

USER GUIDE FOR THE WHO RISK BASED DECISION SUPPORT TOOL FOR BLOOD SAFETY

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Introduction

This user guide was written as an introduction for the use of the WHO Decision Support Tool for Blood Safety. This tool is provided in the form of a Microsoft Excel workbook that allows a structured quantitative and qualitative assessment of various safety interventions to mitigate the risk of infectious disease transmission by blood transfusion.

This user guide is part of a series of three documents (User Guide, User Manual and Case Study), which we recommend reading in this order before accessing and using the tool itself.

The Excel workbook was initially developed as a prototype for the development of an MCDA (Multi-Criteria Decision Analysis) decision support tool for blood safety interventions, but is presented here as a full working model, be it with restricted functionality to enhance its usability. Nonetheless, we hope the tool in its current form will be useful to support the decision making concerning different interventions possible (e.g. screening tests, pathogen reduction technology) to improve blood transfusion safety.

In this document, we will start with a brief introduction to risk-based decision making and will then link this process to the structure and operation of the tool. Next, in the case study document we will discuss the data required, the analyses performed, and outcomes provided by the tool in more detail, as well as providing a discussion on how to interpret various outcomes presented.

We hope that this tool will support you in identifying the most suitable safety intervention for your blood supply and that it will help you in communicating the support for the decisions made.

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Risk-based decision making

Risk-based decision-making concerns the selection of mitigating interventions from a set of candidate interventions to prevent the occurrence (or reduce the probability thereof) of one or more undesired outcomes. All relevant information concerning the occurrence and possibility of one or more outcomes are organized into a broad, orderly structure that helps decision-makers make more informed management choices. When applied to blood safety, this is usually a complex and multi-factorial process involving multiple (stakeholder) parties with different interests and responsibilities. Within the blood transfusion community, the Alliance of Blood Operators (ABO) has developed a [Risk Based Decision Making Framework](#) that addresses various elements of this process, specifically for blood safety.

There is a set of generic elements that can be found in any risk-based decision-making process. These would be comprised of:

1. Problem formulation (define decision context)
2. Define outcomes (favorable / unfavorable effects)
3. Describe safety interventions
4. Assess consequences using reference data ('effects table')
5. Explore trade-offs (benefit-risk balance, outcome importance)
6. Address uncertainty
7. Risk attitude(s) (may be different for different stakeholders)
8. Linked decisions (consistency)
9. Summary of findings

For many practical applications related to blood safety, like the decision to select the most appropriate screening test to reduce the risk of transmission of an infectious disease by blood transfusion, the first few elements are well known. For instance, for the prevention of HIV transmission, the problem formulation (step 1), the outcomes (step 2), and viable safety interventions (step 3) are well known. The difficulty in the decision-making process lies (to some extent) in assessing the consequences (step 4), but most importantly in balancing the perceived impact and trade-offs of various strategies (steps 5-7).

To support the decision-making process with respect to those steps specifically, the WHO Decision Support Tool for Blood Safety was developed.

Structure of the WHO Decision Support Tool for Blood Safety

The WHO Decision Support Tool for Blood Safety consists of six parts (the colors correspond to the colors of the corresponding tabs in the workbook):

- 1) Description of the interventions
- 2) Input of model parameters
- 3) Safety interventions & Outcomes table
- 4) Bar, spider and cost-effectiveness plots
- 5) MCDA assessment
- 6) Qualitative "Step-By-Step" assessment



The core of the decision support tool is the Safety interventions & Outcomes table. This is a table with on the vertical axis various safety interventions and on the horizontal axis various outcomes are shown (see Table 1 below). This format provides a tangible and concise overview of various risk management alternatives and the implications of their implementation.

