

## Risk-Benefit Analysis: Recommendation 1<sup>1</sup>

<p><b>Existing recommendations:</b>  <i>Exclusive breastfeeding is recommended for HIV-infected mothers for the first 6 months of life [unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time].</i></p>	
<p><b>Proposed recommendations:</b>                  Mothers known to be HIV-infected who:</p> <ul style="list-style-type: none"> <li>• are established on lifelong ART, <b>OR</b></li> <li>• are known to have CD4 counts greater than 350, <b>OR</b></li> <li>• whose CD4 count is unknown and do not fulfil clinical criteria for ART,</li> </ul> <p>1a. should .... exclusively breastfeed their infant for the first 6 months of life, <b>and</b>,</p>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Moderate</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span></p> <p><b>Systematic review reported decreased HIV transmission associated with exclusive breastfeeding compared to mixed feeding in populations not on any ARV/ART intervention (Coovadia et al., 2007; Iliff et al., 2005; Kuhn et al., 2008);</b></p> <p><b>Exclusive breastfeeding also associated with reduced mortality in HIV-exposed infants compared to mixed feeding;</b></p> <p><b>Indirect evidence:</b></p> <p><b>High quality evidence from non-HIV settings (not presented) that, especially in resource-limited settings, mixed feeding and non-breastfeeding are associated with increased morbidity and mortality (WHO 2000; Bahl et al., 2005).</b></p>
<p><b>Benefits/desired effects</b></p>	<ol style="list-style-type: none"> <li>1. Reduces risk of HIV transmission compared to mixed breastfeeding.</li> <li>2. Reduces risk of mortality from other non-HIV infectious diseases.</li> <li>3. Breastfeeding induces lactational amenorrhoea.</li> </ol>
<p><b>Risks/undesired effects</b></p>	<p><i>Low persisting risk of HIV transmission to the infant in the context of prophylaxis or treatment versus no breastfeeding</i></p>
<p><b>Values/Acceptability</b></p>	<p><u>In favour:</u></p> <p><i>Transmission risk would be further diminished in presence of ARV interventions;</i></p> <p><i>Follows international recommendations for all other infants;</i></p> <p><i>Culturally acceptable;</i></p> <p><i>Additional developmental and other health benefits for infants who do not become HIV infected;</i></p> <p><i>Reduced stigma and discrimination compared to formula feeding in many settings, as most mothers would be breastfeeding.</i></p> <p><u>Against:</u></p> <p><i>Exclusive breastfeeding (EBF) not commonly practiced;</i></p> <p><i>Medical establishment does not always believe in sufficiency of EBF;</i></p> <p><i>Perceived as double standard versus care offered in well-resourced settings;</i></p> <p><i>By not including a replacement feeding option immediately beside the breastfeeding approach, it may be seen as denying women's right to choose formula feeding;</i></p> <p><i>May inadvertently imply that these three groups of mothers are equally</i></p>

<sup>1</sup> This recommendation was numbered 1a when first presented at the meeting.

	<i>likely to transmit HIV to their infants if breastfeeding.</i>
<b>Costs</b> <i>(consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</i>	<i>Minimal cost implication for health system if no additional counselling and support offered compared to replacement feeding; In HIV-uninfected populations, modelling (Lancet series) demonstrated promotion of EBF to be cost-effective; In HIV-exposed infants, cost-effective depending on model of intervention and if counselling and support extended to entire population (Desmond et al., 2008)</i>
<b>Feasibility</b>	<i>Promotion and support of EBF effective if health system commitment present. Several examples from non-HIV settings and HIV research sites demonstrating effectiveness. Little experience in implementing new PMTCT ART/ARV recommendations. Need to ensure appropriate guidance and support for women who need extended leave for EBF (economic pressure to return to work early).</i>
<b>Final recommendation</b>	<b>Mothers known to be HIV-infected should be provided with life-long antiretroviral therapy or antiretroviral prophylaxis interventions to reduce HIV transmission through breastfeeding according to WHO recommendations.</b>
<b>Strength of recommendation</b>	Strong, <b>or</b> Conditional, <b>or</b> Qualified, <b>or</b> Weak <i>Strong</i>
<b>Quality of evidence that informs recommendation</b>	<b>High / Moderate / Low / Very low</b> <b>Moderate</b>
<b>Comments justifying recommendation</b>	This recommendation is based on the revised WHO recommendations for antiretroviral therapy or prophylaxis to reduce HIV transmission, including through breastfeeding. Including the recommendation in this document emphasizes the care that should be available to all mothers known to be infected with HIV.
<b>Gaps, research needs, comments</b>	<i>More implementation research needed. How often is counselling needed? How effective is it? How best to communicate this recommendation? Effectiveness of recommendation? Impact on infant feeding practice? Modelling of impact on recommendation. How to best communicate changes of guidelines to women/mothers and countries?</i>

