

EIP/GPE/EQC/2003.1

# **GUIDELINES FOR WHO GUIDELINES**



**Global Programme on Evidence for Health Policy  
World Health Organization  
Geneva, Switzerland**

# WHO Practice Guidelines: Recommended Processes

Version: 10 March 2003

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**1. Definition.** **Guidelines** are systematically developed evidence-based statements which assist providers, recipients and other stakeholders to make informed decisions about appropriate health interventions. Health interventions are defined broadly to include not only clinical procedures but also public health actions. Guidelines are formal advisory statements which should be robust enough to meet the unique circumstances and constraints of the specific situation to which they are being applied. The basic nature and intent of guidelines have also been expressed under other formats variously labeled as protocols, best practice, algorithms, consensus statements, expert committee recommendations, and integrated care pathways. This document refers to all formats with the basic nature and intent of guidelines.

**2. WHO Mandate.** In line with Article II of the Constitution, one of the core functions of WHO is setting, validating, monitoring and pursuing the proper implementation of norms and standards. In the performance of this function, WHO has been and will continue issuing recommendations for best practices given the current evidence i.e. guidelines.

**3. Context.** National and international organizations are increasingly issuing their own guidelines (Woolf, 1999). This leads to multiple guidelines on the same topic, which are not necessarily uniform in their process of development or consistent in their recommendations, but are widely circulated and increasingly available on the Internet. They are of growing interest to policy makers as well as to payers, providers and users of health services.

The demand for guidelines has contributed to the development of improved methodologies for basing guidelines on the most rigorous science available (Gyorkos 1994, Woolf 1996, Shekelle 1999, SIGN 1999, NHRMC2000). Key steps, which have been identified, are: selection of the topic, synthesis of evidence, formulation of recommendations, consultation and peer review, dissemination and implementation, review and updating.

Although there is consensus on the essential steps, there has been less progress with ensuring that recommendations of guidelines are implemented and produce better outcomes. A systematic review concludes that explicit, evidence-based guidelines improve the process and outcomes of health care when appropriately implemented (Grimshaw, 1993). The size of the improvement varies considerably, however. At the extreme, a recent study testing the effectiveness of guidelines showed no difference in process measures in the presence of guidelines (van der Wijden, 1999). The authors suggest that greater attention be given to improving the validity and ensuring the feasibility of guidelines.

Work from developing countries show that several factors increase the impact of practice guidelines: involvement of the end-users in guidelines development, launch and introduction of the guidelines, multiple training modalities, feedback to prescribers

on their prescription practices in relation to guidelines and effective monitoring and supervision (Ross- Degnan, et.al, 1997)

Some studies have been undertaken on the characteristics of guidelines which get implemented in clinical practice. The type of recommendations of the guideline, the methods of dissemination, and the extent to which the guidelines impinge on the usual operations of the system determine the degree to which recommendations get implemented. Grol (1998) shows that evidence-based, non-controversial, specific recommendations not requiring large changes in clinical practice routines were more likely to be implemented. A systematic review show that clinicians' practices were more likely to change if strong and multi-faceted dissemination strategies were used (Davis, 1997). More importantly, an in-depth analysis of application of an AHCPR guideline in one hospital (Katz, 1999) showed the importance of envisioning the operationalization of the guideline. This case study showed poor inter-observer reliability in interpretation of the guidelines (not specific enough), limited applicability of recommendations (applied only to 6% of intended population), incomplete specification of exceptions that may require deviations from the guideline, unexpected effects on medical care by increasing the demand for limited ICU beds and unknown effects on patient outcomes.

Considerable work has already been done in the area of guidelines within WHO. A preliminary inventory by the Department of Essential Drugs and Medicines Policy (EDM) of 192 documents with recommendations on drug treatment revealed at least 71 primary treatment guidelines. 73% were produced within the last 6 years. Only 55% of the 71 showed clearly the source of evidence backing each recommendation. A description of the process by which recommendations were developed was present in only 38% and only 1 of those conformed to current expectations of how guidelines should be developed. Only 31 guidelines described the affiliations of the contributors to the guideline. In terms of presentation, the guidelines did not always state clearly the intended audience, target disease or condition. Many WHO guidelines had recommendations which were not conclusive and where it is difficult to find the supporting discussion within the text (Jambert, et.al., 2000).

