensure responsible, transparent relationships in which industry support and other relevant entities have no influence on the content of any scientific or professional material developed, published and diffused under its coverage.
However, the SIE do believe that that experts involved into writing committees who have relationships with industry and other relevant entities, when transparent and properly managed, strengthens the writing effort and final published document. However, part- or full-time employees of industry are prohibited from serving as members of guideline writing committees. The following policy outlines the SIE methodology for ensuring a document development process without improper bias or influence.

9.2 Scope

The SIE requires for all the expert involved in the development of guidelines the periodic disclosure of all relationships with industry and other entities (as defined in Section 9.4) involved in the production, marketing, distribution or reselling of healthcare goods, services, advice or information consumed by patients, investors and/or physicians. This may include relationships with government entities as well as not-for-profit institutions and organizations (see category definitions for details)

9.3 Relationships with Industry (RWI) Versus Conflict of Interest (COI)

The SIE consider as the most appropriate the term Relationships with Industry (RWI) and other entities as opposed to the term Conflict of Interest (COI). RWI, by definition, does NOT necessarily imply a conflict. Indeed, when all relationships are disclosed with the appropriate detail regarding the type, and they are managed appropriately for building consensus and voting, the SIE believes that potential bias can be avoided and the final published document is strengthened since the necessary expertise is accessible.

9.4 General Principles for Managing RWI

9.4.1 The RWI of SIE

The SIE acknowledge the relevant educative value of guideline development and diffusion among physicians and other healthcare operators. Therefore, guidelines preparation is core to the society education missions and no direct influence from industries or from a direct sponsorship is allowed on any aspect of them. However, according to the general principle of a responsible, transparent relationship with industries and other entities bearing interests in the production, marketing, distribution of healthcare goods and services, the SIE reserves the right to allocate for the guideline preparation, publication or diffusion, part of its own resources or unrestricted grant received to support its education activities.

9.4.2 Collecting RWI

Listed below is the information the SIE collects for the purposes of managing relationships with industry and other entities for guideline development.

9.4.3 Reporting Timeframe

The SIE requires the disclosure of all relationships with industry and other entities for the past 12 months. In addition, guideline authors are discouraged from adding new RWI during the writing effort and prior to publication; however, if relevant relationships are added, this information must be verbally disclosed during any conference calls or meetings, as well as added to the author disclosure table.

9.4.4 Relationship Type

The following definitions are used to define categories for reporting relationships with industry and other entities.

REPORTING CATEGORY	DEFINITION
Consultant	Includes relationships resulting in honoraria from a third party, gifts or other consideration, or "in kind" compensation, whether for consulting, lecturing, service on an advisory board, or for any other similar purpose in the prior calendar year.
Speaker's Bureau	Includes compensation from speaker's bureaus.
Ownership/ Partnership *(excluding mutual diversified funds)*	Includes status as any stock, stock option, ownership, partnership, membership or other equity position in an entity regardless of the form of the entity, or any option or right to acquire such position, and any rights and/or royalties in any patent or other intellectual property.
Personal Research	Includes principal investigator (PI) or co-PI (if so, please specify), investigator, steering committee member, collaborator or consultant for pending commercially-funded

Institutional or Organizational *(including but not limited to research)*	Institutional: Includes any institutional relationship between your employer or academic institution and a business or other entity (including government agencies). Examples: a) If your institution is recruiting patients for a trial and you are a sub-investigator or co-investigator and/or if you are a Chief of Division and therefore have administrative authority and/or direct decision-making responsibility (such as support for research grants, fellowships, and institutional supplies); b) If you are participating with any role into the development of guidelines promoted by scientific or business organization other than the SIE. Organizational: Organizational competing relationships include any leadership or governance responsibilities or roles in another professional or other nonprofit organization, whether or not remuneration is received (e.g., Officer, Director, Trustee or other Fiduciary Role, Editor) that may have interests potentially competitive with the SIE.

