



make medicines **child size**

Report of an informal consultation on missing priority medicines for children

14-15 July 2011, WHO HQ, Geneva, Switzerland

This publication contains the Report of an informal consultation on missing priority medicines for children and does not necessarily represent the decisions or policies of the World Health Organization

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Background and objectives

On 14-15 July 2011, an informal consultation was convened to discuss strategies for advancing the availability of a fixed-dose combination (FDC) medicine for treatment of paediatric tuberculosis (TB). While the primary focus was first-line therapies, second-line treatments were also discussed. The meeting was held at the World Health Organization (WHO) headquarters in Geneva, coordinated by the Medicines Access and Rational Use (MAR) unit. Participants included representatives from WHO, academic institutions, nongovernmental organizations, pharmaceutical industry associations, procurement organizations, regulatory agencies, and funder agencies.

While FDCs exist for treating paediatric TB, the available products are based on outdated dosing guidelines. Because these existing formulations are significantly different from current dosing recommendations, it is too complicated to use the products as a long-term solution. Specifically, the ratios of individual medicine components in the existing FDCs do not correspond to those in the revised dosing recommendations. It is overly complicated, and in some cases impossible, to use them and achieve correct dosing. Other options, such as splitting or crushing adult strength tablets as a means of delivering correct doses, are also unrealistic as long term solutions, particularly because of poor compliance and risk of dosing errors. Policies and scientific evidence of the need for a revised FDC are clear, yet progress towards a revised product has been slow.

In consideration of this public health gap, the overall objective of the consultation was to review outstanding issues and identify solutions to barriers impeding the availability of an appropriate FDC for paediatric TB.

The consultation included a review of the process for determining the revised dosing recommendations, followed by a review of challenges experienced to date in promoting a revised FDC. The agenda invited technical experts to present and discuss three critical and relevant areas: 1) policy and scientific activities; 2) regulatory pathway; and 3) procurement/business activities. Discussions were guided by the following key questions:

1. What are we already doing to solve this problem?
2. What are the gaps?
3. For each problem, what is the solution?
4. For each solution, who is the appropriate party to lead?
5. What is the timeline for any recommended activity?

The informal consultation process provided a venue for experts and stakeholders to consider how best to address barriers and move forward in making an appropriate quality FDC available. It concluded with the development of a timeline listing the activities, responsible parties, and time frame for advancing the availability of an FDC.

Policy and scientific activities

WHO provided background details on the processes and actions taken so far to ensure appropriate treatment of paediatric TB. Information on challenges and problems experienced was also provided to inform discussions and proposed solutions. Lead scientists presented summaries of ongoing studies related to dosing in children. These presentations and discussions clarified several misunderstandings, filled information gaps, and highlighted a high level of investment in research on treating children with TB.

While it is generally accepted that a revised FDC is the preferred solution, progress to achieving this goal has been slow. The problem, in part, appears to be related to confusion about the status of the recommendations. WHO has informally received comments and information from multiple sources indicating that there is some misperception regarding:

- the latest dosing recommendations in the 2010 Rapid Advice;
- the formulations listed on the WHO Model List of Essential Medicines (EML);
- the nature and complexity of challenges in reformulating the necessary component medicines.

Process for reaching the 2010 Rapid Advice¹

In 2006, WHO performed a comprehensive review of all TB medicines on the EML and found that the listed products were insufficient for treating children. Another key finding was that doses were too low to obtain therapeutic levels in children. A review was conducted by the Subcommittee on the Selection and Use of Essential Medicines in 2008² and again by the WHO Expert Committee

¹ WHO/HTM/TB/2010.13: Rapid advice : treatment of tuberculosis in children. WHO, 2010. Available at: http://whqlibdoc.who.int/publications/2010/9789241500449_eng.pdf

² WHO Technical Report Series 958: The selection and use of essential medicines. Report of the WHO Expert Committee, 2009 (including the 16th WHO Model List of Essential Medicines and the 2nd WHO Model List of Essential Medicines for Children), page 198. Available at: http://whqlibdoc.who.int/trs/WHO_TRS_958_eng.pdf



on the Selection and Use of Essential Medicines in 2009¹. This was followed in 2010 by the publication of the Rapid Advice guideline providing recommendations for dosages of anti-TB medicines that take into account the risk of hepatotoxicity.