As an example, a systematic review (Jadad, 1995) analyzed the scientific rigor of the evidence base of the WHO ladder for analgesics for cancer pain management. Although the individual drugs are proven pain-killers, there were no rigorous studies which tested the effectiveness of the ladder approach prior to dissemination of the guidelines. Jadad (1995) found 8 studies published since the WHO guidelines were produced but all were of poor design or of limited follow up. Sometimes it will be necessary to issue guidelines where no rigorous studies exist, based on the best available evidence. But after issuance of such guidelines, the opportunity could be taken to undertake rigorous studies to provide missing evidence and to evaluate the effectiveness or impact of the guidelines in the actual settings where they are intended to be used. This would allow them to be revised or updated if needed.

With the increased importance being placed on evidence-based medicine and health policy, it is important to set standards for the process of developing and reporting WHO guidelines. There is also a need to ensure that WHO guidelines add value to the

broader process of guideline development taking place in countries by building on WHO's unique mandate and expertise.

On January 11, 2000, the HQ cabinet recommended that all WHO guidelines should be evidence-based. An EIP-led intercluster initiative developed this document as the recommended approach to development of WHO guidelines. At the same time, a self assessment checklist was also produced to ensure a consistent level of quality in the guidelines. Cluster note 2002/39, dated December 3, 2002, endorsed the recommended process and at the same time, mandated HTP to develop a database of guidelines which met all the criteria in the self-assessment checklist.

#### **4. Added Value of WHO Guidelines:**

Guidelines have, to date, been used primarily to advise practitioners on what interventions to use in their interaction with individuals or patients. As such, many are directly addressed to practitioners although they are been addressed increasingly at patients as well. Most of the time, recommendations are based solely on evidence on efficacy. This is consistent with the approach of the US Task Force on Preventive Services (Woolf, 1996) and the CDC guide to Community Preventive Health Services (Truman, 2000) which explicitly stated that the only evidence on which they base their recommendations is efficacy or effectiveness. On the other hand, the Canadian Medical Association takes a slightly broader approach where the principle of guideline development is that "Clinical practice guidelines should recognize that the physician's primary responsibility is to his or her own patient, although it may have to be balanced against the needs of other people and society in general."

WHO's mandate comes from the constitution adopted by member states and the primary audience it serves is composed of governments, more specifically, the ministries or agencies concerned with health. Although the broader community of practitioners and patients pays close attention to statements issued by WHO, the difference in the audiences for ordinary guidelines and WHO guidelines changes the nature of the development process in WHO. Governments have as their main responsibility the health of the population, rather than the disease of the individual, and must consider other factors in addition to the traditional concern for maximizing the benefit to individual patients. WHO needs to assess the implications for population health of any recommendation as well. This requires explicit recognition that resources to provide health interventions are limited. This involves considering the cost-effectiveness of alternative interventions, the opportunity costs of investing in one intervention versus another, the affordability of the interventions, and the feasibility of applying a set of recommendations in different settings.

In some situations there may be a conflict between recommendations based on maximizing benefits for a single individual (using only efficacy data) and those which seek to make the best use of scarce resources to maximize population health (Birch 1996, Granata 1998). But some agencies are now explicitly exploring the issues of cost-effectiveness in making guideline recommendations (Eccles 2000, Mason 1999, Eddy 1999).

Feasibility is also a major concern for agencies that are accountable for the health of their populations. For many of the countries, the population availing of health

services and the health infrastructure may not be similar to the setting where the original studies on efficacy took place. It is possible that the expected outcomes as predicted by efficacy studies will not be attained when implemented under field conditions (Lohr, 1998).

Finally, WHO takes a global perspective in addressing the needs of 191 member states. Differences in outcome will not only be due to transferring results from a research to a field setting, but also from the different cultural, economic, socio-demographic contexts present in the member-states (Wabitsch1998, Veninga 2000).

## **5. Implications for the WHO guideline development process**

*a. A 3 stage process.* The key part in any guidelines is the set of recommendations and its corresponding link to evidence. The strength of recommendations reflects the extent to which it is possible to be confident that adherence to a recommendation will do more good than harm. The level of evidence is the extent to which one can be confident that an estimate of effect or association is correct (Oxman, 2000). Thus, the strength of the recommendation is very much linked to the level of evidence.

For WHO guidelines, the traditional approach of reviewing and reporting evidence on efficacy and safety is certainly crucial but not sufficient. It can be regarded as the first step, but it is also necessary to examine the implications of applying each possible set of recommendations on a population basis. The initial body of evidence to be considered in WHO guidelines will be identical to that of traditional guidelines, but WHO guidelines will need to go further, to take the second step of spelling out the implications of adopting recommendations on costs and on population health. If done adequately, this will allow decision makers in different settings to take the third step of “localizing” the guidelines to their settings, and deciding where the tradeoff between additional benefit and additional costs should be set. It will also be useful in determining what is acceptable for the end-users.

