

WHO guidelines and the Guidelines Review Committee

Dr Faith McLellan



World Health
Organization

The Problem

WHO guidelines: not transparent, not evidence based

- ↓ **Systematic reviews**
- ↓ **Transparency about judgements**
- ↑ **Expert opinion**
- ↓ **Adaptation of global guidelines to end users' needs**
- ↔ **Tension between time taken and when advice needed**
- ↓ **Resources**

Oxman et al, Lancet 2007;369:1883-9



**World Health
Organization**

WHO response

- **GRC**
- **Standards for:**
 - **Reporting**
 - **Processes**
 - **Use of evidence**
- **Revised WHO handbook for guidelines**
- **Different types of documents for different purposes**



Guideline types

- **Emergency**
 - **Response to acute need, evidence informed, limited consultation, short use-by date**
- **Standard /focused**
 - **Limited topic area, 10-20 'questions', evidence-based, 1 guideline group meeting**
- **Comprehensive**
 - **Disease/policy area, evidence-based, 3-4 meetings**
- **Textbooks**
- **Joint guidelines**



What is a WHO guideline?

- "Guidelines are **recommendations** intended to assist providers and recipients of health care and other stakeholders to make **informed decisions**. Recommendations may relate to **clinical interventions, public health activities, or government policies.**"

WHO 2003, 2007



World Health
Organization

But what is it, really?

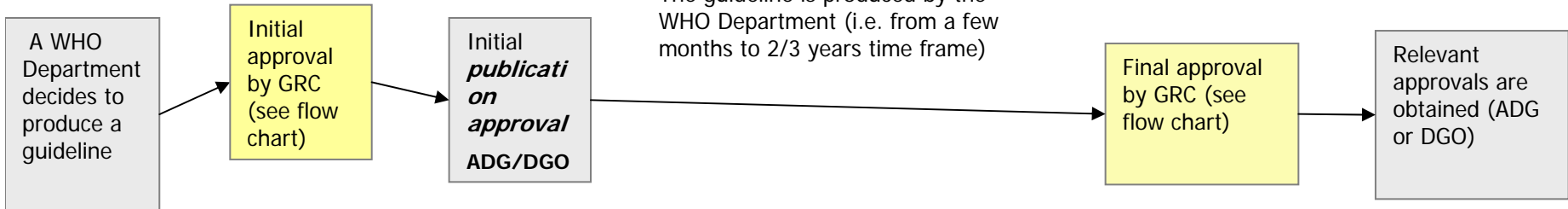
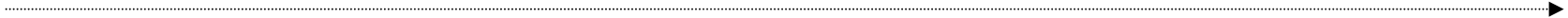
- **YES:** Clinical and public health interventions
- **NO:** Standards (eg pharmacopoeia, food), standard operating procedures, evidence synthesis without recommendations, 'how to' manuals
- **UNCLEAR:** compilations of clinical information without clear recommendations
- **IN ANY CASE:** The *name* is irrelevant