## Risk-Benefit Analysis: Recommendation 2<sup>2</sup>.

<p><b>Existing recommendations:</b>  <i>At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed. All breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided</i></p>	
<p><b>Proposed recommendations:</b></p> <p><i>These mothers should follow the WHO recommended ART / ARV interventions to reduce postnatal transmission while breastfeeding and</i></p> <p><b><u>Option 1</u></b>  Continue breastfeeding until 12 months while introducing complementary foods at 6 months of age, <b>and</b>, after 12 months of age, all breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided.</p> <p><b><u>OR</u></b>  <b><u>Option 2</u></b>  Continue breastfeeding while introducing complementary foods at 6 months of age, <b>and</b>, stop all breastfeeding once a nutritionally adequate and safe diet without breast milk can be provided.</p>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Low</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span></p> <p><b><i>Systematic review provided minimal data to specifically inform the comparative advantage of breastfeeding for different time periods.</i></b></p> <p><b><i>Indirect evidence: Model suggested that continued breastfeeding until 12 months in combination with an ART/ARV intervention to the mother or infant to reduce postnatal transmission improves HIV survival in comparison to formula feeding interventions when implemented in programmatic settings.</i></b></p>
<p><b>Benefits/desired effects</b></p>	<p><i>ARV intervention to infant reduces risk of HIV transmission through breast milk, which should increase the likelihood of infant HIV-free survival; Breastfeeding until 12 months capitalizes on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection versus risk;</i></p> <p><i>Complementary feeds needed by all infants from 6 months onward.</i></p> <p><i>Reference to 'adequacy and safety' to emphasize their importance, especially when subsidiary products formulated, e.g. training courses and job aids.</i></p> <p><i>Easier to formulate nutritionally adequate and safe diet without breast milk for children from 12 months (compared to &lt;12 months), as the child can consume family diet at that point (however, family diet could still be lacking some nutrients).</i></p>
<p><b>Risks/undesired effects</b></p>	<p><i>Specifying a time at which breastfeeding by HIV-infected mothers is recommended to stop may push mothers who are unable to provide an adequate and safe replacement feed to inappropriately stop breastfeeding at 12 months despite their circumstances.</i></p> <p><i>Adherence to PMTCT regimens for mothers and babies.</i></p>
<p><b>Values/Acceptability</b></p>	<p><i>In favour:</i></p>

<sup>2</sup> This recommendation was numbered 1b when first presented at the meeting.

	<p><i>Specifying the time point until which breastfeeding by HIV-infected mothers should breastfeed gives greater clarity to health workers as to what to promote and support;</i></p> <p><i>A recommendation to continue breastfeeding to 12 months would avoid the complex issue of whether to recommend stopping breastfeeding between 6-12 months. Also reduces implication for health system to provide skilled counselling that is needed to assist mothers make appropriate decisions at about 6 months of age. Good programmatic data show that this counselling rarely takes place, and mothers make these decisions by themselves without significant input from health workers;</i></p> <p><i>Moderate evidence of increased serious morbidity and mortality when infants inappropriately stop breastfeeding between 6-12 months. Stopping after 12 months would be much simpler as infant will, by that time, be taking significant amounts of family foods and simpler to stop breastfeeding at this time relative to stopping at 6 months. Presently, ambiguity of recommendations and lack of clear guidance from national authorities has resulted in non governmental organizations and individual counsellors promoting stopping of breastfeeding at about 6 months without any assessment of home circumstances;</i></p> <p><i>Statement of introducing complementary feeding at 6 months explicitly included to clarify the need to introduce complementary foods in the context of HIV when, before 6 months of age, the introduction of foods other than breast milk is strongly dissuaded.</i></p> <p><u><i>Against:</i></u></p> <p><i>A recommendation for HIV-infected mothers may be misunderstood by the general community, and HIV-uninfected mothers may similarly stop breastfeeding at 12 months to the disadvantage of their infants.</i></p> <p><i>May be a hard message to reverse.</i></p>
<p><b>Costs</b> <i>(consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</i></p>	<p><i>Strong financial argument for mothers to breastfeed with ARV intervention versus provision of formula milk as PMTCT strategy;</i></p> <p><i>Ideally cost-saving for programmes that presently do provide formula feeds to reinvest those funds in improved counselling and ARV support to mothers or to promote and support improved infant feeding practices in entire community. Questionable whether this would happen.</i></p>
<p><b>Feasibility</b></p>	<p><i>Simplifying recommendations would assist implementation.</i></p> <p><i>Recommendations that would reduce the complexity of counselling would be a major advantage in terms of feasibility.</i></p> <p><i>Experience of health systems providing other HIV prevention and care interventions, e.g. formula milk and co-trimoxazole, have been very variable and hard to extrapolate to these proposed recommendations.</i></p> <p><i>Quality of diet (nutritional adequacy).</i></p> <p><i>Adherence (to ARV/ART drugs, to follow-up).</i></p>
<p><b>Final recommendation</b></p>	<p>Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life while introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast-milk can be provided.</p>
<p><b>Strength of recommendation</b></p>	<p>Strong, <b>or</b> Conditional, <b>or</b> Qualified, <b>or</b> Weak</p> <p>Strong</p>
<p><b>Quality of evidence that</b></p>	<p><b>High / Moderate / Low / Very low</b></p>

<p><b>informs recommendation</b></p>	<p><b><i>High for first 6 months; low for recommendation re 12 months</i></b></p>
<p><b>Comments justifying recommendation</b></p>	<p>The group identified the following key evidence</p> <ul style="list-style-type: none"> <li>• Systematic review reported decreased HIV transmission in first 6 months of infant life associated with exclusive breastfeeding (EBF) compared to mixed feeding in populations not on any ARV/ART intervention (Coovadia et al., 2007; Iliff et al., 2005; Kuhn et al., 2007);</li> <li>• Exclusive breastfeeding is also associated with reduced mortality over the first year of life in HIV-exposed infants compared to mixed feeding and replacement feeding in both research and programme settings, especially if inappropriately chosen by mothers (Mbori-Ngachi et al., 2001; Thior et al., 2006; Doherty et al., 2007).</li> </ul> <p>Additional indirect evidence:</p> <ul style="list-style-type: none"> <li>• High quality evidence from non-HIV settings that mixed feeding and non-breastfeeding are associated with increased morbidity and mortality (WHO, 2000; Bahl et al., 2005).</li> </ul> <p>Additional considerations that the group placed high value on:</p> <ul style="list-style-type: none"> <li>• Transmission risk would be further diminished in presence of ARV interventions;</li> <li>• Enabling breastfeeding in the presence of ARV interventions to continue to 12 months avoids many of the complexities associated with stopping breastfeeding and providing a safe and adequate diet without breast-milk to the infant 6-12 months of age. This was seen as a major advantage;</li> <li>• Additional developmental and other health benefits for infants who do not become HIV infected.</li> </ul> <p>The group recognized that the risk of HIV transmission continues for as long as the infant breastfeeds.</p> <p>The group reviewed modelling data that suggested that 12 months represents a reasonable cut-off for most HIV-infected mothers, capitalizing on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection versus risk;</p> <p>Data from non-HIV populations indicates that the survival benefits of breastfeeding decrease with age, especially after 12 months of life. However, for the HIV-uninfected mother there are many other health benefits to her infant if she continues breastfeeding until 24 months.</p> <p>A systematic review also examined the effect of prolonged breastfeeding on the health of mothers who are known to be HIV-infected. This review indicated that there was no clear evidence of harm to the mother if she continued breastfeeding. One report that did find increased mortality in breastfeeding mothers was in conflict with several others including one large meta-analysis that did not find this outcome.</p>
<p><b>Gaps, research needs, comments</b></p>	<p>Lack of evidence on relative benefits of continuing breastfeeding to 9-18 months (duration of breastfeeding).</p> <p>Implementation questions.</p>