The three steps are delineated to recognize that different competencies are needed at each step. The initial synthesis of evidence can be done centrally or virtually in any place. However, developing of final recommendations means applying the evidence in the context of local conditions and this is preferably done at the national level by local decision-makers. It is recognized that many countries will not yet have the capacity to localize WHO guidelines to their settings. Accordingly, we suggest that the second part of guidelines developed in WHO, the implications on population health and effectiveness if recommendations are applied on a population basis, should be elaborated for a number of possible scenarios or settings.

In summary, there are 4 questions, which need to be answered in guideline development: what is efficacious? what is cost-effective? what is affordable? and what is beneficial for the population? In many instances, there will not be a single answer to all these questions. It is also to be expected that the answers will vary across countries.

*b. Choice of topics for development of WHO guidelines:*

Guideline development is a process which consumes resources (see Sec VII). They could be developed on almost every health topic or intervention so it is necessary for WHO to decide which topics should be given priority. It is suggested that the following areas be given priority:

- interventions that will require system changes (feasibility concerns) as opposed to those dealing solely with provider/patient interactions. WHO has greater comparative advantage in dealing with governments, for interventions which require inputs and coordination at different levels of the system. It has less comparative advantage on purely provider/patient interactions.
- cost-effective interventions that address a disease burden which is still causing major health losses, implying under-utilization of the technology (population perspective).
- interventions that are of limited or questionable effectiveness but are being used widely (opportunity costs).
- Interventions for diseases which have a high burden in developing countries, or new and emerging diseases for which there are no existing guidelines.
- interventions where there might possibly be a conflict in choices between individual and societal perspectives (political concerns: when countries will need WHO's normative support to make recommendations based on the population perspective especially in the context of other influential organizations espousing guidelines adopting an individual perspective).

### ***c. Synthesizing the evidence.***

Evidence should be gathered in a systematic process to avoid or minimize bias. It is recommended that WHO should follow the Cochrane method of systematic reviews to the extent possible. Because of the additional requirement for improving the basis for making decisions on generalizability, there is more onus than usual to systematically search for evidence, particularly in the grey literature or unindexed local journals and alternative indexing services like extraSCI or extramed or regional databases (LILACS for Latin America, African Index Medicus, IMEMR for Eastern Mediterranean Region c/o WHO Library's virtual reference desk).

While extracting data from the studies, all critical details of characteristics of the population, the setting and the intervention need to be recorded. If information is lacking from published studies, reviewers should contact the authors to get more details. The data should then be analyzed in a way which allows accurate estimation of the treatment effects in different settings and populations.

This is the first phase of the 3-stage process. It will answer the question of what is the best evidence on efficacy, and maybe effectiveness, of different types of strategies. It could develop statements on what types of strategies would maximize the potential benefit to individual patients or a group of patients *if resources were unlimited*.

In case there is not enough evidence on which to base guidelines, WHO may opt to issue consensus statements and acknowledge that these recommendations are based on expert opinion. These consensus statements are to be issued with a limited lifespan during which time WHO will invest in resources to ensure that the necessary research is being done to provide evidence needed the next time around.

#### ***d. Making recommendations.***

The second stage of WHO guideline development will spell out any tradeoffs between the cost of applying possible recommendations on a population basis, and the population health impacts. It would consist of a number of scenarios (or optimal recommendations) – perhaps in the cases of very limited resources, and unlimited resources. This would enable country decision makers to make recommendations as part of the localization process.

During the third step or the localization process, WHO should seek to provide any technical assistance necessary to countries to help them make their own recommendations. This means providing local (regional) cost-effectiveness data on the interventions concerned, data on other interventions which might be of comparable or better cost-effectiveness but which they might not yet be currently providing (to expand their policy choices within the sector), data on the resources required to carry out the interventions, including financial start-up and capital costs. This is one of the roles of GPE.

#### ***e. Disseminating the guidelines***

Dissemination should involve more than physical distribution of guidelines. It means assisting countries to implement the guidelines based on local recommendations. WHO can do this by anticipating countries' needs based on the scenarios and model recommendations which have been developed. Technical assistance can be provided by staff at headquarters or in the regions by provision of training manuals and programs, operations manuals and recommendations for monitoring activities and use of uniform indicators.