Participants agreed that the evidence for the new dosing recommendations was robust and that the process was consistent with other published guidelines. The recommendations have been validated through pharmacokinetic simulation studies performed by scientists (Dr S. Abdel-Rahman and Dr G. Kearns) from the Children's Mercy Hospital in 2009.² While there is still a need for additional data on minority populations, such as children under 3 months of age, this does not preclude the urgency of advancing that availability of an FDC needed for the majority of paediatric populations.

WHO Essential Medicines List (EML) and the WHO Essential Medicines List for Children (EMLc)

Medicines for TB for children were first included on the WHO Model List of Essential Medicines in 1999, when a number of low dose individual medicines and fixed dose combination products were added. Actual corresponding products did not exist at the time they were added to the EML and the strengths were based on extrapolation from adult products. They were later determined to have not adequately accounted for differences in the metabolism of the medicines in children compared to adults.

Some manufacturers eventually produced the specified combinations and they were prequalified by WHO in 2008. These products were then deleted from the Model List in 2009, following the review of evidence on doses required in children. The low dose products resulting from the original 1999 EML cannot be used to deliver the doses needed without being used in complex regimens that are difficult to administer. As such, they do not enhance adherence, which is the main reason to use a FDC product compared to single component products. The FDC's based on the 1999 EML are, therefore, not 'essential' medicines.

¹ WHO Technical Report Series 958: The selection and use of essential medicines. Report of the WHO Expert Committee, 2009 (including the 16th WHO Model List of Essential Medicines and the 2nd WHO Model List of Essential Medicines for Children), page 15. Available at: http://whqlibdoc.who.int/trs/WHO_TRS_958_eng.pdf

² Antituberculosis medicines reports. Geneva, World Health Organization, 2008 and 2009. Available at: <http://www.who.int/childmedicines/progress/TB/en/index.html> (Accessed 25 July 2011).



WHO accepted that the series of decisions in relation to these products has confused manufacturers, and while the recommended doses are now clear, the optimal product specifications for a FDC to deliver them are not. Further, the policy of the WHO Expert Committee on the Selection and Use of Essential Medicines is now not to list products on the EML that do not exist. The current EML therefore lists only existing single component products for TB that can be used in children to ensure that procurement agencies that are guided by the EML to select appropriate products. Global Drug Facility (GDF), however, is still procuring the existing low-dose FDCs for use according to the regimens specified in the dosing recommendations published in 2010. This apparent contradiction is confusing a fragile market even further.

Participants agreed with the need to communicate two messages clearly to manufacturers and procurement agencies: (1) the current products are not optimal and therefore will not be reinstated on the EMLc, but (2) they can be used according to the recommended regimens published in 2010. WHO will continue to work with academics, regulatory authorities and manufactures to finalize specifications for appropriate and feasible FDCs that once available could be included on the EMLc.

Challenges with product development

While an ideal FDC would combine 3 or 4 of the medicines rifampicin, ethambutol, isoniazid and pyrazinamide, there are challenges in developing an actual product. The challenges are related to both the formulation process as well as perceptions that have slowed progress. Examples include:

1. A four-drug combination prototype at the recommended doses resulted in a tablet approximately the size of 2 one euro coins stacked together. Unless this tablet is dispersible and palatable for children, it would be impossible to administer and/or divide to produce a proper age-adjusted dose of the drugs therein.
2. Another prototype formulation gave evidence of an interaction among the drug components and excipients resulting in an unacceptable dosage form after exposure to ambient temperatures (i.e., a gelatinous, amorphous mass).
3. Bioavailability of oral rifampicin is complex, apparently formulation-dependent and highly variable.
4. There are misperceptions that revising the existing FDC is simple, not innovative, and inexpensive, all leading to shortfalls in funding.
5. There are errant perceptions that without an ideal formulation at the ready, the WHO dosing guidelines for the primary antitubercular medicines are therefore not ready for clinical implementation.

6. While the market is assumed to be small, yet growing, market information remains sparse for paediatric TB medicines.
7. Among implementing programmes, there is confusion regarding appropriate use of the EML (including the EMLc) and about regulatory processes.

Additional discussions noted the potential for new challenges and perceptions to emerge, and suggested monitoring the need to consider studying drug interactions, drug-food interactions, and the need for any additional bio-availability studies.