In the example in Table 1, five optional blood safety interventions are given: (1) no testing, (2) screening with a rapid serologic test, (3) screening with a conventional laboratory-based serologic test, (4) NAT testing, and (5) pathogen reduction without testing. The outcomes listed are: (1) the total net costs, (2) the annual number of deaths, (3) the annual cost of the intervention, (4) the annual number of products lost, (5) the technological complexity of the intervention, and (6) the cost-effectiveness (in terms of US\$ per death prevented). Note that the numbers in the cells are contrived for purposes of illustration but are based on a model of interventions for HIV.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Technological complexity	Cost-effectiveness [US\$ per death prevented]
No testing	Baseline situation where no testing is performed	162,000	189	0	0	Low	-
Rapid serologic testing	Screening of all or part of all blood donations	117,840	98	33,600	2,352	Low	-487
Laboratory serological testing	Screening of all or part of all blood donations	212,520	96	129,900	412	Low	546
NAT testing	Screening of all or part of all blood donations	1,233,081	95	1,152,000	88	High	11,346
Pathogen Reduction	Treatment of all or part of all blood donations with PR	689,100	104	600,000	1,500	Medium	6,198

Table 1: Example of a “Safety interventions & Outcomes” table

The outcomes provided in Table 1 may be considered the main drivers for a decision related to the implementation of a blood safety intervention. These include total costs, costs of screening (or treatment), number of deaths (prevented), the number of products lost, the suitability of the technology for the blood supply considered (summarized as the level technological complexity), and the cost-effectiveness in terms of US\$ per death prevented.

It was decided that the tool in its current form would be pre-set for a selection of various screening tests and pathogen reduction technology. These will be described later in this user guide in more detail. However, if one would like to change the underlying models and assessments this is very well possible. The fact that the tool is implemented in the flexible Microsoft Excel environment, allows a more advanced user to change various tables and inputs as desired. All worksheets are protected to prevent accidental changes. However, worksheets can be easily unprotected by the user without entering a password if so required.

Part 1: Description of interventions

On this worksheet in the Excel workbook, the description of five optional safety interventions (as shown in Table 1) and associated outcomes can be changed. The scope of each of the safety interventions and associated outcomes and should remain unchanged, as the underlying models which calculate various outcomes are fixed. However, the details of their descriptions may be

changed. For instance, when opening the tool, three screening tests specific for HIV are indicated. Their descriptions may be changed to that of any alternative test (for instance for a different virus), but only such that the calculated risks remain a correct reflection of the intervention indicated. The same holds for the description for the columns which contain the outcomes considered.

The first safety intervention is labelled the 'no screening' option. This first option should contain the reference option for which the outcomes will be used as a reference for the cost-effectiveness calculations for all other options. Also, options 2, 3 and 4 refer to screening tests, whereas option 5 refers to a (pathogen reduction) treatment intervention.

Part 2: Input Values

On this worksheet, a set of general as well as specific input parameters per safety intervention can be provided. These parameters are used for calculating outcomes that are presented in the Safety interventions & Outcomes table seen on the "Quantitative estimates" worksheet.

The estimates shown in this table are based on a limited set of input parameters and some basic assumptions. These concern:

- Total number of donations made within the blood establishment
- Proportion of active infections among donors (prevalence of infection)
- Characteristics of the screening test (sensitivity/specificity and costs)
- Pathogen reduction effectivity, costs and blood product loss (if applicable)
- Coverage rate of screening when implemented
- Proportion of immune recipients
- Impact of disease on the patient (mortality rate)
- Cost of treatment

In addition to point estimates for each parameter, a range of viable input values is required for the sensitivity analysis provided on the "Sensitivity assessment" worksheet as part of the MCDA assessment (Part 5b). This range is defined by a minimum and a maximum value.

Part 3: Quantitative estimates

This worksheet contains quantitative estimates for each outcome of each safety intervention as shown in Table 1. The quantitative estimates are based on the parameter point estimates entered on the "Input values" worksheet. Note that for each safety intervention, a qualitative indication of the level of technological complexity ('Low', 'Medium' or 'High') may be assigned. For each outcome, a threshold value can be set that will be shown on various charts. This might represent the maximum budget available or the maximum number of deaths considered acceptable.

For each cell of the Safety interventions & Outcomes table, when selected, the formula that is applied for calculating the corresponding estimate will be shown in an easy-to-interpret manner. This allows the user to review, and, if necessary, adapt the calculations performed.