9.4.5 Financial Value/Level of Relationship

Financial disclosures should be classified as *significant, modest, or no financial relationship*. A person is deemed to have a *significant* interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity. A relationship is considered to be *modest* if it is less than *significant* under the preceding definition. *No financial relationship* pertains to relationships for which you receive no monetary reimbursement.

9.5 Disclosure Timing

Relationships are disclosed 1) in writing or online in advance of the writing effort to determine eligibility of members to serve on a writing committee and 2) during the document development process to ensure complete transparency throughout the writing and sign-off processes.
Relationships that develop during the writing process must be reported to the writing group chair immediately.

9.6 RWI Management

9.6.1 Writing Committee Balance (bias)

Chairs: The writing group chair is selected primarily for the competency of effectively managing the writing group. A general working knowledge and competency in the writing topic is also necessary, but the chairperson does not necessarily have to be a leading expert in that topic. The chairperson must be selected to avoid significant RWI* and other relationships that could undermine the credibility of the writing group or its work product.
Committee: A *majority* of writing committee members must be free of significant RWI.* At least 50% of writing committee members, plus the Chair, may have no significant RWI*. The Guideline Steering Committee monitors writing committee composition for RWI, as well as other potential areas of bias, such as intellectual bias/perspectives or organizational relationships potentially competitive with the SIE, and must approve each writing committee before work begins. Once chosen, authors are requested to avoid forming any new significant RWI during the writing effort and prior to publication in order to maintain the RWI balance of the writing committee.

Of note, the Guideline Steering Committee also reviews writing committee balance for other issues such as specialty, geographic location, private practice (versus academic setting/practice), and appropriate organizational/content expertise.

*At the discretion of the Guideline Steering Committee, certain disclosed relationships of the chair, or writing committee members such as participation in government-sponsored or university-managed clinical trial or research, as well as certain institutional/organizational and government/nonprofit relationships may be considered as NOT signif-

icant to the writing of the document.

9.7 Consensus Development

All writing committee members are invited to discuss all aspects of the document, including those for which they have relevant relationships with industry or other entities. The SIE values the expertise of all writing committee members and allows open discussion to inform the writing committee's final deliberation on document content. However, if one or more individuals *appear* to be unduly influencing the outcome of the discussion, whether they have a relevant relationship with industry related to the topic under discussion, a relevant relationship with another (non-industry) entity related to the topic (see above definition), or other bias related to the discussion, the individual may be asked to leave the room or conference call during a portion or all of the discussion at the discretion of the chair.

9.7.1 External Peer Review

There are no RWI restrictions for participation in the external peer review process of a document; however, all reviewers must disclose all relevant relationships with industry and other entities related to the topic for publication in an appendix of the document. This promotes the opportunity for comment on the document from a variety of constituencies/viewpoints to inform final document content.

9.7.2 Public Disclosure of RWI

The SIE disclosure policy is cited in the published document and *significant* relationships with industry and other entities of authors and peer reviewers are published in a document appendix. In addition, to ensure complete transparency, a hyperlink to the *comprehensive RWI* of each author (in effect at the time of the writing effort) and Guideline Steering Committee member (updated in real time) is included in the document. This information resides on www.siematologia.it
SIE requests an annual declaration of potential Conflict of Interest from the following individuals: members of the Strategic Committee, members of the Methodology Committee, members of the Scientific Committee. COI declarations are revised by the Strategic Committee, while COI declarations made by members of the Strategic Committee itself are revised by the Scientific Committees.

The type of COI to be declared regarding last 5 years include:

- PARTECIPATION IN GUIDELINE DEVELOMPENT
    - Have you been involved in the development on any of the guidelines under review (e.g., a member of the guideline development committee)?
- PERSONAL SPECIFIC INTEREST
    - Have you been involved in health-care company-supported projects *relevant to the guideline* you are currently developing?
    - Did you get economic or non-economic paybacks?
    - Which type of economic payback did you get?
        - Consultancies
        - Fee-paid work
        - Shareholding
    - Is the interest current?
- PERSONAL NON-SPECIFIC INTEREST
    - Have you been involved in health-care company-supported projects *irrelevant to the guideline* you are currently developing?

- Did you get economic or non-economic paybacks?
- Is the interest current?