WHO Guidelines Production Process Guidelines Review Committee

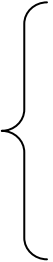
Beginning

End



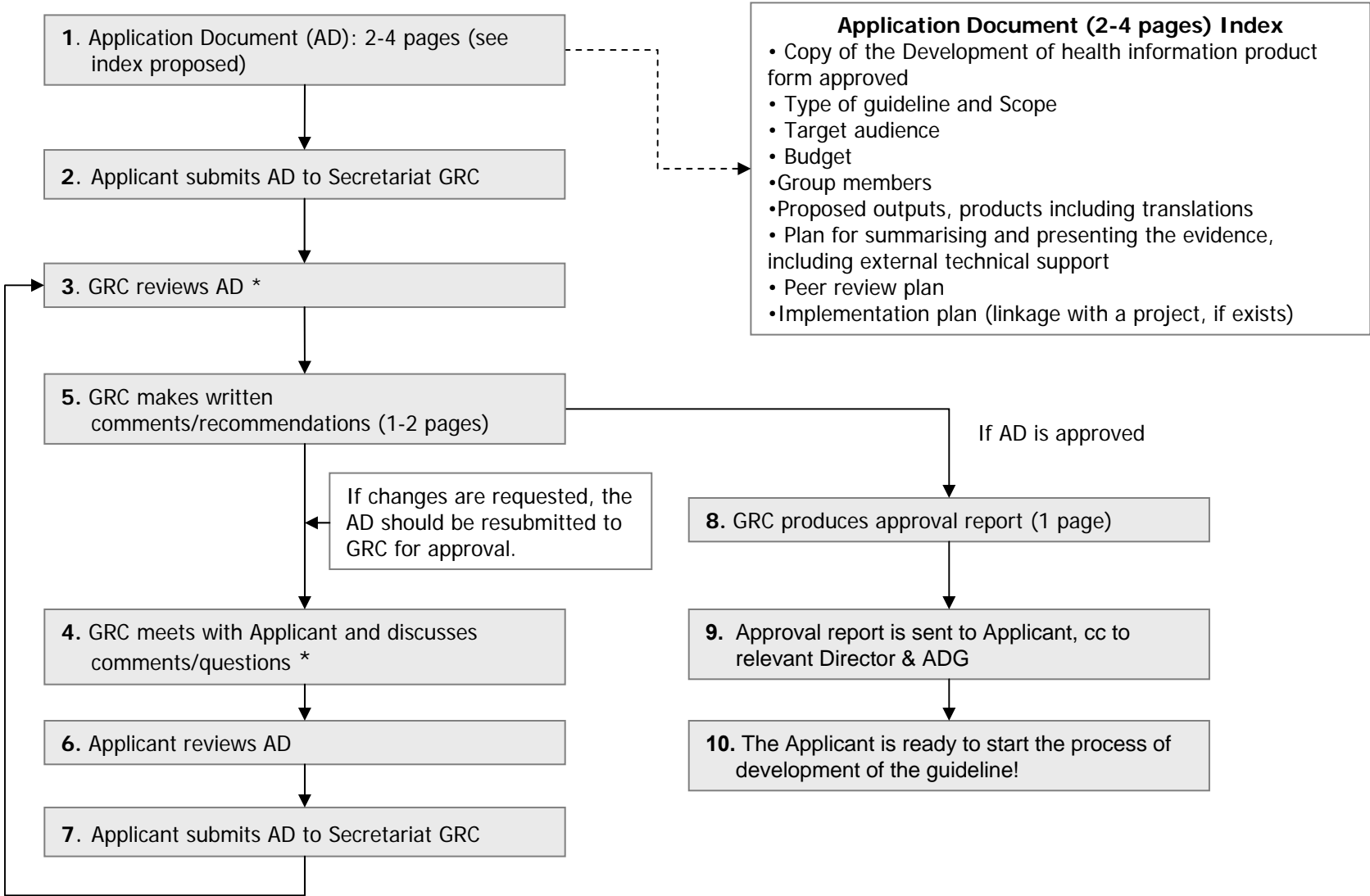
GRC Secretariat
Throughout the process of production of a guideline, the WHO Department can access the resources provided by the GRC Secretariat.