The following formulae are implemented for the calculation of various outcomes:

Outcome	Calculations performed
Annual cost of screening	$\text{NrDonations} * \text{Coverage} * \text{CostsOfScreening}$
Annual number of products lost	For all screening tests: $=\text{NrDonations} * \text{Coverage} * (1 - \text{DonorPrevalence}) * (1 - \text{ScreeningSpecificity})$ For PRT option: $=\text{NrDonations} * \text{Coverage} * \text{ProductionLoss}$
Annual number of deaths	For 'No screening' option: $=\text{NrDonations} * \text{DonorPrevalence} * (1 - \text{ProportionImmuneRecipients}) * \text{MortalityRate}$ For all other interventions: $=\text{NrDonations} * \text{DonorPrevalence} * (1 - \text{ProportionImmuneRecipients}) * (\text{Coverage} * (1 - \text{ScreeningEffectiveness}) + (1 - \text{Coverage})) * \text{MortalityRate}$
Total net costs	For 'No screening' option: $\text{NrDonations} * \text{DonorPrevalence} * (1 - \text{ProportionImmuneRecipients}) * \text{CostsOfTreatment}$ For all other interventions: $=\text{NrDonations} * \text{Coverage} * \text{CostsOfScreening} + \text{NrDonations} * \text{DonorPrevalence} * (1 - \text{ProportionImmuneRecipients}) * (\text{Coverage} * (1 - \text{ScreeningEffectiveness}) + (1 - \text{Coverage})) * \text{CostsOfTreatment}$
Cost-effectiveness	$= (\text{Total net costs [intervention considered]} - \text{Total net costs ['No screening' option]}) / (\text{Annual number of deaths ['No screening' option]} - \text{Annual number of deaths [intervention considered]})$

Part 4: Bar, spider and cost-effectiveness plots

Different chart types (bar chart, stacked bar chart and a spider plot) are provided to visualize the relative contribution of various options to each of the defined outcomes. This should help provide insights into the strengths and weaknesses of each of the options. In the plots, any negative values (which these plots are unable to accommodate) are indicated with deviating patterns: stripes in the bar charts and dots in the spider plot.

In the graphs, the quantitative estimates from Table 1 are shown for each outcome, scaled to the maximum value (or sum of values). Next to the bar and spider plots, a cost-effectiveness plot ("Costs vs Effects plot") is provided which shows the costs and effects for each of the options relative the first option, which in this case is the 'No Screening' option.

Part 5a: MCDA (Multi-Criteria Decision Analysis) assessment

The difficulty when comparing various safety interventions is that each of the options, when implemented, will have different consequences. There will never be one option that will have the most favorable outcome of all alternatives considered for all outcomes. Where one option will result in a more effective reduction of the number of fatalities, its costs will be higher. Where one option the technology applied will be less complex and hence the process will be more robust, the false positive error rate and therefore the number of discarded blood products will be higher. So how to balance these differences in outcomes?

This so-called Multi-Criteria Decision Analysis (MCDA) is a field of research on its own and many approaches exist to solving this (difficult!) problem. The simplest approach, however, is by providing each of the individual outcomes a weight to represent its relative importance. For each option, each of the individual outcome estimates is multiplied by its outcome weight to obtain a weighted score. Finally, all the weighted scores are summed up per option to obtain a final MCDA score. As all of the outcomes have negative consequences (more fatalities, more disease, more money spent), the option with the lowest overall score is the preferred option.

In Table 2, an MCDA score table is shown that is based on the outcomes from Table 1. For each outcome a weight is provided. Based on this weight for each individual outcome a score is calculated, as well as the total MCDA equivalent score per option. Note that for the qualitative outcomes the scores are obtained by summation of the appropriate weights instead of by multiplication. The lower the score, the more favorable the option.

The weights map individual outcomes on a common denominator (an MCDA equivalent), which is very often a monetary unit. So, a weight of 1 for the outcome 'Total net costs' indicates that the outcome is expressed in US\$. In that case, as the MCDA equivalent is expressed in US dollars, a weight of 150.000 for 'Annual number of deaths' would indicate that the monetary equivalent for one death would be 150.000 US\$.

One way to obtain meaningful and applicable values for the weights is to imagine for which value of the two outcomes one would be indifferent as to which to prefer. For instance, in the example above, one should be indifferent to either spending 150.000 US\$ or accepting one additional fatality. If one is indifferent to spending more money in order to prevent one additional fatality, this means that the weight of 150.000 US\$ is too low.