	Nutritional questions.
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### Risk-Benefit Analysis: Recommendation 2<sup>3</sup>.

<p><b>Existing recommendations:</b>  <i>[HIV-infected] Women who need anti retrovirals (ARVs) for their own health should receive them.</i></p>	
<p><b>Proposed recommendations:</b>                  Mothers known to be HIV-infected and who are also known to be at high risk of transmitting HIV to their infants through breastfeeding i.e. found to have CD4 counts less than 350 or fulfil clinical eligibility criteria for ART, <b>and</b>,                  Who not yet on lifelong ART should:                  2a. Be started on ART immediately or, if the antenatal clinic does not have the resources then be referred for urgent initiation of ART, <b>and</b>,  <b>Option 1.</b>                  As per Recommendation #1 and Option 1 .  <b>OR</b>  <b>Option 2.</b>                  2b. provide either heat-treated breast milk or a safe replacement feed;                  2c. If neither of these are safe and feasible alternatives to breastfeeding then follow Recommendation #1.</p>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>High</b> (re. maternal ART)  <b>Low</b> (re. infant feeding elements) (High / Moderate / Low / Very low)  <b>Systematic review</b>  <b>Indirect evidence:</b></p>
<p><b>Benefits/desired effects</b></p>	<p><i>Improved survival for mothers fulfilling eligibility criteria for ART;                  Improved HIV free survival of infants born to this group of mothers.</i></p>
<p><b>Risks/undesired effects</b></p>	<p><i>Option 1. Increased risk of transmission if mother has not been on ART for long enough to suppress viral load. Late initiation of ART has greatest implication for peripartum transmission risks to infant. However, will also apply, even if to a lesser degree, to risk of HIV transmission through breastfeeding;                  Option 2. Increased risk of death from non-HIV infectious diseases and malnutrition, especially in countries that do not have health systems capable of supporting safe replacement feeding such as by providing reliable and prolonged supply of formula milk, safe water interventions and high quality counselling to reduce likelihood of unsafe formula milk preparation.</i></p>
<p><b>Values/Acceptability</b></p>	<p><b><u>In favour:</u></b>                  Option 1.                  Simplifies implementation - no special considerations needed for women on ART, regardless of time they have been on ART. This is especially so if PMTCT-ARV recommendations support use of ARV intervention to infant if mother has only recently initiated ART;                  Does not include need for health workers to assess and confirm duration of ART in order to classify which mothers fall into this group.                  Option 2.</p>

<sup>3</sup> The group decided to delete this Recommendation as the relevant issues were covered in Recommendation 1.

	<p>Addresses the high risk of transmission that these infants are exposed to. Heat treatment of breast milk could be viewed as a interim approach until viral suppression has been achieved. Then breastfeed as normal.</p> <p><u>Against:</u></p> <p>Option 1.</p> <p>Lack of nuance of recommendations for high risk mothers. ?Implications for credibility of recommendations and acceptability.</p> <p>Option 2.</p> <p>The increased transmission risk for these infants is mitigated with each week of ART taken by the mother (especially if taken antenatally) while the risk of serious morbidity and mortality associated with replacement feeding remains throughout, especially the first 12 months of life;</p> <p>Heat-treatment of breast milk is not widely understood as a safe option and would take considerable effort to familiarise and persuade health workers and mothers re. its potential use.</p> <p>Formula feeds are the only replacement feed that are adequately formulated nutritionally for the first 6 months of life. However, serious concerns about their safe use in settings that are anything other than ideal. Very hard to assess if circumstances are 'ideal'. Inappropriate usage of formula milk associated with high risk of death.</p>
<p><b>Costs</b> (consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</p>	<p>Similar significant financial savings if BF and ARVs implemented as per recommendation #1. However, cost-effectiveness considerations will be different for replacement feeding options as these mothers and infants represent higher transmission risk groups.</p>
<p><b>Feasibility</b></p>	<p>If Option 1 is decided, need to outline contingency for mothers who are too sick to BF and how therefore infant would be fed, especially in situations where formula feeds would be deemed unsafe due to environmental circumstances. Otherwise see feasibility considerations for Rec 1a.</p> <p>Feasibility of safely providing formula feeds highly dependent on environmental circumstances (High quality evidence).</p>
<p><b>Final recommendation</b></p>	<p>Included in Recommendation 1</p>
<p><b>Strength of recommendation</b></p>	<p>Strong, <u>or</u> Conditional, <u>or</u> Qualified, <u>or</u> Weak</p>
<p><b>Quality of evidence that informs recommendation</b></p>	<p><i>High / Moderate / Low / Very low</i></p>
<p><b>Comments justifying recommendation</b></p>	
<p><b>Gaps, research needs, comments</b></p>	