## **6. Operationalizing the standard process for development of WHO guidelines**

### **A. Selection of partners**

The Director General of WHO has encouraged the development of partnerships. Departments within WHO interested in the development of guidelines can decide to work with other organisations with a view to co-sponsoring guidelines with them.

In the selection of partners, the following should be considered:

- Is the organization global or international in scope?
- Does the organization share the objectives of WHO ?
- Is the organization credible professionally, with no conflict of interest relating to the guidelines under development?
- Is there value added by WHO partnering the organization?

If the answer to any of these questions is no, there is little reason to partner that organisation.

### **B. Organization of guideline groups:**

For each guidelines, it is suggested that the following groups be organized:

- **Guideline Steering Group**

This will be an in-house steering group composed of WHO staff with the general function of overseeing the development of each step of the guideline development process.

***Specific functions:***

1. define the general parameters of the proposed technical guideline
2. draft the terms of reference (TOR) for the technical guideline development group (TDG)
3. select the chair and members of the TDG based on pre-specified criteria
4. orient the TDG to the specific TOR and the standard process of guideline development
5. monitor regularly the development of the guidelines
6. ensure external review of the guidelines
7. review final draft of the guideline for approval by the Executive Director

***Composition:***

Chair: Representative from the cluster/department issuing the guideline

Members: 2-4 persons from within or from other clusters who together will have the following skills and expertise:

1. guideline development and evidence based methodologies
2. familiarity with implementation of programmes in developing countries in the area related to the guideline development (if feasible, preferably from regions or country offices most affected by the issue being addressed in the guideline)
3. subject /topic/content of the guideline

Note: If there is a co-sponsor, a liaison group may be constituted composed of representatives from WHO and its partners. The representatives from WHO could be the same individuals in the steering group. It must be clarified, however, which of the key decisions (approval of topics for guideline development, approval of nominated chair and members for the TDG, approval of process and timetable for guideline development, approval of draft guidelines and documentation to be forwarded to Executive Director for approval, approval of dissemination plan) will be delegated to the liaison group.

➤ **Technical Guideline Development Group (TDG)**

***Functions:***

- a. define the specific issues to be addressed by the guideline
- b. undertake a systematic search for evidence (see taskforces)
- c. review the evidence available
- d. develop recommendations linked to the strength of the evidence
- e. draft guidelines
- f. discuss and incorporate, where relevant, comments of external reviewers
- g. draft final version of the guidelines
- h. make recommendations on dissemination strategy
- i. document the process of guideline development

***Composition:***

1. Chair (to be selected by the steering group)

criteria for selection:

Should be credible and commands respect in the field/subject area

Should have good people skills in a small-group situation

Should have experience in guideline development

2. Members (multidisciplinary, around 8-12 individuals) to represent:

a. stakeholders and to ensure that the right issues are identified and facilitate early buy-in for the guidelines)

Professionals

Disease experts

Primary care/public health (MOH)

End users

Patients

b. Methodologists (to ensure scientific rigour)

Practice Guideline Development

Systematic Review (at least 2)

Cost Effectiveness (1-2)

Health services/systems

- **Taskforces** – can be designated as needed to undertake systematic reviews of evidence or conduct consultations from experts if evidence is lacking. Ideally, it is to be constituted as a subgroup within the technical development group, or if needed, outside experts can be invited.
- **Secretariat:** administrative support to be provided by WHO staff.

Note 1: All individuals involved in the guideline development process will be asked to sign a declaration of interest form (attached as annex a).

Note 2: Selection of members should be done to in a way which ensures geographic and gender balance.

Note 3: If resources are limited, this should not be a barrier to selection of individuals from distant countries. The use of modern communication technology can facilitate participation even if from a distance.

Note 4: It is recommended that WHO staff participate in all the steps with the regional and country staff specifically involved in step 3.

See fig. 1 on relationships of sponsoring organizations, steering groups, liaison groups, technical guideline development group, taskforces, and secretariat

### C. Process of developing guidelines:

The most detailed and methodologic reference is NHRMC 2000.

1. Refine the topics/questions

To identify the issues to be addressed, it is helpful to develop a logic and analytical frameworks guide (Woolf, 1994)

2. Undertake systematic review

It is recommended that the systematic review be undertaken.

(<http://hiru.mcmaster.ca/cochrane/cochrane/hbook.htm>)

After the studies have been identified and critically appraised, and the evidence synthesised, evidence should be graded.