Note that an evaluation based on quantified outcomes and (linearly applied) weights is a very simple approach to balancing various outcomes, which might not do justice to the complexity of the interpretation of these outcomes by the user. One might be willing to spend 150.000 US\$ to prevent one fatality, but not 1.500.000 US\$ to prevent 10 fatalities. Alternative and/or additional considerations may therefore be relevant that are not facilitated by this kind of assessment.

Optional Safety Interventions		Total net costs [US\$]	Annual number of deaths [US\$]	Annual cost of the intervention [US\$]	Annual number of products lost [US\$]	Technological complexity [US\$]	Overall MCDA score
<i>Option reference:</i>	<i>Description:</i>	Values provided (with the exception of the qualitative outcome) are the product of the column weight (bottom row) and the corresponding values provided on the 'Quantitative estimates' worksheet.					Overall score is calculated as the sum of all weighted outcomes presented. These are the product of quantitative estimates and outcome weights
No testing	Baseline situation where no testing is performed	162,000	27,972,000	0	0	0	28,134,000
Rapid serologic testing	Screening of all or part of all blood donations	117,840	14,545,440	0	348,096	0	15,011,376
Laboratory serological testing	Screening of all or part of all blood donations	212,520	14,265,720	0	60,917	0	14,539,157
NAT testing	Screening of all or part of all blood donations	1,233,081	13,999,986	0	13,054	300,000	15,546,121
Pathogen Reduction	Treatment of all or part of all blood donations with PR technology	689,100	15,384,600	0	222,000	100,000	16,395,700
Weights:		1	148,000	0	148	100,000	
						300,000	

Table 2: MCDA score table, the data are derived from the example shown in Table 1

Part 5b: MCDA sensitivity assessment

The MCDA assessment provides an “optimal” decision by balancing various outcomes. It uses the outcomes calculated using the input values provided and the weights for each of the individual outcomes. However, as the point estimates used in the MCDA assessment may not be completely fixed and possibly also subject to uncertainty, the question arises as to how robust this optimal decision is, and if the optimal decision will change when individual parameters change.

To help provide this insight, on the ‘Input Values’ worksheet (as well as on the ‘MCDA Sensitivity assessment’ worksheet in the Excel workbook), in addition to point estimates for each input value a range of viable values is provided. This range is defined by a minimum and maximum viable value. Within the viable range of values the optimal decision, the decision with the lowest MCDA score, may change. Therefore, for each parameter within the range of viable input values, the values for which the optimal decision changes, the ‘changepoints’ are calculated. These values are derived by varying the value of that parameter while holding all other parameters fixed at their point estimates. For each of the changepoints the change in the preferred safety interventions is given as well. In the changepoint descriptions, numbers are used to reference the optional safety interventions. The legend for the numbers used for various safety interventions is given at the bottom left of the worksheet.

Further, this worksheet contains a copy of all the input and range definitions found on the “Input Values” worksheet. In addition, the weights from the MCDA assessment are listed here and for these a range of viable values (Min and Max values) can be entered here.

Current preferred option: Laboratory serological testing

Model parameter description	Value	Units	Min Value	Max Value	Changepoints
Number of donations	60,000	-	60,000	60,000	
Prevalence among donors	2%	-	1%	20%	At 10% a change from 3 to 4;
Proportion recipients not affected	10%	-	1%	20%	
Coverage rate for the safety intervention	50%	-	50%	100%	
Costs of treatment (per patient)	150.00	US\$	100.00	200.00	
Mortality rate of infected patients	17.5%	-	10%	20%	
Sensitivity of Rapid serologic testing	96.0%	-	65%	99.99%	At 99.4% a change from 3 to 2;
Specificity of Rapid serologic testing	92.0%	-	80.0%	99.99%	
Costs of Rapid serologic testing (per donation)	1.12	US\$	0.50	2.50	
Sensitivity of Laboratory serological testing	98.0%	-	75%	99.99%	At 94.6% a change from 2 to 3;
Specificity of Laboratory serological testing	98.6%	-	98.0%	99.99%	
Costs of Laboratory serological testing (per don.)	4.33	US\$	3.25	5.40	
Sensitivity of NAT testing	99.9%	-	99.4%	99.99%	
Specificity of NAT testing	99.7%	-	99.6%	99.80%	
Costs of NAT testing (per donation)	38.40	US\$	24.90	59.50	
Effectivity of Pathogen Reduction	90.0%	-	75%	99.99%	
Costs of Pathogen Reduction (per donation)	20.00	US\$	15.00	30.00	
Production loss of Pathogen Reduction	5.0%	-	3%	7%	
MCDA weights for					
Total net costs	1.00	-	1	1	
Annual number of deaths	148,000	US\$/death	0	1,500,000	At 1.203 a change from 1 to 3; At 708.830 a change from 3 to 4;
Annual cost of the intervention	0	-	0	0	
Annual number of products lost	148	US\$/product	0	5,000	At 3.262 a change from 3 to 4;
Medium Technological complexity	100,000	US\$	0	1,500,000	
High Technological complexity	300,000	US\$	0	1,500,000	