- NON-PERSONAL SPECIFIC INTEREST is to be declared if the department he/she is working at was involved in the last 5 years in company-sponsored projects *relevant to the guideline* but he/she did not get any personal revenue.
  - Which kind of payback did you get from the company?
    - Grants
    - Fellowships
  - Is the interest current?
- NON-PERSONAL, NON-SPECIFIC INTEREST relates to payments from healthcare industry to the department he/she is working at but *without any link to the guideline* under construction.
- PERSONAL FAMILY INTEREST either specific or non-specific
  - Consultancies
  - Fee-paid work
  - Shareholding

Relevance of company-sponsored projects to the guideline under construction is judged by the Strategic Committee, which is allowed to request further details in order to complete the evaluation. COI declarations will be fully transparent, therefore, they will be accessible to all the members of the Guideline Project before the start of the Project itself.

10 – References

1. ADAPTE manual. www.adapte.org. version 2.0 (March 2010)
2. GRADE project. www.gradeworkinggroup.org
3. GUIDE system. www.openclinical.org
4. Ciccarese P, Caffi E, Boiocchi L, Quaglini S, Stefanelli M. A guideline management system. Medinfo. 2004;2004:28-32.
5. Micieli G, Cavallini A, Quaglini S. Guideline Compliance Improves Stroke Outcome - A Preliminary Study in 4 Districts in the Italian Region of Lombardia. Stroke 2002; 33:1341-1347.

11 – Appendix 1- AGREE checklist

The AGREE Assessment Tool asks to score each of 23 items from 1 (strongly disagree) to 7 (strongly agree).

Domain		
1	Scope & purpose	**The overall objective(s) of the guideline is (are) specifically described**
		The health question(s) covered by the guideline is (are) specifically described.
		The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

2	Stakeholder involvement	**The guideline development group includes individuals from all relevant professional groups.**
		The views and preferences of the target population (patients, public, etc.) have been sought.
		The target users of the guideline are clearly defined.
3	Rigour of development	**Systematic methods were used to search for evidence.**
		The criteria for selecting the evidence are clearly described.
		The strengths and limitations of the body of evidence are clearly described.
		The methods for formulating the recommendations are clearly described.
		The health benefits, side effects, and risks have been considered in formulating the recommendations.
		There is an explicit link between the recommendations and the supporting evidence.
		The guideline has been externally reviewed by experts prior to its publication.
		A procedure for updating the guideline is provided.
4	Clarity of presentation	**The recommendations are specific and unambiguous.**
		The different options for management of the condition or health issue are clearly presented.
		Key recommendations are easily identifiable.
5	Applicability	**The guideline describes facilitators and barriers to its application.**
		The guideline provides advice and/or tools on how the recommendations can be put into practice.
		The potential resource implications of applying the recommendations have been considered.
		The guideline presents monitoring and/or auditing criteria.
6	Editorial independence	**The views of the funding body have not influenced the content of the guideline.**
		Competing interests of guideline development group members have been recorded and addressed.
Overall guideline assessment		

Scoring will be calculated for each domain by normalization: scores for each n-item of the domain will be summed up and then normalized according to minimum and maximum score as below:

(SUM - n*1)/n*(7-1) = (SUM-n)/6n

12 – Appendix 2- Sources for guidelines search

Modified from ADAPTE manual.