R
E
S
O
U
R
C
E
S



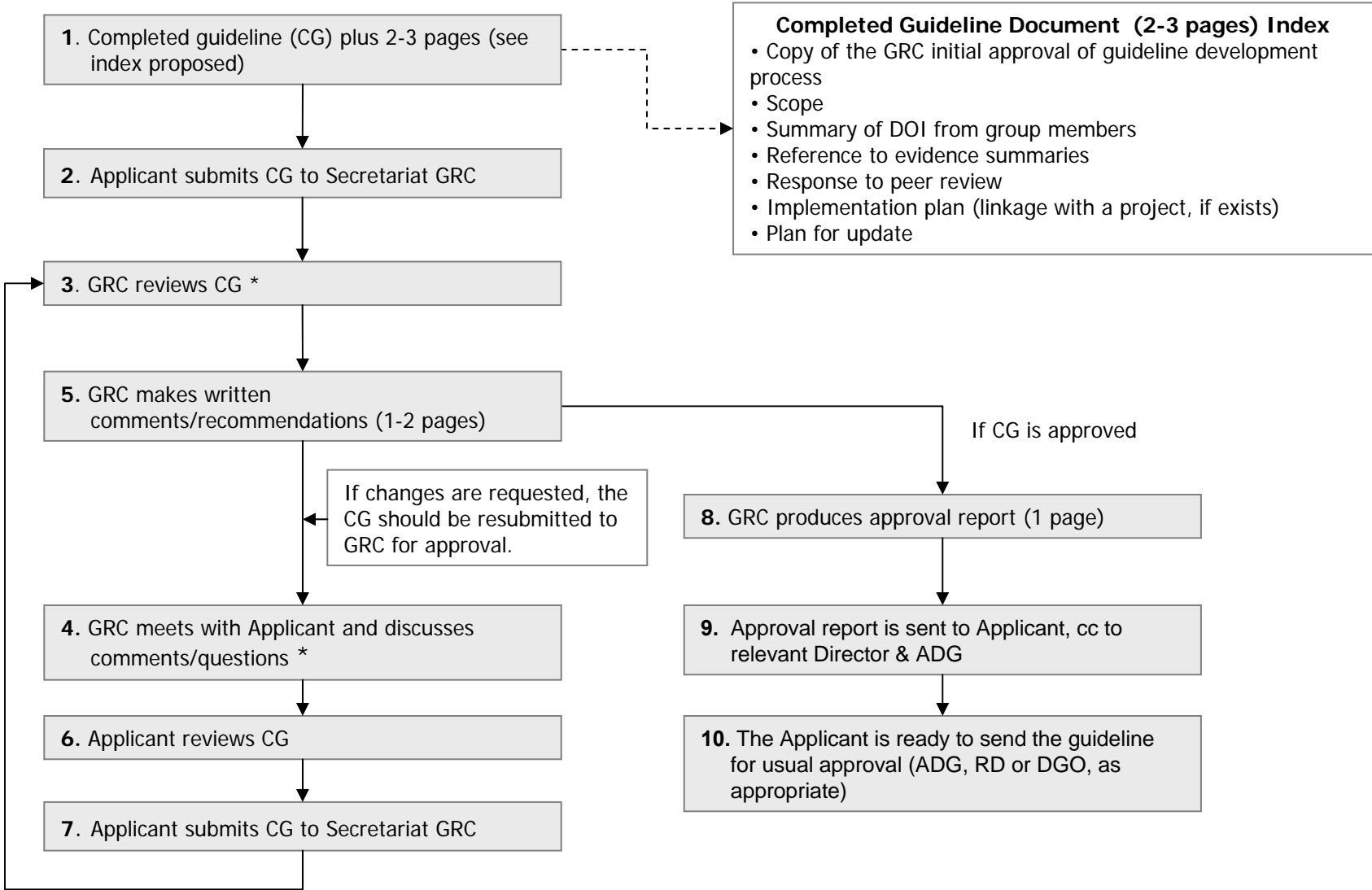
- Advice and support from the GRC Secretariat
- Advice and support from members of the GRC
- Advice and support from WHO Collaborating Centres
- Advice and support from GRC through WHO list of technical expert
- Advice and support from external experts on guideline production

Initial approval flow-chart for WHO guidelines



* Evaluation and discussion could require a meeting with the GRC and some technical support from GRC Secretariat. Methodological support to the group for framing, formulating the questions and revising the evidence could be offered.

Final approval flow-chart for WHO guidelines



* Evaluation and discussion could require a meeting with the GRC and some technical support from GRC Secretariat. Methodological support to the group for framing, formulating the questions and revising the evidence could be offered as methodological support.



WHO Standards for guidelines

**Reporting, process and use of
evidence**



**World Health
Organization**

Title, responsible person, WHO Department
- responsible of the clearance process, WHO Departments involved, CC involved,

1. Scoping the document: reasons for choosing the topic, problems with existing guidelines, variations and gaps,

2. Group composition (or consultations)

3. Conflict of interest

4. Formulations of the questions and choice of the relevant outcomes

5. Evidence retrieval, evaluation and synthesis (balance sheet, evidence table)

6. Benefit/risk profile: integrating evidence with values and preferences, equity and costs

7. Formulation of the recommendations

8. Implementation and evaluation of impact

9. Research needs or areas of further research

10. Peer-review process and updating

Reporting standard and process

Standards for evidence: GRADE system

Reporting standard and process

Conflict of interest sample

Dr N.C. reported being an investigator on trials for GlaxoSmithKline, Quintiles, Uriach and Biomarin but not any products or related products to those being considered at the meeting, and also holding shares in Biota. He, therefore, excluded himself from discussion of the late item on antivirals.

Dr M.R. reported having been a consultant for Roche about drug research and development and is currently a member of a data safety and monitoring board for them; receiving royalties through the NIH on the use of gossypol for cancer, being a consultant to several start up companies none of which have products on the market. As there were no products related to any of these items on the agenda no action was required.

Dr A.F. reported a family member being an employee of Merck, Sharpe and Dohme, Brazil. He, therefore, excluded himself from review or discussion of the product applications from Merck on this agenda.