Risk management options considered:

- 1: No testing
- 2: Rapid serologic testing
- 3: Laboratory serological testing
- 4: NAT testing
- 5: Pathogen Reduction

Table 3: MCDA sensitivity analysis for the example from tables 1 and 2. Note that the numbered options indicated at the changepoint descriptions are indicated at the bottom of the table under 'Risk management options considered'. Note that the MCDA weight for the 'Annual number of products lost' shows multiple changepoints

Step 6: Qualitative Step-by-step assessment

As previously mentioned, there are many approaches in selecting the best option in a multi-criteria decision problem. There are various drawbacks to the linear weighting approach described above. Next to the fact that the weights often vary according to the actual size of the outcome (so applying linear weights would not properly reflect the perceived balance of preferences), interactions between various outcomes may also affect perceived preferences. Hence, the model also provides a fully qualitative approach where the best option is directly selected on basis of the estimated outcomes. Support for the preference is formulated in terms of a description of the argumentation and underlying considerations. This allows consideration of various aspects that may apply, but that are not captured or reflected in the outcomes directly. To support the thought process, we created a step-by-step assessment in which the best option is initially selected presuming that only the two most relevant outcomes would be applicable. This could for instance be: the annual cost of

screening and the annual number of deaths. The argumentation and underlying considerations leading to the preference are made explicit on the worksheet. Next, the third most important outcome is added and the impact of this additional criterion on the previous assessment is made explicit by updating the argumentation and considerations for the currently perceived preference. This process is repeated until all (relevant) criteria are included. In Table 4, the tables for the first two steps of a step-by-step assessment for the example from the previous tables are shown (with the column with considerations left blank).

After setting the order of importance for each of the criteria by the user, the set of evaluation sheets will be generated on which the user can fill out the considerations for the selection of a preferred option at each step of the assessment.

The advantage of the step-by-step assessment is that in addition to the “hard” quantitative outcomes, other considerations may be included and made explicit in the assessment as well. Such a refinement may result in a more balanced and acceptable selection than one derived from a purely theoretical/quantitative analysis of outcomes alone.

Optional Safety Interventions		Annual number of deaths [-]	Annual cost of the intervention [US\$]	Comments / Considerations
Option reference:	Description:	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	
No testing	Baseline situation where no testing is performed	189	0	
Rapid serologic testing	Screening of all or part of all blood donations	98	33,600	
Laboratory serological testing	Screening of all or part of all blood donations	96	129,900	
NAT testing	Screening of all or part of all blood donations	95	1,152,000	
Pathogen Reduction	Treatment of all or part of all blood donations with PR technology	104	600,000	

Table 4a: First step in the step-by-step assessment for the example from the previous tables, considering two outcomes only.

Optional Safety Interventions		Annual number of deaths [-]	Annual cost of the intervention [US\$]	Annual number of products lost	Comments / Considerations
Option reference:	Description:	Total number of deaths given that the safety intervention indicated is implemented	Includes the total cost of the intervention (including costs of personnel, equipment training etcetera)	The proportion of blood products that are discarded/lost due to the safety intervention applied	
No testing	Baseline situation where no testing is performed	189	0	0	
Rapid serologic testing	Screening of all or part of all blood donations	98	33,600	2,352	
Laboratory serological testing	Screening of all or part of all blood donations	96	129,900	412	
NAT testing	Screening of all or part of all blood donations	95	1,152,000	88	
Pathogen Reduction	Treatment of all or part of all blood donations with PR technology	104	600,000	1,500	

Table 4b: Second step in the step-by-step assessment for the example from the previous tables, considering two outcomes only.