All evidence, including that on safety, should be clearly laid out in an evidence table.

Meta-analysis should be done when the data permit.

The final results should be presented in a balance sheet (see Annex B)

3. Draft different scenarios and develop model recommendations (Annex B)  
To maximise representation and inputs from the different stakeholders, formal group processes should be used when possible (Murphy, 1998)
4. Make recommendations for research and updating of guidelines
5. Ensure peer review  
Circulate widely to experts, professional organizations, regional offices, countries
6. Make dissemination plans including plans for localization and evaluation.
7. Complete documentation of the guideline development process (Hayward, 1993).
8. Submit to the steering group for approval of draft guidelines

Note: It is recommended that a uniform, readily-recognizable printing format be developed for WHO guidelines.

#### **D. Guiding values**

The following are proposed as the guiding values in the WHO guideline development process:

- Population perspective
- Scientific integrity
- Sensitivity to local contexts
- Transparency.

#### **VI. Self-test kit**

After development, it is suggested that the draft guideline be subjected to a self test (Annex C) by the technical development and the steering/liaison groups.

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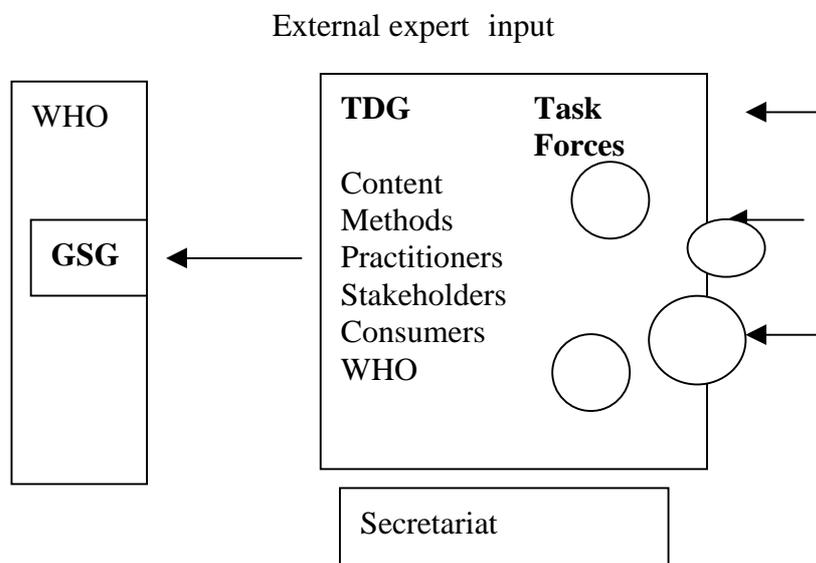
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**Figure 1. General guideline development**  
(adapted from WHO/NCD 2000 HPN guideline meeting report)



## Annex A: DECLARATION OF INTERESTS FOR WHO EXPERTS



**Title of meeting or work to be performed, including description of subject-matter, substance (compounds and organisms), technology or process to be considered:** \_\_\_\_\_

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Public health considerations have a primary importance in all WHO technical work. Measures need to be taken to ensure that the best possible assessment of scientific evidence is achieved in an independent atmosphere free of either direct or indirect pressures. Thus, to assure the technical integrity and impartiality of WHO's work, it is necessary to avoid situations in which financial or other interests might affect the outcome of that work.

Each expert is therefore asked to declare any interests that could constitute a real, potential or apparent conflict of interest, with respect to his/her involvement in the meeting or work, between (1) commercial entities and the participant personally, and (2) commercial entities and the administrative unit with which the participant has an employment relationship. "Commercial entity" refers to any company, association (e.g., trade association), organization or any other entity of any nature whatsoever, with commercial interests.

In addition, as a result of WHO's strong stance against tobacco use, it is considered relevant for the Organization to know whether experts working with it have, or have had, any relationship with any part of what may be called "the tobacco industry". Nevertheless, declaration of such an interest would not necessarily be considered a reason to disqualify an expert.

### **What is a conflict of interest?**

Conflict of interest means that the expert or his/her partner ("partner" includes a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship, has a financial or other interest that could unduly influence the expert's position with respect to the subject-matter being considered. An apparent conflict of interest exists when an interest would not necessarily influence the expert but could result in the expert's objectivity being questioned by others. A potential conflict of interest exists with an interest which any reasonable person could be uncertain whether or not should be reported.