1-i	www.g-i-n.net	Guidelines International Network (G-I-N)
2-i	www.guidelines.gov	National Guidelines Clearinghouse (NGC)
3-i	www.library.nhs.uk/guidelinesfinder/	
4-i	www.icsi.org/knowledge/	Institute for Clinical Systems Improvement (ICSI)
5-i	www.uptodate.org	UPTODATE
	NATIONAL GUIDELINE REPOSITORIES	
1-n	www.nzgg.org.nz/	New Zeland Guidelines Group
2-n	www.nhmrc.gov.au/	AU
3-n	www.sign.ac.uk/guidelines/index.html	Scottish Intercollegiate Guidelines Network (SIGN)
4-n	afssaps.sante.fr	Agence Francaise de Securite Sanitaire des Produits de Sante (AFSSAPS)
5-n	www.nice.org.uk/page.aspx?o=ourguidance	National Institute for Clinical Evidence (NICE)
6-n	mdm.ca/cpgsnew/cpgs/index.asp	
7-n	kaypahoito.fi	Finnish Medical Society Duodecim
8-n	doccismef.chu-rouen.fr/servlets/Simple?Mot=recommandations+professionnelles&aff=4&tri=50&datt=1&debut=0&rechercher.x=29&rechercher.y=18	CHU de Rouen – Catalouge & Index des Sites Mèdicaux Francophones (CISMef)
9-n	www.bmlweb.org/consensus.html	Bibliothèque mèdicale AF Lemanissier
10-n	www.msss.gouv.qc.ca/sujets/prob_sante/cancer/index.php?id=76,105,0,0,1,0	Direction de la lutte contre le cancer – Ministère de la santè et des services sociaux du Quèbec
11-n	www.fnclcc.fr/-sci/sor/index.htm	SOR: Standards, Options et Recommandations
12-n	rnao.org	Registrered Nures Association of Ontario
	aezq.de	Agengy for Quality in Medicine (Germany)
13-n	cancercare.on.ca	Cancer Care Ontario Practice Guideline Initiative
14-n	www.gacguidelines.ca	Ontario Guidelines Advisory Committee (GAC) Recommended Clinical Practice Guidelines
15-n	www.cadth.ca	Canadian Agency for Drugs and Technology in Health
16-n	cancer.gov	National Cancer Institute
	HEMATOLOGY-ONCOLOGY SOCIETIES	
1-s	www.siematologia.it	SIE
2-s	www.bcshguidelines.com	BCSH
3-s	www.leukemia-net.org	ELN
4-s	www.sisetonline.org	SISET
5-s	www.dgho.de www.onkopedia-guidelines.info	DGHO DGHO & OeGHO
6-s	www.hematology.org	ASH
7-s	www.nccn.org	National Comprehensive Cancer Network
8-s	www.asco.org	ASCO (US)
9-s	www.esmo.org	ESMO
10-s	www.aieop.org	AIEOP
11-s	www.ehaweb.org/eha-partners/collaborations/national-societies/listing-of-national-societies/	EHA list of European Societies
	HIGH-LEVEL EVIDENCE (HTA, SR)	
1-e	www.cochrane.org/reviews	The Cochrane Library
2-e	www.crd.york.ac.uk/crdweb http://www.york.ac.uk/inst/crd/crddatabases.htm#HTA	Centre for Reviews and Dissemination Health Technology Assessment Database
3-e	www.campbellcollaboration.org	The Campbell Library
4-e	www.eppi.ioe.ac.uk/cms/	Evidence for Policy and Practice Information and Co-ordinating Centres

5-e	health-evidence.ca	
6-e	sante.fr/anaes/anaesparametrage.nsf/Page?ReadForm&Section=/anaes/SiteWeb.nsf/wRubriquesID/APEH3YTFUH?OpenDocument&Defaut=y&132.203.128.28/medecine/repertoire/repertoire.asp	ANAES
7-e	has-sante.fr/anaes/anaesparmetrage.nsf/Page?ReadForm&Section=/anaes/SiteWeb.nsf/wRubriquesID/APEH-3YTFUH?OpenDocument&Defaut=y&	Haute Autoritè de Santè (HAS)
8-e	www.ianahta.org	IANAHTA
9-e	euroscan.org.uk	Euroscan – International Network on New and Emerging health Technologies
10-e	aquas.gencat.cat	AQuAS – Agencia de Qualitat i Avauacio Sanitaries de Catalunya
11-e	mdm.ca/cpgsnew/cpgs/index.asp	Canadian Medical Association Infobase
12-e	www.fda.gov/cder/guidance/index.htm	Food and Drug Administration
13-e	www.ema.europa.eu	EMA
14-e	www.132.203.128.28/medecine/repertoire/repertoire.asp	Directory of evidence-based Information Web sites