DNDi
Drugs for Neglected Diseases *initiative*

World Health Organization

NEOAMR Expert Meeting

WHO-DND*i* Global Antibiotic Research and Development Partnership (GARDP)

2-3 August 2016

DND*i* office: 15 Chemin Louis Dunant, 1202 Geneva

Background

Neonates and young infants are at high risk of severe bacterial infections (SBIs) with significant associated morbidity and mortality. Because of the non-specific presentation of SBI in this patient group, at least initially most treatment is empiric (i.e. covering a range of possible target bacteria). This results in many infants being treated who are unlikely to have a bacterial infection, although neonates with confirmed bacterial sepsis have a high mortality. This balance between potential over and under treatment is made more complex by the concern that empiric treatment is increasingly likely to be inadequate in terms of antibiotic cover in settings where there is a high prevalence of antimicrobial resistance. Multidrug-resistant Gram-negative bacteria (MDRGNB) are a major global health threat, and MDRGNB SBI is associated with a very high mortality amongst neonates and young infants. Several reviews have identified lower- and middle-income countries (LMICs), as having high MDRGNB prevalence, but outbreaks and endemicity of MDRGNB have also been described for neonatal units in high-income countries (HIC).

The overall possible SBI (pSBI) incidence in non-premature neonates in Latin America, Africa and South Asia has been estimated to be around 8% with a case-fatality risk of nearly 10%, and pSBI is thought to account for nearly ¼ of deaths in this patient group in LMICs (Seale, TLID 2014). In HICs, the incidence of early-onset sepsis, one of the most severe forms of neonatal SBI, is around 1 per 1000 live births. The case fatality risk for these infants is similar to that described for LMICs (Weston, PIDJ 2013). Hospital-born babies in LMICs are at particular risk of neonatal SBI (3-20 times higher than in HICs), and GNB account for nearly 60% of culture-proven infections in this group (Zaidi, Lancet 2005). Recent modelling puts neonatal sepsis deaths due to resistant organisms in China, India, Pakistan, Nigeria and the Democratic Republic of Congo alone at 215,000 (Laxminarayan, Lancet 2016).

In HIC settings, guidelines defining the recommended empiric antibiotic regimens are highly variable (Spyridis, ADC 2016), perhaps in response to statements such as those made by the “Surviving Sepsis Campaign” that “antibiotic choices should be guided by local prevalence patterns of bacterial pathogens and susceptibility data” (Dellinger, ICM 2013). However, data from Europe suggest that broader-spectrum options used in some settings may not necessarily provide better cover when microbiological epidemiology is taken into account (Bielicki, JAC 2015). In LMICs, a standard regimen of an aminopenicillin plus gentamicin is recommended for neonatal SBI (WHO pocket book, 2013). However, based on available limited surveillance data, a substantial proportion of neonatal and young infant SBI cases would not be adequately covered with this regimen (Downie, ADC 2012), particularly when considering GNB (Le Doare, JPIDS 2015). Together with an increasing proportion of hospital births in LMICs, this may explain that meropenem was amongst the antibiotics accounting for the top 90% of prescriptions to hospitalized neonates in Africa, Asia and Latin America (Versporten, JAC 2015).

DNDi
Drugs for Neglected Diseases *initiative*

World Health Organization

Objectives

1. To review and evaluate the NEOAMR proposal.
2. To determine observational study details, notably countries most feasible in terms of laboratory capacity, exportation of isolates etc.
3. To review in detail and adjust any preparatory work to be done in advance of clinical trials.

Outcomes

1. Consensus on the way forward for the proposal, including content and financing opportunities.
2. Timelines and workstream required to reach the GARDP Scientific Advisory Group meeting on 12 October 2016.

DNDi
Drugs for Neglected Diseases *initiative*

World Health Organization

Agenda

Tuesday, 2 August 2016

Time	Topics	Resource speaker	Facilitator
9:00	Arrivals and coffee		
9:10	Welcome	**Anthony Costello**, WHO, Switzerland (TBC)	
9:20	Opening and objectives - GARDP	**Manica Balasegaram**, GARDP, DND*i*, Switzerland	
9:45	Global clinical epidemiology on pSBI and MDR NNUs	**Anna Seale,** LSTHM, UK	
10:15	Global burden of Neonatal AMR Overview, current treatment options NeoAMR project introduction	**Mike Sharland**, St George's University London, UK	
11:15	Coffee break		
11:30	Global variations in molecular AMR	**Herman Goossens**, University of Antwerp, Belgium	
12:00	MDR in neonates in Africa	**Gary Reubenson,** University of the Witwatersrand, South Africa	
12:30	MDR in neonates in India	**Ramesh Agarwal,** AIIMS, India	
13:00	Lunch at DND*i*		
13:45	Landscape analysis of old drugs to treat MDR gram-negatives	**Céline Pulcini**, University of Lorraine, CHU Nancy, France	**Samir Saha**, Child Health Research Foundation at the Bangladesh Institute of Child Health, Dhaka Shishu Hospital in Dhaka, Bangladesh (TBC)
14:30-18:00	NeoAMR work packages	**Mike Sharland**, St George's University London, UK	**Manica Balasegaram,** GARDP, DNDi, Switzerland

Dinner TBD

DNDi
Drugs for Neglected Diseases *initiative*

World Health Organization

Agenda

Wednesday, 3 August 2016

Time	Topics	Resource speaker	Facilitator
9:00	Welcome and coffee		
9:10	Objectives of the day – Building on existing networks		**Mike Sharland**, St George's University London, UK
9:15	Role of global infectious disease networks	**Herman Goossens**, University of Antwerp, Belgium	
10:00	Global neonatal networks and regulatory aspects	**Mark Turner,** University of Liverpool, UK	
10:30	Learning from ANISA – building and running large neonatal infection studies (+ other LMIC AMR projects)	**Samir Saha**, Child Health Research Foundation at the Bangladesh Institute of Child Health, Dhaka Shishu Hospital in Dhaka, Bangladesh (TBC)	
11:00	Coffee break		
11:30	Running global paediatric infection trials – learning from experience	**Carlo Giaquinto,** PENTA-ID (TBC)	
12:15	Strategic AMR trial design	**Sarah Walker,** MRC-CTU, UK (TBC)	
13:00	Lunch at DNDi		
14:00	Policy and pharmaceutical approaches to facilitate conservation and sustainable access strategies • Key elements of stewardship from local to global • Distribution models What R&D incentives or how can risk be reduced?	**Manica Balasegaram**, GARDP, DND*i*, Switzerland	
14:45	Neonatal sepsis guidance / EMLc	**Anthony Costello**, WHO, Switzerland	**Liz Tayler,** WHO, Switzerland
15:00	Target Product Profiles - Purpose / indication - Characteristics	**Jutta Heim**, GARDP, DND*i*, Switzerland	
16:00	NeoAMR Proposal discussion		**Mike Sharland**, St George's University London, UK
17:00	Conclusions and next steps		**Manica Balasegaram**, GARDP, DND*i*, Switzerland