Challenges and Successes of the FACT Project

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Partnership in India and Beyond

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## Malaria Endemic Areas

### Percentage Contribution of Population, Malaria Cases, Pf Cases and Deaths in 2009 (Compared to the country total)

<table>
<thead>
<tr>
<th>States</th>
<th>% Population</th>
<th>% Malaria cases</th>
<th>% Pf cases</th>
<th>% Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.E. States</td>
<td>4</td>
<td>13</td>
<td>17</td>
<td>46</td>
</tr>
<tr>
<td>Other high endemic states*</td>
<td>42</td>
<td>67</td>
<td>77</td>
<td>43</td>
</tr>
<tr>
<td>Other</td>
<td>54</td>
<td>20</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

*Andhra, Chhattisgarh, Gujarat, Jharkhand, MP, Maharashtra, Orissa, Rajasthan

Source: NVBDCP
Malaria Control Strategy: EDPT

- Case Detection & management
- Disease Surveillance
- Epidemic Preparedness

Scaling up ACT

- ACT in millions

Scaling-up RDT

- RDTs in thousands

Source: NVBDCP
Malaria Control Strategy: IVM

- Indoor Residual Spraying
- Insecticide treated Bednets (ITNs) & Long Lasting Insecticidal Nets (LLINs)
- Source Reduction

Scaling up LLIN

Source: NVBDCP
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973</td>
<td>First evidence of CQ resistance</td>
</tr>
</tbody>
</table>
| 1982 | Drug policy drafted for the first time, Presumptive therapy CQ: (600 mg)  
      | PQ RT (5d), SP introduced in resistant Pf areas |
| 1995 | Presumptive treatment with full dose of Chloroquine |
| 1997 | Registration of artemisinin derivatives |
| 2001 | Introduction of αβ arteether for severe malaria in programme |
| 2007 | No more presumptive treatment, PQ for 14 days  
      | ACT (AS+SP) introduced in India in NER and clusters with >10% resistant Pf districts |
| 2008 | Trials of AS+AQ, AS+MQ, Artekin, Pyramax accomplished  
      | AS+SP extended to 117 districts |
| 2009 | Registration of AS+AQ  
      | Ban on Artemisinin monotherapy |
| 2010 | ACT extended to Pf cases all over India |
| 2011 | ?Registration of AS+MQ FDC |
Do we need partnerships?

- Little financial incentive for Industry for malaria
- Only 21 drugs for tropical diseases between 1975 and 2004
- Partnerships bring together academia and industry
- Success stories in India: DNDi & MMV
- GF partnerships with countries limited to distribution of products and 5-10% for evaluation
Partners for ACT studies

- NIMR
- Industries
- NVBDCP
- DNDi
- Public Health System
- Medical Colleges
- Corporate Hospitals
- MMV
Development of ASAQ
Partnership with DNDi: ASAQ

- ASAQ registered in 30 African countries
- 70 million doses distributed
- Phase III trials in India
- Registration with regulatory authority in 2009

Cure Rates (Before and After PCR Correction)

<table>
<thead>
<tr>
<th></th>
<th>Cure rate (%)</th>
<th>Cure rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (AS/AQ)</td>
<td>92.42 (Before PCR correction)</td>
<td>92.42 (After PCR correction)</td>
</tr>
<tr>
<td>Group B (AQ)</td>
<td>82.98</td>
<td>98.99</td>
</tr>
</tbody>
</table>

Parasite Clearance Time (PCT)

<table>
<thead>
<tr>
<th></th>
<th>Mean parasite clearance time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (AS/AQ)</td>
<td>1.5</td>
</tr>
<tr>
<td>Group B (AQ)</td>
<td>2.1</td>
</tr>
</tbody>
</table>
### Partnership with DNDi: ASMQ

#### 63 Day Cure rate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with ACPR</td>
<td>65 (98.48)</td>
</tr>
<tr>
<td>Cure rate (%)</td>
<td>98.48</td>
</tr>
<tr>
<td>95% CI of cure rate</td>
<td>91.8, 100.0</td>
</tr>
</tbody>
</table>