World Health
Organization



Standards for evidence



World Health
Organization

Practicalities

- **Synthesis of all available evidence**
- **Formal assessment of quality of evidence**
- **Evidence summaries for group meetings using standard template**



Practicalities, cont'd

- **Consideration of resource use and costs**
- **Link evidence to recommendations, explaining reasons for judgements**



World Health
Organization

**System for assessing evidence for interventions:
GRADE (Grading of Recommendations Assessment,
Development and Evaluation)**

Quality of evidence

The extent to which one can be confident that an estimate of effect or association is correct.

Suggested categories:

High

Moderate

Low

Very low



**World Health
Organization**

Quality of evidence

Table 2 : GRADE quality assessment criteria

Quality of evidence	Study design	Lower if *	Higher if *
High	Randomized trial	Study quality: -1 Serious limitations -2 Very serious limitations	Strong association: +1 Strong, no plausible confounders, consistent and direct evidence**
Moderate			
Low	Observational study	-1 Important inconsistency	+2 Very strong, no major threats to validity and direct evidence***
Very low	Any other evidence	Directness: -1 Some uncertainty -2 Major uncertainty -1 Sparse data -1 High probability of Reporting bias	+1 Evidence of a Dose response gradient +1 All plausible confounders would have reduced the effect

* 1 = move up or down one grade (for example from high to intermediate)

2 = move up or down two grades (for example from high to low)

** A statistically significant relative risk of >2 (< 0.5), based on consistent evidence from two or more observational studies, with no plausible confounders.

*** A statistically significant relative risk of > 5 (< 0.2) based on direct evidence with no major threats to validity.

QUESTION: Should active management of the third stage of labour be used by skilled providers for all women to prevent postpartum hemorrhage (PPH)?

Quality assessment					
No of studies (Ref)	Design	Limitations	Consistency	Directness	Other considerations
Benefits:					
Maternal deaths					
0	-	-	-	-	-
Admission to intensive care unit					
0	-	-	-	-	-
Blood loss \geq 500 ml					
4 PW 00 ¹ Ad 97 Br 88 Du 90 Hi 98	RCT	serious limitation ² ,3,17 -1	no important inconsistency	some uncertainty about directness ^{4,5} -1	none
Blood loss \geq 1000 ml					
4 PW 00 ¹ Ad 97 Br 88 Du 90 Hi 98	RCT	serious limitation ² ,3,17 -1	no important inconsistency	some uncertainty about directness ^{4,5} -1	none

Recommendations versus evidence

- **Recommendations are judgements**
 - **Quality of evidence**
 - **Trade off between benefits and harms**
 - **Costs**
 - **Values and preferences**



Why bother about grading?

- **People draw conclusions about the**
 - quality of evidence
 - strength of recommendations
- **Systematic and explicit approaches can help**
 - protect against errors
 - resolve disagreements
 - facilitate critical appraisal
 - communicate information



Strength of a recommendation

Although the degree of confidence is a continuum, two categories are used: strong and weak.

A **strong recommendation** is one for which the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.

A **weak recommendation** is one for which the panel concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is not confident about these trade-offs. Reasons for not being confident can include:

- absence of high quality evidence;
- presence of imprecise estimates of benefits or harms;
- uncertainty or variation in how different individuals value the outcomes;
- small benefits;
- the benefits may not be worth the costs (including the costs of implementing the recommendation).



World Health
Organization

Strength of a recommendation

Strong vs. weak?

Examples of implications of a strong recommendation are:

- **For patients:** Most people in your situation would want the recommended course of action and only a small proportion would not.
- **For clinicians:** Most patients should receive the recommended course of action. Adherence to this recommendation is a reasonable measure of good quality care.
- **For policy-makers:** The recommendation can be adapted as a policy in most situations. Quality initiatives could use this recommendation to measure variations in quality.

Examples of implications of a weak recommendation are:

- **For patients:** The majority of people in your situation would want the recommended course of action, but many would not.
- **For clinicians:** Be prepared to help patients to make a decision that is consistent with their own values.
- **For policy-makers:** There is a need for substantial debate and involvement of stakeholders.



World Health
Organization

Strength of a recommendation

Strong vs weak?

- **Strong/weak**
- **Strong/conditional**
- **Strong/qualified**



For assistance, advice, and further information

■ Guidelines HELP CLINIC

- Thursdays, 1400 to 1600, Rooms 4336 and 4341
- GRC Secretariat contacts:
- Dr Faith McLellan mclellanf@who.int
- Dr Gunn Vist vistg@who.int
- Ms Silke Walleser wallesers@who.int



World Health
Organization