### Risk-Benefit Analysis: Recommendation 3<sup>4</sup>.

<p><b>Existing recommendations:</b>  <i>For HIV-infected women who choose to exclusively breastfeed, early cessation of breastfeeding (before six months) is no longer recommended, unless their situation changes and replacement feeding becomes AFASS.</i></p> <p><i>Abrupt or rapid cessation even at six months is not generally recommended because of possible negative effects on the mother and infant.</i></p>	
<p><b>Proposed recommendations:</b>                  Mothers known to be HIV-infected who decide to stop breastfeeding at any time should stop over a period of 3 days to 3 weeks. Stopping breastfeeding abruptly is not advisable</p>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Moderate</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span>  <b>Very low</b></p> <p><b>Systematic reviews:</b> <i>No data included in systematic review</i></p> <p><b>Indirect evidence:</b></p>
<p><b>Benefits/desired effects</b></p>	<p><i>Avoids the detrimental effects of rapidly stopping breastfeeding that have been reported in association with cessation over very short periods, e.g. 1-2 days, including serious morbidity and mortality in infants and increased breast health problems in mothers. (The evidence for this is not clear.) Facilitates promotion of breastfeeding.</i></p>
<p><b>Risks/undesired effects</b></p>	<p><i>Breastfeeding, especially in the absence of ARV interventions either to the mother or infant, will be viewed as having no risk and therefore no value in shortening the duration of breastfeeding and exposure to HIV. If a mother stops before 6 months, the duration of mixed feeding will be greater. Longer ART exposure for mother and infant.</i></p>
<p><b>Values/Acceptability</b></p>	<p><u><i>In favour:</i></u>  <i>Clarifies to health workers and mothers the approximate period over which stopping breastfeeding should be achieved by mothers with HIV infection.</i></p> <p><u><i>Against:</i></u>  <i>Mothers known to be HIV uninfected may adopt the same practice.</i></p>
<p><b>Costs</b>  <i>(consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis)</i></p>	<p><i>No cost difference compared with counsellors and mothers trying to implement very rapid cessation over 1-2 days.</i></p>
<p><b>Feasibility</b></p>	<p><i>Should assist counsellors and mothers to plan and implement cessation when the time is determined appropriate.</i></p>

<sup>4</sup> This recommendation was numbered 3a when first presented at the meeting.

<p><b>Final recommendation</b></p>	<p><i>Mothers known to be HIV-infected</i> who decide to stop breastfeeding at any time should stop gradually within one month. Mothers or infants who have been receiving ARV prophylaxis should continue prophylaxis for one week after breastfeeding is fully stopped. Stopping breastfeeding abruptly is not advisable.</p>
<p><b>Strength of recommendation</b></p>	<p>Strong, <u>or</u> Conditional, <u>or</u> Qualified, <u>or</u> Weak <i>Strong</i></p>
<p><b>Quality of evidence that informs recommendation</b></p>	<p><i>High / Moderate / Low / Very low</i> <i>Very low</i></p>
<p><b>Comments justifying recommendation</b></p>	<p>The group noted that the overall quality of direct evidence informing this recommendation was very low. No research studies have ever been designed and implemented to compare the health outcomes of HIV-exposed infants following a longer or shorter period of breastfeeding cessation. However, research and programmatic experience, including reports from well-conducted qualitative studies, were very consistent: namely, that rapid and abrupt cessation breastfeeding was associated with adverse consequences for the infant such as growth failure and increased prevalence of diarrhoea. Breast-milk viral load is also known to spike with rapid cessation of breastfeeding. While this has not been shown to be associated with increased transmission or adverse outcomes in the infant, there is biological plausibility that this would be detrimental. The group felt that WHO should make a recommendation, even if based on very little objective data, on the duration over which mothers should stop breastfeeding. This was considered better than saying nothing and devolving this responsibility to health workers who would probably base their recommendations to mothers on very little evidence. The revised WHO recommendations for antiretroviral therapy or prophylaxis to reduce HIV transmission indicate that whichever ARV prophylaxis is provided to prevent HIV transmission through breast-milk, the prophylaxis should continue for one week after all exposure to breast milk has ended.</p>
<p><b>Gaps, research needs, comments</b></p>	<p><i>Comparison of effects of different time periods for cessation.</i></p>

### Risk-Benefit Analysis: Recommendation 4<sup>5</sup>.

<p><b>Existing recommendations:</b>  <i>At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed. All breastfeeding should stop once a nutritionally adequate and safe diet without breast milk can be provided</i></p>	
<p><b>Proposed recommendations:</b>                  Mothers known to be HIV-infected who decide to stop breastfeeding at any time should provide their infants with safe and adequate replacement feeds to enable normal growth and development.</p> <p>3a. Alternatives to breastfeeding include:  <i>For infants less than 12 months of age:</i></p> <ul style="list-style-type: none"> <li>• Heat-treated breast milk;</li> <li>• Commercial powdered infant formula milk as long as home conditions outlined in #4 below are fulfilled;</li> </ul> <p><i>For children over 12 months of age:</i></p> <ul style="list-style-type: none"> <li>• Other age-appropriate replacement feeds.</li> </ul>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Moderate to Very low</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span></p> <p><b>Systematic reviews</b></p> <p><b>Indirect evidence: Very low</b></p>
<p><b>Benefits/desired effects</b></p>	<p><i>Infants who are not breastfed from birth or whose mothers stop breastfeeding at some point in time, receive safe and adequate alternatives to breast milk;</i></p> <p><i>Heat-treatment of breast milk, if correctly done, inactivates HIV and is nutritionally adequate to support normal growth and development;</i></p> <p><i>Commercial powdered infant formula averts all risk of HIV transmission and is nutritionally adequate if correctly reconstituted and can be safe if prepared under good conditions;</i></p> <p><i>In children older than 12 months, other replacement feeds can be adequate to enable normal growth and development.</i></p>
<p><b>Risks/undesired effects</b></p>	<p><i>Mothers do not consistently heat-treat breast milk correctly in order to inactivate HIV and infants placed at risk of transmission;</i></p> <p><i>Formula milk not consistently prepared hygienically and infants placed at increased risk of serious morbidity;</i></p> <p><i>Health systems unable to consistently provide formula milk, and as a result infants put at increased risk of malnutrition;</i></p> <p><i>Infants, especially between 6-12 months of age, often do not receive adequate replacement feeds. In this age group (compared with infants more than 12 months of age) providing replacement feeds other than formula milk is still difficult and without a strong evidence base to demonstrate effectiveness.</i></p>

<sup>5</sup> This recommendation was numbered 3b when first presented at the meeting.

