

Outsourcing and Procurement Considerations in High Risk Countries

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Views and opinions are those of the author and do not necessarily represent official policy or position of MMV

MMV team November 2018



A foundation of over 90 people working towards
the same mission, to reduce the burden
of malaria in disease-endemic countries by
DISCOVERING, DEVELOPING and DELIVERING
new, effective and affordable antimalarial drugs

Malaria remains a public health imperative

Estimated
435 000 deaths
worldwide



61%
deaths occur in
children <5 years

High Risk Definition

“likely to result in failure, having a lot of risk”

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Barriers for conducting clinical trials in developing countries

- **Lack of financial and human capacity**
 - Funding
 - Skilled personnel
 - Awareness and motivation
- **Ethical and regulatory system obstacles**
 - Delay of approval decisions
 - Unskilled authorities
 - Complex and strict system

Alemayehu et al, March 2018, International Journal for Equity in Health

Barriers for conducting clinical trials in developing countries

- **Lack of research environment**
 - Infrastructure
 - Materials, facilities
 - Conducive scientific atmosphere
- **Operational barriers**
 - Unsupportive administrative system
 - Lack of/difficult patient recruitment
- **Competing demands**
 - Time
 - Competing priorities



Outsourcing/Procurement Risks

- **Failure To Secure Supply**
- **Insufficient Lead Time**
- **Misrepresentation of the Facts, Unethical Practise & Breach of Confidentiality**
- **External Factors**
- **Inappropriate Strategy/Evaluation Criteria**

Failure To Secure Supply

- **Experienced and Available PIs and Site Staff**

- Robust training and oversight processes to ensure meet required standards

- **Clinical laboratories**

- Local (TATs / capacity building [staff/infrastructure] – healthcare compliance)
- Central – sometimes limited regional capacity. Africa ship from/to Europe (↑ courier costs and time for shipments)
- Sample shipment (↑ frequency)

- **Monitoring and site management**

- Availability of experienced CRAs (↑ costs including expenses)
- Note CRO travel bans (e.g., DRC) – how integrate?



Failure To Secure Supply

- **eCRF connectivity issues**
 - Off-line access (most CROs moving away)
 - Record on paper and enter when connectivity resumes
 - Satellite links
- **Trial documentation**
 - eTMF connectivity issues
 - Limited site archiving



Insufficient Lead Time

- **Approvals (6-12 months)**
- **Laboratories and IMP**
 - Bureaucratic import/export (MTAs)
- **Site readiness**
 - Start GCP and other training early (mixture of e-learning/F2F)
- **Pharmacovigilance**
 - Can take time to confirm some reporting times and processes (default to those of EMA/FDA)



Misrepresentation of the Facts, Unethical Practise & Breach of Confidentiality

- **IMP**

- IB Management & Dissemination SOP rigorously followed (AoR). Some countries PI submits RAs/ECs (note use of public domains – Yahoo)

- **Investigator sites**

- SEV F2F and preferably with final protocol
- Financial audits (F2F/remote)
- Specify analyse their own samples (Zambia)
- Site in Benin, did not meeting recruitment target, however payment for capacity building, not able to get money refunded – payment plan

- **Training**

- Ethiopia – trainer from South Africa provider complained about conditions (Trainer from Europe)



External Factors

- **Instability**

- Terrorist attacks in Burkina Faso. Couldn't get CRAs in or samples and auditors out
- Gabon election violence (CRAs, samples, auditors) plus put patient recruitment on hold
- Ethiopia (last week) 22 people killed, postponed SIV
- Earthquake in Indonesia (damaged undersea cable – time to repair). Communication issues somewhat improved with whatsapp. However daily back-up hindered / cleaning wait until internet connection resumed

- **Health**

- DRC – ebola outbreak (CRAs/samples etc.,)
- Cameroon – auditor hospitalised (update to date with injections)

External Factors

- **Cultural**
 - Tanzania – remote (pregnant women) – issues with taking samples. Consulted with social anthropologist, plan in place for community engagement/education
- **Travel Risk Policy (International SOS)**

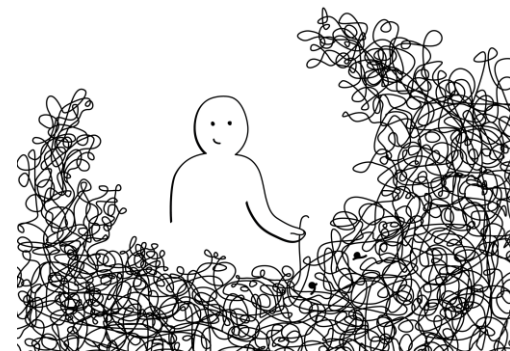
Risk Level	Risk Factors	Mitigation Measures
MEDIUM	<ul style="list-style-type: none">• communal, sectarian or racial violence.• Violent crime rates are likely to impact on foreigners as well as the local population.• Inadequacies in the security and emergency services.	<ul style="list-style-type: none">• with precautions.• Approval for travel given by direct supervisor / manager, unless there is a travel restriction in place (in which case it will be ELT), the Travel Coordinator will advise.
HIGH	<ul style="list-style-type: none">• Regular periods of political instability and associated problems of poor governance.• Protests are frequently violent and may target or disrupt foreigners.• Communal, sectarian or racial violence is common, foreigners may be directly targeted.• Violent crime rates are typically high and often have police complexity.• Infrastructure, internal security and emergency services are poor.• Areas are inaccessible or off-limits.	<ul style="list-style-type: none">• Restricted operations.• Essential travel only.• Evacuations / contingency plans in place and ready for activation.• Monitoring of traveller (regular "check-in").• Approval for travel given by ELT.
CRITICAL & EXTREME	<ul style="list-style-type: none">• State of war, failed states or states in which the government has lost control of significant portions of the country.• Government control and law and order may be minimal or non-existent.• There is a serious threat of violent targeted attacks against international organizations and / or NGO staff.• Foreigners are likely to have no access to significant parts of the country.	<ul style="list-style-type: none">• No operations.• Exceptional travel only.• Evacuation plans in place and executed.• Monitoring of traveller (regular "check-in").• Approval for travel given by CEO only.

A report prepared for Medicines for Malaria Venture
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Inappropriate Strategy/Evaluation Criteria

Recommend reviewing current strategy if new to working in these countries:

- Clinical laboratories
- Sponsor presence in the region?
 - In-house clinical operations
 - CRO PM/Monitoring
- Appropriate resourcing
 - Seniority
 - “sufficient” – ensure oversight
- Technology/ies?
- RBM?
- Post-registration study in Brazil, PI wanted to perform data management



Outsourcing/Procurement Process

- **Early identification of potential partners**
- **Perform robust due diligence**
- **Careful review of proposals which accounts for total value (cost), to minimise failure**
- **Select partners and execute the contracts**
 - With appropriate financial controls and payment plans
 - Consider “force majeure”, unforeseeable circumstances that prevent someone from fulfilling a contract
- **Thorough and frequent monitoring of oversight, performance and risk**
- **Timely establishment and implementation of issue escalation plan**
- **Conduct close out activities (including lessons learned)**

Key Messages

- Determine the barriers that operate in your country /ies
- Start planning early, ensure you focus on appropriate mitigation of risks with regular review
- Csíkszentmihályi (Hungarian-American psychologist). Chaos – Flow Theory - "the emotions are not just contained and channeled, but positive, energized, and aligned with the task at hand"

THANK YOU!
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Questions?