Ongoing scientific studies

The high level of investment in ensuring appropriate treatment of paediatric TB was evidenced by the presentations from leading experts. It was noted that there is a general paucity of clinical studies in children relative to adults; however, this is not specific to TB and should not be confused with an absence of data to support the Rapid Advice document. The studies presented covered issues related to expanding the evidence base for optimal dosing (particularly in infants < 3 months old, or weighing < 5 kg), TB dosing with HIV co-infection, monitoring of treatment, second-line TB treatment drugs, and an overview of study initiatives. There were studies from two leading universities in South Africa, where TB burden in children is among the highest in the world. It was noted that both the research capacity and its high TB burden highlight the importance of collaboration with South African institutions.

Discussions about the presentations included technical feedback on study designs and potential collaborations. Studies included the following:

- Optimal dosing of 1st line antituberculosis and antiretroviral drugs in children (Dr Helen McIlleron, University of Cape Town).
- Low cost monitoring strategy to optimize tuberculosis treatment in children (Dr Susan Abdel-Rahman, Children's Mercy Hospitals and Clinics).
- Current research initiatives in paediatric TB drugs (Prof Anneke Hesselning, Stellenbosch University).
- Second-line antituberculosis drugs in children (Prof Simon Schaaf, Stellenbosch University).

Weight banding

There has been informal discussion regarding the potential for weight banding TB medicines for children. The interest is based on three issues. First is the need to manage infants and children up to 30 kg without under or over dosing. Second is the non-linear relationship between drug absorption and weight in children under 30 kg. Finally, the close relationship to HIV/AIDS treatment programmes, where weight banding is used, has led to suggestions that TB treatments follow a similar approach to avoid confusion.

A presentation by Professor Nunn provided information about a tool that was developed to determine the weight bands for anti-retroviral (ARV) medicines for treatment of paediatric HIV/AIDS. Weight banding was initially developed to reduce confusion in administering the ARVs, improve compliance, and provide for weight-appropriate doses of medicine. The tool calculates the resultant mg/kg dose of each drug that would result from administration of a given drug product at a specified dosing interval and then compares this information to the pediatric dose ranges for the TB drugs recommended by WHO. The presentation highlighted that weight banding would be possible, but that there were outstanding questions as to whether the same weight bands used for ARVs would be appropriate for TB medicines. Professor Nunn agreed to perform some initial simulations using the tool, and presented his findings later in the day. The outcome was not entirely conclusive, but indicated potential. The outcome indicated potential but the value of using the tool was put into question as the high burden HIV countries are not the same as the high burden TB countries. As noted in the follow up activities, Professor Nunn will perform additional simulations to develop a clear recommendation.

Regulatory pathway

A revised FDC will necessarily undergo some level of regulatory submission and market authorization. There have been questions regarding what level of clinical detail would be required by Stringent Regulatory Agencies (SRAs) and by the WHO's Prequalification of Medicines Programme (PQM) in a submission for a revised product. In addition, there have been questions regarding whether an appropriate regulatory strategy should include both SRA submissions and PQ certification, or PQ certification alone. The two SRAs that have active involvement in paediatric TB medicines include the United States Food & Drug Administration (FDA) and the European Medicines Agency (EMA). While the FDA was not able to attend the consultation meeting, representatives from the EMA and WHO/PQM participated.

WHO Prequalification of Medicines Programme (WHO PQP)

A comprehensive overview of the requirements and processes for PQ certification was provided by the WHO/PQM team. The presentation from Dr Milan Smid also covered activities with other regulators that have been developed to encourage submissions, such as those for HIV medicines. While examples such as accelerated review programmes, grants, and waivers of fees for submissions of HIV medicines exist, they do not extend to TB medicines.

WHO PQ certification can be pursued with or without an SRA submission. A submission without an SRA approval requires a more rigorous review from PQP, and takes additional time, investment, and site inspections. WHO/PQM works closely with global regulators, and reduces its review requirements for medicines with approvals from an SRA. The PQP has advantages, including technical assistance for developing country manufacturers and clear eligibility for procurement through UN programmes.

Clarifying a frequently asked question about efficacy data in children, there was consensus that pediatric effectiveness can be extrapolated from adequate and well-controlled efficacy studies in adults usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic and safety studies. Studies may not be needed in each pediatric age group, if data from one age group can be extrapolated, although some key age groups (e.g. children below 2 years of age) require specific attention. A decision to require additional studies would depend on the available data and would be treated on a case-by-case basis by regulators or the WHO/PQM team.