<p><b>Values/Acceptability</b></p>	<p><u>In favour:</u></p> <p>Heat-treated breast milk (HTBM) allows the mother to continue to give her own breast milk, especially if she is living in very resource-constrained conditions. Can also be seen as an interim practice, e.g. until ART achieves effective viral suppression or if the infant is preterm and receiving specialized care;</p> <p>Widespread use of formula milk indicates its availability and familiarity within communities;</p> <p>Other replacement feeds have been developed for older children in some countries and could therefore be available.</p> <p><u>Against:</u></p> <p>HTBM has not gained widespread support and belief. Despite limited published literature, HTBM is seen as complex, difficult and questionably acceptable within communities;</p> <p>Multiple reports demonstrating difficulties of individual mothers to safely and correctly reconstitute formula milk and inability of health systems to maintain consistent supplies to facilities and mothers. Some major stock-outs reported;</p> <p>Multiple reports highlighting the failure of counselling in health systems to effectively guide mothers, known to be HIV infected, to make appropriate choices regarding infant feeding. Counselling frequently prescriptive and not guided by maternal circumstances;</p> <p>Lack of evidence base for adequacy and safety of replacement feeds other than commercial formula milks.</p>
<p><b>Costs</b> (consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</p>	<p>No comparative costs for HTBM. Formula milk considerations as previously reflected.</p>
<p><b>Feasibility</b></p>	<p>The feasibility of promoting and supporting successful HTBM has not been assessed at scale;</p> <p>Programme reports illustrate mixed experiences re the use of formula milk. The inconsistency between reports indicates how sensitive the safety and adequacy of formula milk is dependent on context.</p> <p>If breastfeeding stops after 12 months, animal milk may be a safe and adequate alternative.</p>
<p><b>Final recommendation</b></p>	<p><b>When mothers known to be HIV-infected</b> decide to stop breastfeeding at any time, infants should be provided with safe and adequate replacement feeds to enable normal growth and development.</p> <p>Alternatives to breastfeeding include:</p> <ul style="list-style-type: none"> <li>• For infants less than 6 months of age:             <ul style="list-style-type: none"> <li>– Commercial infant formula milk as long as home conditions outlined elsewhere are fulfilled,</li> <li>– Expressed, heat-treated breast-milk;</li> </ul> </li> </ul> <p><b>*Home-modified animal milk is not recommended as a replacement food in the first six months of life</b></p> <ul style="list-style-type: none"> <li>• For children over 6 months of age:             <ul style="list-style-type: none"> <li>– Commercial infant formula milk as long as</li> </ul> </li> </ul>

	<p>home conditions outlined elsewhere are fulfilled,</p> <ul style="list-style-type: none"> <li>- Animal milk (boiled for infants under 12 months), as part of a diet providing adequate micronutrient intake. Meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day.<sup>6</sup></li> </ul> <p>All children need complementary foods from six months of age.</p>
<p><b>Strength of recommendation</b></p>	<p>Strong, <u>or</u> Conditional, <u>or</u> Qualified, <u>or</u> Weak</p> <p><i>Strong</i></p>
<p><b>Quality of evidence that informs recommendation</b></p>	<p><i>High / Moderate / Low / Very low</i></p> <p><i>Low for formula; very low for HTBM</i></p>
<p><b>Comments justifying recommendation</b></p>	<p>There was little direct evidence from HIV-exposed populations to inform this recommendation. However, the group considered that the very considerable evidence from non-HIV exposed populations was relevant and justifiable to use to inform how HIV-infected mothers should feed their infants in the absence of breast-milk.</p> <p>The explicit statement that home-modified animal milk should not be used as a replacement feed in infants less than 6 months of age was included in the 2007 United Nations recommendations on HIV and Infant Feeding; the group considered it important to include it in these recommendations again.</p> <p>The text referring to alternatives to breast-milk for infants more than 6 months of age is taken from the WHO <i>Guiding principles for feeding non-breastfed children 6-24 months of age</i>.</p>
<p><b>Gaps, research needs, comments</b></p>	<p><i>Feasibility of heat treatment.</i></p> <p><i>HIV-free survival conditional on breastfeeding to 6 months versus breastfeeding to 12 months.</i></p>

<sup>6</sup> Guiding principles for feeding non-breastfed children 6-24 months of age. WHO 2005. ISBN 92 4 159343 1

