Investing in the development of new antibiotics and their conservation: A proposal for a global antibiotic research and development facility

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MSF and AMR

MSF can no longer safely assume the efficacy of simple antibiotics

• Bacterial infections one of the most common presentations in MSF projects
  – Including lethal invasive bacteria infections (IBI) such as bacteremia, meningitis, pneumonia and dysentery

• Risk of ineffective initial antibiotic treatment higher in MSF set-ups
  – Patients present later, with advanced disease, fewer safety nets for those inappropriately managed

• Antibiotic resistance (ABR) has emerged in most contexts where MSF works

• ABR is growing in severity; all regions of the world are affected to varying extents
  – High, middle and low IC countries affected
  – Many of the gaps in ABR surveillance exist where MSF operates
  – This in turn makes it difficult to understand true needs and gaps
Key problems

• Field surveillance

• Diagnostics
  – Especially to promote rationale use

• Drugs
  – Better formulations, combinations, regimes and new treatments/protocols where there is resistance
Key problems: diagnostic tools

In the field settings MSF cannot diagnoses bacterial infections with a high degree of sensitivity or specificity

Not enough national data exists to guide empirical choices

Lack of tools to distinguish bacterial infections from mycobacteria and non bacterial pathogens (eg viruses, parasites)
Cannot distinguish infections caused by sensitive / ABR bacteria

Microbiological capacity very limited in most MSF contexts (eg gram stain or blood culture not available)
Key problems: drugs

Marked increased in broad-spectrum antibiotics use:
• 3rd generation cephalosporins: ceftriaxone
• Fluroquinolones: ciprofloxacin
• β-Lactam/β-lactamase inhibitors: amoxicillin-clavulanate

This strategy has major costs:
• May drive further ABR
  – Most children leaving MSF ITFC are colonized with ESBL-producing gram negative bacteria (Niger, 2011)
• Unsustainable “arms race”
  – Bacteria evolve new resistance mechanisms
  – Highly ABR strains emerging in L&MICs eg Enterobacteriaceae strains expressing NDM-1
  – Few antibiotics in the development pipeline

However, improving access & patient care is our priority!
Recent MSF field experience

CNS infection study, Mbarara, Uganda (2011)

- S pneumoniae with intermediate sensitivity to PCN, resistant to cotrimoxazole
- H influenzae resistant to amoxicillin, chloramphenicol
- ESBL E coli and Kleb pneumo
- Salmonella typhi resistant to cipro

Diarrhea, Niamey & Maradi, Niger (2009)

ESBL Salmonella documented
1/3 bacteria were resistant to all antibiotics available in Niger
What is needed?

- Strong global health perspective: defined priorities, TPPs etc
- Monitoring & surveillance
- Diagnostics (new tools, improved lab capacity)
- Updated guidelines and policies (international and national)
- Education and local capacity
- Regulation
- Rational use linked with access strategies
- Coordinated procurement and supply
- Appropriate uptake, compliance
- Clinical research capacity and platforms
- Alternative incentives to promote innovation and conservation
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The facility: scientific added value

- R&D that will not be taken by other actors; improved formulations, combinations and updated dosing schedules – DNDi already has a track record
- Focus on specific diseases, especially where trials needed in LMIC context
- Potential focus on upstream ideas where risk taking can be encouraged
- PDPs (eg DNDi) have significant space to work on research, policy and early implementation in tandem with others including WHO and multilaterals (GF, UNITAID)
The facility: conservation and access

- Critical to have strong focus on LMIC and most vulnerable population access
- Diagnostics key in improving rationale use
  - improved integrated approach of fever management can significantly aid conservation
- Key role of essential medicines list (to ensure best policy) and WHO PQ (to promote uptake of best quality products)
- Facility could play similar role to The GDF for TB drugs (eg linking drug demand to supply and monitoring)
- Specific country level strategies need to be developed through further consultations
- Traditional incentive systems do not work: conservation & access promoted by different model based on de-linkage. Plenty of proposals that are ready for implementation!
The facility: set up

Real potential to develop a facility that will be global health focussed

Governance is key:
• Mandate and involvement of WHO but outside formal WHO structure (for flexibility)
• DNDi board/SAC serving as starting models (and allows time to develop the final governance structure)
• Governance not just a round table of donors
  – Independence must be ensured
  – Needs to ensure stays true to mission; takes and mitigates risks
  – Needs to provide required strategic technical and political input
  – Developing country presence is important
  – Technical expertise from a wide range of actors

Financing:
• Long term and sustainable
• Country commitments & contributions
Challenges for the facility

• Good understanding of needs and gaps for developing countries
  – Implementation of all aspects of GAP is therefore important to ultimately drive R&D agenda

• Political support and member state buy-in
  – Willingness of global health community and member states to implement something different to go beyond just talking about “alternative business models”
  – Sustainable, long term financing (including from developing countries)

• Identifying and implementing conservation strategies
  – Link with WHO critical
  – Important that WHO also has member state’s support to play a key role in AMR

• Creation of an open source and knowledge innovation model