European Medicines Agency

In most EMA member countries, TB treatment medicines are authorized, but mostly in adult strengths. For children, rifampicin is authorized as a liquid formulation. Following the release of the 2010 Rapid Advice by WHO, the EMA is also investigating dosing requirements for a paediatric FDC formulation, including consideration of strengths and combinations. The presentation from Dr Agnes Saint Raymond also provided suggestions on appropriate regulatory steps for authorization sought through the EMA.

The critical steps in the pathway for pursuing authorization from the EMA are noted below and Illustration 1 provides a visual representation excerpted from Dr Saint Raymond's presentation.

Scientific advice

A specific and critical step would be requesting formal scientific advice on the need for pharmacokinetic studies to document the validity of the current WHO dosing guidelines which were derived following modeling and simulation using available pediatric data for both pharmacokinetics and pharmacodynamics from the literature. Additional advice should be requested to clarify the reference drugs that would be accepted for bioequivalence i.e., would it require an FDC or could the individual component drugs be used. There was also interest in requesting a global reference product so that data could be used for multiple submissions.

Regarding the request for formal scientific advice, it was determined that the best approach would be for the scientific experts present at the meeting to draft questions as an output of the meeting. The questions that will be used to formulate an eventual request for scientific advice are in Annex 1.

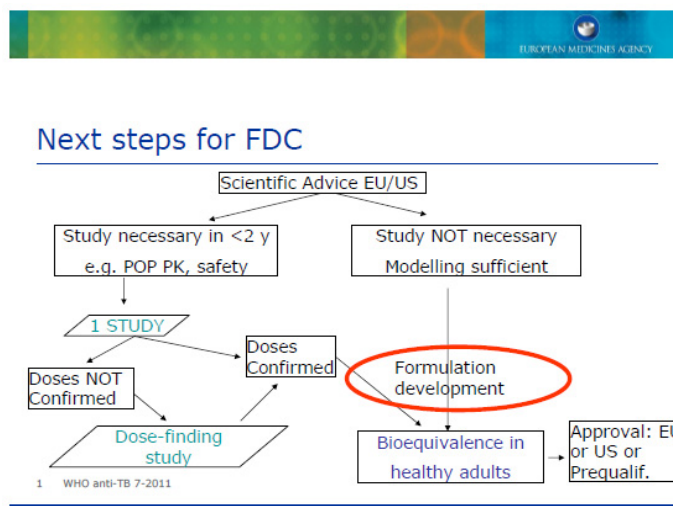
Bioequivalence studies

Depending on the outcomes of the advice, the remaining steps for submitting and requesting approval from the EMA would at a minimum include bioequivalence studies of a proposed product. Generally, these studies would be performed in panels of healthy adult volunteers conducted by the manufacturer of the drug product(s). In subsequent studies of a given drug formulation in a population of children with TB, appropriately constructed population-based pharmacokinetic analyses could be used to validate bioequivalence data from healthy young adult volunteers.

Submission under Article 58

Depending on the manufacturer making the submission, the most likely approach would be through the processes known as "Article 58" which provides review and authorization of products that are not marketed in the European Union. As additional background on pursuing limited authorization under Article 58, the demand for paediatric TB medicines is low in Europe and pursuing full European market authorization would not be cost effective at present.

Illustration 1, Excerpt from "Regulatory pathways for anti-TB paediatric medicines"



Reference products

In a separate yet related discussion, participants noted that it would be very useful to have a list of reference drugs for global application, especially for use in bioequivalence studies. It was recognized that regulations vary from country to country. For example in South Africa the confidence interval for C_{MAX} has been widened from 0.8-1.25 to 0.75-1.33 and therefore the requirements are different from those used in submissions to other regulators. If a list of appropriate reference products that could be used globally could be produced then issues of substitution could be minimized.

Business and procurement strategies

In order for a revised FDC to be available, it needs to be developed and produced. It also needs to be included in the procurement planning and supply systems that deliver medicines to countries that need them. Manufacturers need to be able to understand market trends in order to plan appropriate production and costing, and TB programme managers need information about the product to manage forecasting and transition planning for a new medicine. Presentations from UNITAID and GDF provided background on procurement funding for TB medicines and on available market information. Presentations from industry associations and from an industry feedback survey covered additional issues affecting interest in manufacturing as well as uptake.



GDF is currently the largest single procurer of TB medicines. Funding for TB drug procurement has been stable for the past three years and there is optimism that funding will continue. Total spending over the past three years has been over USD 9 million, mainly on adult medications, with the majority of distribution across African countries. There is a limited number of suppliers of paediatric formulations, and only one supplier of TB FDCs producing PQP-approved medicine.