Different *types of financial or other interests*, whether personal or with the administrative unit with which the expert has an employment relationship, can be envisaged and the following list, which is not exhaustive, is provided for your guidance. For example, the following types of situations should be declared:

1. a current proprietary interest in a substance, technology or process (e.g. ownership of a patent), to be considered in - or otherwise related to the subject-matter of - the meeting or work;
2. a current financial interest, e.g. shares or bonds, in a commercial entity with an interest in the subject-matter of the meeting or work (except share holdings through general mutual funds or similar arrangements where the expert has no control over the selection of shares);
3. an employment, consultancy, directorship, or other position during the past 4 years, whether or not paid, in any commercial entity which has an interest in the subject-matter

of the meeting/work, or an ongoing negotiation concerning prospective employment or other association with such commercial entity;

4. performance of any paid work or research during the past 4 years commissioned by a commercial entity with interests in the subject-matter of the meetings or work;
5. payment or other support covering a period within the past 4 years, or an expectation of support for the future, from a commercial entity with an interest in the subject-matter of the meetings or work, even if it does not convey any benefit to the expert personally but which benefits his/her position or administrative unit, e.g. a grant or fellowship or other payment, e.g. for the purpose of financing a post or consultancy.

With respect to the above, an interest in a competing substance, technology or process, or an interest in or association with, work for or support by a commercial entity having a direct competitive interest must similarly be disclosed.

**How to complete this Declaration:** Please complete this Declaration and submit it to the Secretariat. Any financial or other interests that could constitute a real, potential or apparent conflict of interest should be declared (1) with

respect to yourself or partner, as well as (2) with respect to the administrative unit with which you have an employment relationship. Only the name of the commercial entity and the nature of the interest is required to be disclosed, no amounts need to be specified (though they may be, if you consider this information to be relevant to assessing the interest). With respect to items 1 and 2 in the list above, the interest should only be declared if it is current. With respect to items 3, 4 and 5, any interest during the past 4 years should be declared. If the interest is no longer current, please state the year when it ceased. With respect to item 5, the interest ceases when a financed post or fellowship is no longer occupied, or when support for an activity ceases.

**Assessment and outcome:** The information submitted by you will be used to assess whether the declared interests constitute an appreciable real, potential or apparent conflict of interest. Such conflict of interest will, depending on the situation, result in (i) you being asked not to take part in the portion of the discussion or work affecting that interest, (ii) being asked not to take part in the meeting or work altogether, or (iii) if deemed by WHO to be appropriate to the particular circumstances, and with your agreement, you taking part in the meeting or work and your interest being publicly disclosed.

Information disclosed on this Form may be made available to persons outside of WHO only when the objectivity of the meeting or work has been questioned such that the Director-General considers disclosure to be in the best interests of the Organization, and then only after consultation with you.

**Declaration:** Have you or your partner any financial or other interest in the subject-matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential or apparent conflict of interest?

**Yes:**  **No:**  **If yes, please give details in the box below.**

Do you have, or have you had during the past 4 years, an employment or other professional relationship with any entity directly involved in the production, manufacture, distribution or sale of tobacco or any tobacco products, or directly representing the interests of any such entity?

**Yes:**  **No:**  **If yes, please give details in the box below.**

Type of interest, e.g. patent, shares, employment, association, payment (including details on any compound, work, etc.)	Name of commercial entity	Belongs to you, partner or unit?	Current interest? (or year ceased)

Is there anything else that could affect your objectivity or independence in the meeting or work, or the perception by others of your objectivity and independence?

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I hereby declare that the disclosed information is correct and that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to inform you of any change in these circumstances, including if an issue arises during the course of the meeting or work itself.

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name

\_\_\_\_\_  
Institution

Annex B: (From: GRADE 2002 revised)

## GRADE JUDGEMENTS

**Please read the information and instructions below carefully before starting.**

### Instructions

The evidence summary and balance sheet have been prepared based on information from a systematic review.

Do not second guess what is in the tables. Use only the information presented in the tables as the basis for your judgements.

Please note any disagreements and comments you may have about the tables.

#### 1. Quality of evidence across studies for each outcome

When grading the quality of evidence for each outcome (across studies), please refer to and use the following guidelines.