#### PCR corrected 63 Day Cure rate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patient available for PCR genotyping</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>No. of patients with new infection</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>No. of patients classified as cured after PCR genotyping</td>
<td>66 (100%)</td>
</tr>
<tr>
<td>95% CI of cure rate</td>
<td>94.6, 100.0</td>
</tr>
</tbody>
</table>
Partnerships: NVBDCP
Therapeutic efficacy of ACT in Drug Policy

- Baran, n=67, cure rate 100%
- Khanvel, n=94, cure rate 98.8%
- Kanker, n=70, cure rate 100%
- Gadchiroli, n=82, cure rate 93.8%
- North Goa, n=55, cure rate 100%
- Mangalore, n=76, cure rate 100%
- Chhindwara, n=44, cure rate 97.6%
- Purulia, n=80, cure rate 98.7%
- Ranchi, n=71, cure rate 100%
- Simdega, n=60, cure rate 100%
- Dhenkenal, n=76, cure rate 98.2%
- Sambalpur, n=70, cure rate 100%
- Nagaon, n=51, cure rate 100%
Partnerships:

- Development of two FDC’s
  - Eurartesim
  - Pyramax for Pf and Pv
- Packaging for Pyramax
- Plans for implementation research
- Representation in technical committees

An Open-Label, Randomised Study of Dihydroartemisinin-Piperaquine Versus Artesunate-Mefloquine for Falciparum Malaria in Asia

Neena Valecha\textsuperscript{1}, Aung Pyae Phyo\textsuperscript{2}, Mayfong Mayxay\textsuperscript{3,4}, Paul N. Newton\textsuperscript{3,5}, Srivicha Krudsood\textsuperscript{6}, Sommay Keomany\textsuperscript{7}, Maniphone Khanthavong\textsuperscript{8}, Tiengkham Pongvongsa\textsuperscript{9}, Ronnattrai Ruangveerayuth\textsuperscript{10}, Chirapong Uthaivil\textsuperscript{11}, David Ubben\textsuperscript{12}, Stephan Duparc\textsuperscript{12}, Antonella Bacchieri\textsuperscript{13}, Marco Corsi\textsuperscript{13}, Bappanad H. K. Rao\textsuperscript{14}, Prabash C. Bhattacharya\textsuperscript{15}, Nagesh Dubhashi\textsuperscript{16}, Susanta K. Ghosh\textsuperscript{17}, Vas Dev\textsuperscript{18}, Ashwani Kumar\textsuperscript{19}, Sasithon Pukittayakamee\textsuperscript{6}
Efficacy of new ACTs (2005-09)

- Trials with fixed dose ACTs & new drugs
- Teams have been trained For GCP – ICH
- Linkages
  - Ispat General Hospital Rourkela
  - Community Welfare Society Rourkela
  - Kasturba Medical Hospital Mangalore
  - Maha Devi Birla Hospital Ranchi
  - Goa Medical College Goa
  - Civil Hospital Maihar
  - TATA Main Hospital Jamshedpur

Collaborators / Sponsors
- MMV
- DBT
- IISc, Bangalore
- Ranbaxy
- DNDi
- Sigma Tau
- Shing Poong
Partnership for Access/ Implementation

• Collaborative process with Input from Govt./Stakeholders
• Work with manufacturer on no profit/no loss structure
• Focus on lowering price outside profit/competition motive and by technology transfer
• Farmanguinhos in Brazil, Cipla in Asia, Sanofi Aventis in Africa
• Advocacy to improve representation of products, pharmacovigilance
Partnership Gains

Country
- GCP
- Clinical Network Infrastructure
- Resources
- Part of global teams

Industry
- Product Credibility

Organization
- Credibility
- Accomplishing the mission

Quality product
- Disease Control

Affordable Medicine

Community
Partnership for development of ACT in India: SWOT Analysis

**Strengths**
- Involvement of academia
- Acceptable to all partners
- Financial support

**Weaknesses**
- Variable epidemiology
- Common protocols may not be acceptable
- Delay in approvals
- Restriction in material / data sharing

**Opportunities**
- PPP
- Initiatives to promote rational treatment

**Threats**
- Apprehension of industry
- Sustainability
Focus on portfolios and disease control rather than specific products
Acknowledgements

- Govt. of India
- DNDi
- Collaborating Hospitals
- NVBDCP
- State Health Authorities
- NIMR & Its Field Units