### Risk-Benefit Analysis: Recommendation 3c<sup>7</sup>.

<b>Existing recommendations:</b> <i>Home-modified animal milk is no longer recommended as a replacement feeding option to be used for all of the first six months of life.</i>	
<b>Proposed recommendations:</b> Home-modified animal milk is not recommended as a replacement feeding at any time in the first six months of life.	
<b>Quality of Evidence</b> <i>(for outcomes deemed critical)</i>	<b>Moderate</b> (not presented) <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span>
<b>Benefits/desired effects</b>	<i>Clarify that home-modified animal milk is not recommended **Existing WHO recommendation**</i>
<b>Risks/undesired effects</b>	<i>Use of home-modified animal milk in infants less than 6 months is associated with hypernatraemic dehydration and death; Home-modified animal milk is also nutritionally inadequate.</i>
<b>Values/Acceptability</b>	<i><u>In favour:</u> Clarifies safe and best practices for health workers and mothers. <u>Against:</u> Required manipulation and preparation increase the risk of bacterial contamination; In some communities and cultures, use of animal milk as a replacement feed for young infants is practised, even in the absence of maternal HIV infection.</i>
<b>Costs</b> <i>(consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</i>	<i>In young infants who are not breastfed, formula milk is a more expensive option for mothers and families compared with local animal milks. However, the safety concerns associated with using home-modified animal milks over-ride cost considerations.</i>
<b>Feasibility</b>	<i>Relatively straightforward for health workers to recommend against use of home-modified animal milk. However, health workers then need to be competent to assist mothers with alternatives, which has implications for training and job aids.</i>
<b>Final recommendation</b>	<i>See previous recommendation.</i>
<b>Strength of recommendation</b>	<i>Strong, <b>or</b> Conditional, <b>or</b> Qualified, <b>or</b> Weak Strong</i>
<b>Quality of evidence that informs recommendation</b>	<i>High / Moderate / Low / Very low Low</i>
<b>Comments justifying recommendation</b>	<i>See previous recommendation.</i>
<b>Gaps, research needs, comments</b>	<i>None noted.</i>

<sup>7</sup> The group decided to delete this Recommendation as the relevant issues were covered in new Recommendation 4.

### Risk-Benefit Analysis: Recommendation 5<sup>8</sup>.

<p><b>Existing recommendation:</b>  <i>When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended.</i></p>	
<p><b>Proposed recommendations:</b>                  For infants who are known to be HIV exposed and who are uninfected or who are of unknown HIV status, giving commercial powdered infant formula milk as a replacement feed in the first six/twelve months of life is only advisable when:</p> <ol style="list-style-type: none"> <li>safe water and sanitation are assured at the household level <b>OR</b> within a community, <b>and</b>,</li> <li>the mother, or other caregiver, is confident that she/he can reliably provide sufficient formula milk to support normal growth of the infant, <b>and</b>,</li> <li>can prepare it cleanly and frequently enough so that it is safe and carries a lower risk of diarrhoea and malnutrition, <b>and</b>,</li> <li>the mother can, in the first six months, give the formula milk exclusively (i.e. avoids mixed feeding).</li> </ol>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Low</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span></p> <p><b>Systematic reviews</b></p> <p><b>Indirect evidence:</b></p>
<p><b>Benefits/desired effects</b></p>	<p><i>Defining the environmental conditions that make replacement feeds a safe option for HIV-exposed infants will improve HIV-free survival of infants:</i></p> <ul style="list-style-type: none"> <li><i>guiding health workers regarding what to assess and communicate to mothers to assist appropriate decision-making;</i></li> <li><i>Previous terms used to define the same considerations, i.e. AFASS, have been replaced with simpler language to clarify needs.</i></li> </ul>
<p><b>Risks/undesired effects</b></p>	<p><i>Reducing the factors down to 4 points oversimplifies the issues;</i>  <i>Not all the contextual factors or determinants of HIV-free survival, including the counselling capacity of health workers, are reflected in the 4 points of the proposed recommendation.</i></p>
<p><b>Values/Acceptability</b></p>	<p><i>In favour:</i>  <i>AFASS has been a difficult concept to translate into routine practice. Using 'common language' should assist implementation;</i>  <i>To consider whether environmental conditions should be considered for the community or for the individual mother. Whichever approach is agreed has implications for nature of counselling services that health services will then need to offer.</i></p>

<sup>8</sup> This recommendation was numbered 4 when first presented at the meeting.

	<p><u>Against:</u></p> <p><i>Oversimplification may limit opportunities for individual mothers to fully consider the opportunities and conditions needed to safely replacement feed or not;</i></p> <p><i>Some issues, while known to have a bearing on feeding practices, for example, income of the mother or household, have been omitted because considered too complicated to effectively assess within a reasonable period of time.</i></p>
<p><b>Costs</b> (consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</p>	<p><i>The quality of counselling is likely to reflect the complexity of information and concepts in the recommendations and communicating clearer and simpler concepts should be more efficient and feasible. This should result in more cost-effective counselling strategies, i.e. higher quality of counselling resulting in appropriate choices by mothers;</i></p> <p><i>Financial outlay by mothers/families should have more direct relationship to outcome in infants.</i></p>
<p><b>Feasibility</b></p>	<p><i>Experience from programmes and limited research reports highlight the difficulties with counselling approaches using current guidelines based on AFASS terminology;</i></p> <p><i>To consider whether a population- based approach should be adopted or to continue with individual assessments. Significant feasibility implications.</i></p>
<p><b>Final recommendation</b></p>	<p><b><i>Mothers known to be HIV-infected</i></b> should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status, when specific conditions are met: (<i>referred to as AFASS - affordable, feasible, acceptable, sustainable and safe in the 2007 United Nations recommendations on HIV and Infant Feeding</i>)</p> <ol style="list-style-type: none"> <li>a. safe water and sanitation are assured at the household level and in the community, <b>and,</b></li> <li>b. the mother or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant, <b>and,</b></li> <li>c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition, <b>and,</b></li> <li>d. the mother or caregiver can, in the first six months, exclusively give infant formula milk, <b>and,</b></li> <li>e. the family is supportive of this practice, <b>and,</b></li> <li>f. the mother or caregiver can access health care that offers comprehensive child health services.</li> </ol>
<p><b>Strength of recommendation</b></p>	<p>Strong, <b>or</b> Conditional, <b>or</b> Qualified, <b>or</b> Weak</p> <p><i>Strong</i></p>
<p><b>Quality of evidence that informs recommendation</b></p>	<p><b>High / Moderate / Low / Very low</b></p> <p><b>Low</b></p>
<p><b>Comments justifying</b></p>	<p>The group strongly endorsed this recommendation while</p>