Table 1. Quality of evidence across studies for each main outcome		
<b>Observational studies</b>	<b>Quality of the evidence</b>	<b>Randomized trials</b>
Extremely strong association and no major threats to validity	High	No serious flaws in study quality
Strong, consistent association and no plausible confounders	Intermediate	Serious flaws in design or execution or quasi-experimental design
No serious flaws in study quality	Low	Very serious flaws in design or execution
Serious flaws in design and execution	Very low	Very serious flaws in design and execution
Additional factors that lower quality are: <ul style="list-style-type: none"> <li>• important inconsistency of results</li> <li>• some uncertainty about directness</li> <li>• high probability of reporting bias</li> <li>• sparse data</li> </ul> Major uncertainty about directness can lower the quality by two levels.		
Additional factors that may increase quality are: <ul style="list-style-type: none"> <li>• all plausible residual confounding, if present, would reduce the observed effect</li> <li>• evidence of a dose-response gradient</li> </ul>		

## 2. Relative importance of outcomes

Please indicate for each of the outcomes presented, the relative importance of this outcome for making a decision about the question posed at the top of the evidence table.

- Outcomes with a mean of 7 or above will be considered critical outcomes
- Outcomes with a mean between 4 and 6 will be considered important, but not critical to the decision. These should be used in judgements about tradeoffs and recommendations, but not in judgements about the overall quality of evidence across the critical outcomes.
- **Outcomes with a mean of 3 or below will be removed from the evidence table and balance sheet and should NOT be considered further in the judgements about the overall quality of evidence, tradeoffs or recommendations.**

## 3. Overall quality of evidence across the critical outcomes

The overall quality of the evidence across the critical outcomes, should be based on the lowest quality of evidence for the outcomes that are critical to making a decision.

## 4. Balance of the benefits and harms

Based on the critical and other important outcomes, what is the balance between benefits and harms. Your judgements about the balance between benefits and harms and the recommendations should not YET take into account costs.

## 5. Recommendation

This should be based on the

- trade-offs, including costs
- quality of evidence (for critical outcomes)
- translation of evidence into practice in the specific situation (may use different scenarios)
- uncertainty about baseline risk (may use different scenarios)

## 6. Comments and suggestions

Please note comments and suggestions regarding this particular evidence summary and balance sheet or generally about how the evidence summary and balance sheets can be improved.

Please specify any special circumstances that should have been specified, but were not.

## **EXAMPLE: GRADE JUDGEMENTS**

Name:

Date:

Question: Should SSRIs be used instead of tricyclics for depressed patients in primary care?

Reference: The choice of antidepressants for depression in primary care, North of England evidence-based guideline development project, 1997

1. For each of the following outcomes indicate the quality of evidence across studies:

Depression severity

- High
- Intermediate
- Low
- Very low

Transient side effects

- High
- Intermediate
- Low
- Very low

Poisoning fatalities

- High
- Intermediate
- Low
- Very low

2. What is the overall quality of evidence across the above outcomes?

- High
- Intermediate
- Low
- Very low

3. What is the balance between the above benefits and harms?

- Net benefits
- Trade-offs
- Uncertain net benefits
- Not net benefits

4. Which of the following recommendations would be appropriate for this intervention?

- Do it
- Probably do it
- Toss-up
- Probably don't do it
- Don't do it

**EXAMPLE: evidence summary (NOT to be used for actual decision making)**

Name: Gunn Vist, Martin Eccles, Andy Oxman  
 Date: February 2003

Question: Should depressed patients be treated with SSRIs or tricyclics?

Setting: Primary care

Baseline risk: Moderately depressed adult patients

Reference: The choice of antidepressants for depression in primary care, North of England evidence-based guideline development project, 1997

**SSRIs vs tricyclics**

Outcome: <b>Depression severity</b> (measured with Hamilton Depression Rating Scale after 4 to 12 weeks)							
Studies	Design	Quality	Consistency	Directness	SD*	SA*	PB*
8 trials Citalopram 38 trials Fluoxetine 25 trials Fluvoxamine 2 trials Nefazodone 18 trials Paroxetine 4 trials Sertaline 4 trials Velafaxine	RCTs	No serious flaws	No important inconsistency	Some uncertainty about directness (outcome measure)	No	No	No
Outcome: <b>Transient side effects resulting in discontinuation of treatment</b>							
8 trials Citalopram 50 trials Fluoxetine 27 trials Fluvoxamine 4 trials Nefazodone 23 trials Paroxetine 6 trials Sertaline 5 trials Velafaxine	RCTs	No serious flaws	No important inconsistency	Direct	No	No	No
Outcome: <b>Poisoning fatalities</b>							
Office for National Statistics (British)	Observational data	No serious flaw**	Only one study	<i>Direct</i>	No	++	No

\*SD= Sparse data

\*SA= Strong association (+ = strong, ++ = extremely strong)

\*PB= Publication bias

\*\*Although there is not a flaw in how the study was done, there is a major threat to the validity of the results.