UNITAID has been assessing market dynamics related to TB products, including diagnostics and medicines. The market for paediatric medicines is assumed to be small, but there is concern about the lack of capacity to diagnose paediatric TB and the link to uptake of medicines. Market assessments are underway for diagnostics and the work on medicines will be managed later in 2011.

Manufacturers have faced challenges in several areas. While it was clarified that the 2010 Rapid Advice is final and should be used, industry has expressed lack of clarity on an ideal FDC product specification. Information from user assessments, market surveys, and other experts will be important in developing clear priorities for what the ideal product should be. For example, clear information on weight banding, the number of drugs to be included in an FDC, and which drugs can be realistically included in a child-friendly formulation needs to be available. Manufacturers have reported through informal interviews and surveys that additional challenges faced include fragmented markets and high registration burdens. Another long-standing problem is that once a quality drug is developed, registered, and made available, copies of the drug from non-quality approved sources can create unfair competition, especially in private markets where procurement systems do not require quality certification. It is unclear if this situation is as relevant for paediatric TB medications but reassurances need to be given to industry.

A presentation on innovative tableting technologies was also presented for future consideration. The Universities of Parma and Ferrara have developed a modular tablet design (Dome Matrix) where different pieces of a tablet are produced and then joined together by clicking. This technology and others like it may offer options to reduce pill burden in the future. Should a manufacturer have interest in this technology, it would be advisable to discuss the cost, regulatory, programmatic, and formulation implications.

Summary and considerations

Through the discussions and a wrap up session, participants identified issues and action points that need to be taken. The issues and action points generally include those noted below and they are additionally summarized in the attached timeline:

- The group should issue a joint consensus statement from the meeting in support of the dosing guidelines and submit it for publication in a peer-reviewed journal.
- Ensure availability of current first-line TB therapy products while continuing to develop an appropriate FDC formulations for the long-term.
- Improve the perception of the current guideline by developing communication materials to clarify that the 2010 Rapid Advice is final and should be implemented.
- Promote the 2010 Rapid Advice as well as the instructions on using current FDCs as an interim measure.
- Develop plans to address regulatory issues and a plan for moving forward.
- Convey messages that previous dosing regimens do not provide adequate therapeutic levels in children and that the current dosing recommendations should be implemented.
- The research community should continue with technical studies to inform TB medicine needs for children, especially ensuring that there is a collaborative platform to sharing the information with other researchers and critical stakeholders.
- Use the October 2011 conference in Lille as a platform for disseminating technical and other information.
- Consider the benefit of partnering with HIV programmes as a conduit to encourage uptake.
- Pursue weight banding, pill burden, treating children with HIV co-infection and other paediatric formulation issues to provide clear guidance to industry.
- Develop a joint statement to the Committee for Medicinal Products for Human Use (CHMP) to clarify reference products and other technical advice (see Annex 1 for the recommended questions).
- Identify all products available and with market authorization in South Africa.

The meeting concluded with a clear list of activities and a timeline. See Annex 2 for details. Participants agreed on the timeline and on who would take the lead responsibility. If additional consultations are required, they will continue via email unless otherwise agreed.

Annex 1: Draft topics for Committee for Medicinal Products for Human Use (CHMP) scientific advice

The premise of these questions are based on the fact that TB is a global disease that requires urgent attention, in particular for the treatment of paediatric patients.

This requires that a different approach be followed to facilitate the drug product development process and will necessarily require collaboration between all role players viz., academia, industry, regulators, and practitioners.

In particular, bioequivalence is of importance.

Specific questions

1. What process would be considered appropriate for registration of FDC of TB drugs. Would all authorities consider an abbreviated new drug application (ANDA) approach for such products?
2. Guidelines for the conduct of bioequivalence studies must be clear and cover aspects such as, how the reference product(s) should be dosed. For example would it be appropriate to dose three or four single component products versus an FDC product?
3. Would all regulatory authorities consider the registration of pharmaceutical alternatives as dosages for single component and FDC products are likely to be different? Would consensus on this issue be possible.
4. What would the reference products be? Would it be possible to name a single set of appropriate reference products for global use? If not would a continent based approach be adequate?
5. How would the PQ framework and other authorities combine, in particular with Pharmaceutical Inspection Cooperation Scheme (PIC/S)?