<p><b>recommendation</b></p>	<p>acknowledging that the quality of direct evidence from HIV-exposed infants and mothers was limited. There is no possibility of conducting a clinical research study that would deliberately expose infants with the conditions listed above, to the risks of replacement feeding. It would be unethical to do so. The group considered the health outcomes of HIV-exposed infants from a range of programmatic settings and observational studies of HIV exposed infants that indirectly reported on the influence of these household, environmental and social factors on child survival (Andresen et al., 2007; Doherty et al., 2007; Creek et al., 2009).</p> <p>The group also drew from programmatic experience and evidence from non-HIV populations in which there is considerable observational data that quantify the risks of not breastfeeding (WHO, 2000; Bahl et al., 2005) and using commercial infant formula milk in settings that are sub-optimal.</p> <p>The group also chose to explicitly define the conditions, using common everyday language, rather than referring to the acronym AFASS (<i>affordable, feasible, acceptable, sustainable and safe</i>) that was adopted in previous recommendations. It was felt that more carefully defining the environmental conditions that make replacement feeds a safe (or unsafe) option for HIV-exposed infants will improve HIV-free survival of infants. It was considered that such language would better guide health workers regarding what to assess, and communicate to mothers who were considering if their home conditions would support safe replacement feeding.</p> <p>Using these descriptions does not invalidate the concepts represented by AFASS but gives simpler and more explicit meaning to them.</p>
<p><b>Gaps, research needs, comments</b></p>	<p><i>None noted.</i></p>

### Risk-Benefit Analysis: Recommendation 7<sup>9</sup>.

<p><b>Existing recommendations:</b>  <i>Breastfeeding mothers of infants and young children who are known to be HIV-infected should be strongly encouraged to continue breastfeeding as per the recommendations for the general population, that is up to two years or beyond.</i></p>	
<p><b>Proposed recommendations:</b>                  No change <u>or</u>                  Infants who become HIV infected should continue to <i>(what if they are not being BF?)</i> be breastfed up to 24 months of age in order to reduce the risks of non-HIV infectious morbidity and mortality, while introducing complementary foods at 6 months of age.                  Health services should give support as appropriate to mothers to assist them to re-lactate or initiate breastfeeding. <i>(Include and if so, then as recommendation or principle? Falls under the general principle to support mothers in their choices.)</i></p>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Low</b> (re. benefit to infants) <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span>  <b>Very low</b> (re. prolonged breastfeeding and maternal health)</p> <p><b>Systematic reviews</b>  <i>Only one study reporting significant reduction in mortality (Kuhn et al., 2008). Note: small sample size and original study not designed with mortality in these infants as the primary outcome. Sample size not powered accordingly. Three other observational studies reported no significant effect of breastfeeding versus replacement feeding re mortality. These 3 studies each had small sample sizes and were not powered to assess this question.</i></p> <p><b>Indirect evidence:</b>  <i>Several recent- published studies (included in systematic review) report increased serious morbidity, especially diarrhoea and also growth failure, in HIV-exposed but not infected infants who breastfeed versus replacement feeding, especially in 6-12 months.</i>  <i>Very low evidence that prolonged breastfeeding by HIV-infected mothers is detrimental to mothers' health.</i>  <i>Strong evidence base from non-HIV infected populations (not reviewed) to support plausibility that breastfeeding would prolong survival. Note: exclusive breastfeeding and continued breastfeeding to 24 months are standing WHO recommendations for all infants where there is no justification for not breastfeeding (e.g. possible HIV transmission).</i></p>
	<p><b>Benefits/desired effects</b> <i>Improved nutritional status of infants already infected with HIV</i></p>

<sup>9</sup> This recommendation was numbered 5 when first presented at the meeting.

	<i>Reduced non-HIV infectious disease such as diarrhoea and pneumonia.</i>
<b>Risks/undesired effects</b>	<i>Adverse consequences for HIV-infected mothers who breastfeed for long periods.</i>
<b>Values/Acceptability</b>	<p><i><u>In favour:</u></i>  <i>breastfeeding perceived as demonstration of care of mother for infant;</i>  <i>May prolong the infant's survival long enough to be identified by health systems and initiated on ART.</i></p> <p><i><u>Against:</u></i>  <i>Health workers view that breastfeeding of infant already infected results in HIV re-infections that are detrimental.</i></p>
<b>Costs</b> (consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )	<i>Avoids re-direction of home resources to infant formula.</i>
<b>Feasibility</b>	<i>Very feasible, but re-lactation may require skilled counselling and support.</i>
<b>Final recommendation</b>	<i><b>If infants and young children are known to be HIV-infected,</b> then mothers are strongly encouraged to exclusively breastfeed for the first 6 months of life and continue breastfeeding as per the recommendations for the general population, that is, up to two years or beyond.</i>
<b>Strength of recommendation</b>	<i>Strong, <u>or</u> Conditional, <u>or</u> Qualified, <u>or</u> Weak</i> <i>Strong</i>
<b>Quality of evidence that informs recommendation</b>	<i><b>High / Moderate / Low / Very low</b></i> <i><b>Moderate</b></i>
<b>Comments justifying recommendation</b>	<p>This same recommendation appeared in the 2007 United Nations recommendations on HIV and Infant Feeding. The systematic review identified reports from two studies that were not included in the review that supported that guideline and that directly reported on the mortality of HIV-infected infants according to their early feeding practices. In a randomized controlled trial in Zambia, infants of HIV-infected breastfeeding mothers either stopped all breastfeeding at 4 months of age or continued to breastfeed. Among infants who were already HIV-infected, mortality at 24 months was 54% among those randomized to continued breastfeeding compared to 74% among those who stopped breastfeeding early (Kuhn et al., 2008). In a study in Botswana that randomized HIV-exposed infants to either breastfeed or receive infant formula, among infants that were already HIV-infected mortality at 6 months of age was 7.5% in those who breastfed compared to 33% in those randomized to receive infant formula only (Lockman et al., 2006). The group concluded that there was a</p>