Fatality data may be influenced by which pills are given to whom, and it is uncertain if changing antidepressant would deter suicide attempts.

**EXAMPLE: BALANCE SHEET (NOT to be used for actual decision making)**

Name: Gunn Vist, Martin Eccles, Andy Oxman

Date: February 2003

Question: Should depressed patients be treated with SSRIs or tricyclics?

Setting: Primary care

Baseline risk: Moderately depressed adult patients

Reference: The choice of antidepressants for depression in primary care, North of England evidence-based guideline development project, 1997

Outcome	SSRI	Tricyclics	Effect		Quality	Relative importance
			Relative (95% CI)	NNT		
Depression severity	5044 patients	4510 patients	WMD 0.034 (-0.007 to 0.075)	No difference		
Transient side effects	1948/7032 (28%)	2072/6334 (33%)	RRR 0.13 (0.05 to 0.20)	20		
Poisoning fatalities*	1/100,000 per year of treatment	58/100,000 per year of treatment	RRR 98% (97% to 99%)	1754		

\*Uncertainty about baseline risk

CI = confidence interval  
 NNT = number needed to treat  
 WMD = weighted mean difference  
 RRR = relative risk reduction

## Annex C

<b>Checklist for WHO Treatment Guidelines</b>			
This Checklist is intended for the following purposes: (1) As a guide for developing or updating WHO treatment Guidelines (2) As a check-list for Executive and Regional Directors when giving final approval for publication. To qualify for publication and inclusion in the WHO database of treatment guidelines, a tick mark signifying YES must be placed beside all the 24 criteria, except 11a.			
	Yes	Questions	Reference Points
		<b>Origin</b>	
1		Are the Cluster and Department issuing the guidelines clearly identified ?	Introduction
		<b>Objective, target audience</b>	
2		Does the guideline list its objectives, including the patient categories and situation(s) for which the guidelines are intended?	Introduction
3		Does the guideline describe the professional groups to which it is addressed?	Introduction
		<b>Guideline Development Group</b>	
4		Does the Guideline Development Group include all relevant professional groups, public health experts and end users, including individuals from geographic areas where the guidelines will be applied?	List of members of the guideline development group
5		Does the Group include methodological experts in fields such as search methodology, critical appraisal and cost-effectiveness analysis?	List of members of the guideline development group
		<b>Conflict of interest</b>	
6		Are all funding sources named, and is there no conflict of interest?	List of funding sources
7		Have all members of the Guideline Development Group and external reviewers declared their interests, and have these interests been recorded in the guideline document?	Annex on documentation of process
8		Does the document describe the method used to minimize any undue influence on the Guideline Development Group and the external reviewers?	Annex on documentation of process
		<b>Evidence</b>	
9		Was there a systematic comprehensive search for evidence, and has the search strategy been recorded in the guideline?	Annex on documentation of process
10		Has the strength and quality of the evidence on effectiveness been graded?	Annex on documentation of process; evidence table
11a		What percent of recommendations are evidence-based?*	Summary of recommendations
11b		Are the recommendations which are not evidence-based explicitly labelled as "expert opinion" based?	Summary of recommendations
12		Is there explicit consideration of other issues, such as safety and potential misuse in a variety of settings?	Annex on documentation of process; evidence table
13		Is there explicit consideration of issues of cost effectiveness?	Annex on documentation of process; evidence table
14		Is the strength of the recommendation linked to the evidence?	Summary of Recommendations
15		Do the recommendations take into account potential resource constraints?	Implementation issues
		<b>Review</b>	
16		Were the comments by the external peer review adequately addressed?	Annex on documentation of process
17		Did all members of the Guideline Development Group approve the final document?	Annex on documentation of process
18		Did all members of the Steering Group approve the final document?	Annex on documentation of process
19		Is there a plan for reviewing new evidence and updating the guideline?	Introduction
		<b>Presentation, clarity</b>	
20		Are the recommendations clearly formulated?	Summary of Recommendations
21		Does the guideline identify and advise on ineffective practices?	Summary of Recommendations
		<b>Implementation plan</b>	
22		Is there a plan for dissemination and local adaptation of the guideline?	Companion document
23		Are funds available for dissemination and local adaptation for the guideline?	Companion document
24		Are there suggested criteria for monitoring the use in intended settings?	Implementation Issues

\*these are recommendations based on information other than expert opinion.