Note: *A comment on the meeting notes suggest that question 3 be revised. The suggestion was based on a concern that this may not be an appropriate question for CHMP.*

Annex 2: Proposed activity plan

Work stream	Activities	Responsible agency	Timeline						
			2011		2012				
			Q3	Q4	Q1	Q2	Q3	Q4	
Business	Mapping the TB market	UNITAID, Stop TB							
	Pursue the development of a secondary packaging format	GDF							
	Review potential for public private partnerships, advance purchase agreements and other industry incentive options	GDF							
	Clarify procurement funding	UNITAID							
	Review potential procurement strategy to focus on a limited number of formulations	GDF							
Guidelines	Professor Nunn to apply his model to create a weight banding strategy using existing products	Prof Nunn							
	Develop clear messaging to distinguish the need for more research in drug efficacy in children generally (including TB) from the concerns that more guidance is needed to support the guidelines. This needs to be ready for the LILLE Conference in October 2011	WHO							
	Develop clear statements regarding the role of the guidelines, i.e., that they reflect current thinking with an intention to be flexible and adaptable. Include substantiating data , e.g., that presented by Dr Greg Kearns	WHO, Dr Greg Kearns, Dr Susan Abdel-Rahman							

Work stream	Activities	Responsible agency	Timeline					
			2011		2012			
			Q3	Q4	Q1	Q2	Q3	Q4
	Redevelop interim instructions to address use of "kits" with existing formulations.	WHO						
	Report on countries successfully implementing the guidelines compared to challenges faced.	WHO					D3	
	Define the reference product for purposes of bioequivalence studies.	WHO						
	Develop a specific request for scientific advice based on the outcomes of the July 2011 consultation	Rod Walker and WHO						
	Identify all products registered by the MCC and marketed in South Africa to inform regulatory coordination efforts	Rod Walker						
	Obtain CHMP opinion for EU regulatory pathway (September CHMP meeting)	EMA (St. Raymond)						
	Request CHMP advice on whether historic PK data would be acceptable for regulatory purposes (Note: EMA informally already indicated that it would be acceptable. This item is finished).	EMA (St. Raymond)						
	Develop a plan for clinical studies needed to support an actual product i.e., required for submission by a manufacturer	PPP						
	Promote and discuss a global regulatory concept with African regulators. Note: this action remains under advisement pending outcomes and agreement on other regulatory pathway issues.							
	Promote the global approach i.e., using a single reference product, to the PMRN. The approach could include a regional option if necessary. The PMRN meeting in October will be the forum.	WHO						
Scientific	Obtain evidence on PK in children < 2 years of age and those under 5 kg, including those who are HIV+	WHO					D2	
	Add paediatric TB drugs to the extemporaneous drug survey (to accompany general WHO guidance on ext. dosing)	Prof Nunn						

Work stream	Activities	Responsible agency	Timeline					
			2011		2012			
			Q3	Q4	Q1	Q2	Q3	Q4
	Develop a paediatric TB consortium. Note: this item remains under advisement pending discussions with STB	WHO						
	Assess user acceptability and product transition issues	WHO and Union						
	Address the ideal product (3 or 4 drug, dispersible formulation, tablet burden)						D1	
	Complete a PK study to support regulatory submission for a FCD	PPP						



Annex 3: Meeting agenda

Overall Objective: To review and finalize a scientific, regulatory and business strategy needed to encourage the development and supply of fixed dose combination drugs for paediatric TB.

Day One: 14 July Chair: Dr Suzanne Hill, WHO			
Session/Time	Title	Presenter/Facilitator	Materials
08:30 –09:00	Registration		
09:00 - 09:15	Opening remarks	WHO	
09:15 – 09:30	Review of agenda and administrative details	Ms Lisa Hedman, WHO	
Theme 1: Policy and scientific activities			
Session 1 09:30 - 10:30	Review of 2009 dosing guidelines: rationale, process, and products	Dr Suzanne Hill, WHO Dr Malgorzata Grzemska, WHO	-Excerpts (pages 198-199) from rational medicines publication -Presentations
10:30- 11:00	Tea break		