	<p>clear benefit for continued breastfeeding.          Additional studies reported morbidity outcomes such as increased diarrhoea and malnutrition, and the group considered that these supported the mortality evidence that continued breastfeeding is beneficial to the infant who is already HIV-infected.</p>
<p><b>Gaps, research needs, comments</b></p>	<p><i>None noted.</i></p>

## Risk-Benefit Analysis: Recommendation 6<sup>10</sup>

<p><b>Existing recommendations:</b>  <i>No specific recommendation re. HTBM. Reference in Guidelines, training and counselling tools.</i></p>	
<p><b>Proposed recommendations:</b>                  Mothers known to be HIV infected may consider expressing and heat treating breast milk as an alternative to breastfeeding:  <b>Would NVP be recommended to the infant?</b>  <i>As an interim feeding strategy:</i></p> <ol style="list-style-type: none"> <li>In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed;</li> <li>When the mother is unwell in the neonatal period and is unable to breastfeed or has a temporary breast health problem such as mastitis;</li> <li>As an interim measure while the mother is being started on ART or if waiting for antiretroviral drugs to become available.</li> </ol> <p><i>For the full duration of breastfeeding:</i></p> <ol style="list-style-type: none"> <li>When antiretroviral drugs are not available to the mother or infant;</li> <li>When mothers prefer this option.</li> </ol>	
<p><b>Quality of Evidence</b>  <i>(for outcomes deemed critical)</i></p>	<p><b>Low - Very low</b> <span style="float: right;"><i>(High / Moderate / Low / Very low)</i></span></p> <p><b>Systematic reviews</b>  <i>Evidence down graded because of few reports describing inactivation of virus under different circumstances and effect on nutritional composition of milk.</i></p> <p><i>Possible publication bias given that most reports are from one single research group.</i></p> <p><b>Indirect evidence:</b>  <i>Non-HIV data indicates that pasteurization using commercial equipment does not significantly alter nutritional composition of milk.</i></p>
<p><b>Benefits/desired effects</b></p>	<p><i>Provides the mother with an alternative to replacement feeding that if correctly implemented, does not put the infant at risk of HIV transmission yet offers the nutritional and protective effects of breastfeeding</i></p> <p><i>Provides an option for mothers and health services in special settings when alternatives may not be readily available.</i></p>
<p><b>Risks/undesired effects</b></p>	<p><i>Incorrect or inconsistency heat-treating will result in HIV in breast milk not being inactivated and the infant being placed at risk of HIV transmission.</i></p>

<sup>10</sup> This recommendation was not numbered when first presented at the meeting.

<p><b>Values/Acceptability</b></p>	<p><u>In favour:</u>  <i>Feasible if women motivated.</i>  <i>Provides an additional alternative for certain circumstances.</i></p> <p><u>Against:</u>  <i>Questionable feasibility to implement at scale. However, intensity of work needed to correctly perform would not be much different from <u>correct</u> preparation of formula feeds.</i>  <i>Health workers would need significant training and motivation to be able to offer to this alternative to mothers.</i></p>
<p><b>Costs</b>  <i>(consider actual costs, modeling; incremental cost of new recommendation; cost effectiveness analysis )</i></p>	<p><i>Minimal costs to health system. Would need demonstration facilities at clinic.</i>  <i>Training costs of staff to demonstrate correct implementation.</i>  <i>Modest costs to mothers - not assessed.</i></p>
<p><b>Feasibility</b></p>	<p><i>Motivated mothers can perform at home with very modest resources. Nurseries and mothers in hospital could heat-treat milk either using reported home methods or could use commercial pasteurization equipment.</i></p>
<p><b>Final recommendation</b></p>	<p><b><i>Mothers known to be HIV-infected</i></b> may consider expressing and heat-treating breast-milk as <i>an interim feeding strategy</i>:</p> <ul style="list-style-type: none"> <li>• In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; <b>or</b></li> <li>• When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis; <b>or</b></li> <li>• To assist mothers stop breastfeeding; <b>or</b></li> <li>• If antiretroviral drugs are temporarily not available.</li> </ul>
<p><b>Strength of recommendation</b></p>	<p>Strong, <b>or</b> Conditional, <b>or</b> Qualified, <b>or</b> Weak  <i>Weak</i></p>
<p><b>Quality of evidence that informs recommendation</b></p>	<p><b><i>High / Moderate / Low / Very low</i></b>  <b><i>Very low</i></b></p>
<p><b>Comments justifying recommendation</b></p>	<p>Laboratory evidence demonstrates that heat-treatment of expressed breast milk from HIV-infected mothers, if correctly done, inactivates HIV. Several different methods of heat-treatment have been tested in a range of controlled and 'real life' conditions. The methods of heat-treatment do not appear to significantly alter the nutritional composition of breast milk; hence breast milk treated in this way should be nutritionally adequate to support normal growth and development. For these reasons, heat-treatment of expressed breast milk from mothers known to be HIV-infected could be considered as a potential approach to safely providing breast milk to their exposed infants.</p> <p>The group noted the paucity of programmatic data that demonstrates its acceptability and sustainability at scale as an infant-feeding strategy to improve HIV-free survival. While</p>

	<p>reports are beginning to emerge describing its use in neonatal units or as a short-term approach in specific communities, the group was not confident to recommend this approach for all HIV-infected mothers who wish to breastfeed. More data is needed from a range of settings to understand what is needed from health systems to effectively support mothers in this approach. Evidence is needed to demonstrate that mothers can sustain adhering to the methodology over prolonged periods of time. Given the efficacy of antiretroviral drugs to prevent HIV transmission through breastfeeding, the role of heat-treatment of expressed breast milk as a truly feasible HIV prevention and child survival strategy is yet to be clarified. Until then, the group positioned the approach as an 'interim' strategy to assist mothers over specific periods of time rather than for the full duration of breastfeeding.</p>
<p><b>Gaps, research needs, comments</b></p>	<p><i>Continued research on feasibility as HIV prevention and child survival strategy.</i></p>