Chair: Ms Lisa Hedman, WHO			
Session 2 11:00 - 12:20	Scientific studies in process	Dr Helen McIlleron, <i>University of Cape Town</i> Dr Susan Abdel-Rahman, <i>The Children's Mercy Hospitals and Clinics</i> Dr Annেকে Hesselning and Dr Simon Schaff, <i>Stellenbosch University</i>	-Presentations
Session 3 12:20 - 13:00	Open discussion: Timelines of current studies Discussion of outstanding policy, scientific data or formulation studies needed to advance an FDC.	Plenary discussion	
13:00 – 13:45	<i>Lunch (WHO cafeteria, non-hosted)</i>		
Session 4 13:45 – 14:45	Formulation	Dr Tony Nunn, Consultant	-Presentations
Theme 2: Regulatory pathway			



Chair: Dr Sue Hill, WHO			
Session 5 14:45 – 15:30	Requirements and process for critical regulator submissions	Dr Milan Smid, WHO Dr Lembit Rago, WHO	-Presentations -Hand-outs from PaATH initiative
15:30 - 16:00	Tea break		
Session 5 (continued) 16:00 - 17:00	Update on EMA review of paediatric dosing guidelines	Dr Agnès Saint Raymond, <i>European Medicines Agency</i>	-Presentations
17:00 – 17:30	Start of open discussion on outstanding regulatory activities needed to advance an FDC	Plenary discussion	
Close of Day 1			
18:30 - 19:30	Cocktail social, Venue: Atlantide, M-building		
Day Two: 15 July Chair: Dr Suzanne Hill, WHO			
Theme 2: Regulatory pathway (continued)			
09:00 - 09:30	Brief review of day 1		
Theme 3: Business strategy			
Session 6 09:30 - 10:00	Industry Perspective	Mr Mukul Jerath	-Presentation

Session 7 10:00 - 10:30	Review of informal industry feedback: India case study	Ms Deirdre Dimancesco, WHO	-Presentation
11:00 – 11:30	Tea break		
Session 8 10:30 - 12:30 (tea break incl.)	Perspectives of global procurers	Ms Hanne Pedersen UNICEF; Ms Emma Hannay, UNITAID; Dr M. Grzemska, TBP/WHO	Presentation Hand outs on GDF
Session 9 12:30 - 13:00	Discussion with industry associations	Plenary discussion	
13:00 – 14:00	Lunch (WHO cafeteria, non-hosted)		
Session 9 14:00 - 15:00	Open discussion on what outstanding business information or actions are needed to advance an FDC.	Plenary discussion	
Theme 4: Consolidated review			
Session 10 15:00 - 15:30	Review and prioritization of activities identified from all previous sessions	Plenary discussion	
15:30 – 16:00	Tea break		
Session 12 16:00 - 16:30	Discussion of outcomes	Ms Lisa Hedman, WHO	
Session 13 16:30 - 16:45	Meeting wrap up and close	Dr Susanne Hill, WHO	

Annex 4: List of participants

Dr Susan Abdel-Rahman, The Children's Mercy Hospitals and Clinics, United States

Dr Grania Brigden, Médecins Sans Frontières, Switzerland

Dr Thomas Chiang, USAID, United States

Dr Gaia Colombo, Dept. Pharmaceutical Sciences, University of Ferrara, Italy

Professor Anneke Hesselning, Desmond Tutu TB Centre, Stellenbosch University, South Africa

Dr Gregory Kearns, The Children's Mercy Hospitals and Clinics, United States

Dr Helen McIlleron, University of Cape Town, South Africa

Ms Heidrun Hildebrand, Bayer Schering Pharma AG, Germany on behalf of the International Federation of Pharmaceutical Manufacturers and Associations

Mr Mukul Jerath, Lupin Limited, India on behalf of the Indian Pharmaceutical Alliance

Ms Cécile Macé, International Union Against Tuberculosis and Lung Disease, France

Professor Anthony Nunn, Independent Consultant, United Kingdom

Mrs Hanne Bak Pederson, UNICEF Supply Division, Denmark

Dr Agnès Saint-Raymond, European Medicines Agency, United Kingdom

Professor Simon Schaaf, Desmond Tutu TB Centre

Stellenbosch University, South Africa

Professor Roderick Walker, Rhodes University, South Africa

Ms Claire Wingfield, Treatment Action Group, United States

In attendance representing WHO

Ms Deirdre Dimancesco, EMP/MAR

Dr Emma Jane Hannay, UNITAID

Ms Lisa Hedman, EMP/MAR

Dr Suzanne Hill, EMP/MAR

Dr Anna Ridge, EMP/MAR

Dr Milan Smid, EMP/QSM/PQM