Rational Pharmaceutical Management Plus
Unclogging the ARV Drug Pipeline Meeting, January 20, 2005: Trip Report

Helena Walkowiak

March 10, 2005
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About RPM Plus

The Rational Pharmaceutical Management Plus (RPM Plus) Program, funded by the U.S. Agency for International Development (cooperative agreement HRN-A-00-00-00016-00), works in more than 20 developing countries to provide technical assistance to strengthen drug and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

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### Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AHF</td>
<td>AIDS Healthcare Foundation</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>antiretroviral therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>antiretroviral [drugs]</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
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<td>RPM</td>
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Background

The AIDS Healthcare Foundation (AHF) is a provider of antiretroviral therapy (ART) care to over 2,800 people in six developing countries. AHF recognizing that drug supply line problems have become a significant hindrance to ART scale-up in their programs organized a meeting entitled “Unclogging the Antiretroviral (ARV) Drug Pipeline.” This one-day meeting sponsored by Boehringer-Ingelheim, Abbott Laboratories, Gilead Pharmaceuticals, and AHF was held in Amsterdam, the Netherlands, on January 20, 2005. The purpose of the meeting was to examine the issues involved and to suggest solutions. A consensus statement was to be drafted at the end of the meeting for publication.

Purpose of Trip

Ms Helena Walkowiak, Senior Program Associate, Rational Pharmaceutical Management Plus (RPM Plus) traveled to Amsterdam, the Netherlands with funding from the United States Agency for International Development/Washington to attend the meeting held on January 20, 2005 to make a presentation on “Market Factors Impacting ART Scale Up” and to participate in discussions and drafting of the consensus statement.

Scope of Work

1. Give a presentation to identify the 2–3 most important market factors for pharmaceuticals used in the treatment of HIV/AIDS causing difficulties in scale-up for ART programs in least-developed and middle-income countries
2. Participate in discussions to identify issues, suggest solutions and draft a consensus statement to “Unclog the ARV Drug Pipeline”
Activities

1. **Give a presentation to identify the 2–3 most important market factors for pharmaceuticals used in the treatment of HIV/AIDS causing difficulties in scale-up for ART programs in least-developed and middle-income countries**

   The agenda of the meeting is attached as Annex 1. Ms Walkowiak’s presentation entitled *Unclogging the Antiretroviral Drug Pipeline: Market Factors* was very well received and is attached as Annex 2.

   Presentations given by other participants are also attached in the annexes


   *Supply Chain Issues*: Mr. Alain Pierre, Interchurch Medical Assistance – Annex 5


   *Supply Chain*: Consensus/Action; Ms. Bianca Kamps, International Dispensary Association – Annex 6

   *Market Factors*: Consensus/Action; Mr. Robert Dintruff, Abbott Laboratories – Annex 7

2. **Participate in discussions to identify issues, suggest solutions and draft a consensus statement to “Unclog the ARV Drug Pipeline”**

   The morning discussions concentrated on identifying 2-3 key issues that were constraining ARV scale up in developing and middle income countries in the following key areas:
   - Patent approvals, Patents, and Quality Assurance
   - Supply Chain
   - Market Factors

   The afternoon discussions concentrated on identify solutions and agreeing on a consensus statement. The draft consensus statement includes:

   *Patent approvals, Patents, and Quality Assurance*: Consensus/Action

     1. Work towards and consolidate approval processes for registration of products.
     2. Standardize dossiers required from companies between countries and international agencies.
     3. Provide "fast-track" assistance for registration of ARV products in country.
     4. United Nations Agencies should update ART standard treatment guidelines more frequently.
5. Development of paediatric formulations for ARV drugs should be a high priority for companies and agencies.

Supply Chain
   6. Countries should eliminate taxes, fees, and duties for ARVs.
   7. Extending the actual shelf-lives of ARV products should be thoroughly investigated.
   8. Paperwork at all levels should be streamlined.

Market factors
   9. The development and production of simpler therapies and more convenient formulations should be encouraged.

Collaborators and Partners

World Health Organization
   Marte Everard
   F. Amolo Okero

Global Fund to Fight AIDS, Tuberculosis, and Malaria
   Guido Bakker

Axios International
   Laurence Phillips

Interchurch Medical Assistance
   Alain Pierre

Salvation Army World Service Office
   W. Bramwell Bailey

PA Consulting Group -- Infrastructure and Development Services
   Robert Bonardi
   Howard Lyons

International Dispensary Association BV
   Bianca Kamps
   Machiel Wierdsma

AIDS Healthcare Foundation
   Michael Weinstein
   Henry Chang
   Charles Farthing
   Sarynina Nieuweboer
   Steve Schulte
   Clint Trout
Abbott Laboratories
Robert Dintruff

Aurobindo Pharma Limited
Gita Rao

Boehringer-Ingelheim
Helene Clary
Thomas Fischer

Bristol-Myers Squibb
Donne Newbury

Gilead Sciences, Inc.
Alan Taylor

Guava Technologies
David Ferrick
Next Steps

Immediate Follow-up Activities

AHF will draft the consensus statement for comment and final agreement. AHF and partners will use the statement to advocate for and develop a plan of action to address constraints identified in this meeting to improve the availability of ARV drugs to the service delivery points in developing countries and middle income countries.
Annex 1. AGENDA: "Unclogging the Drug Pipeline"

January 20, 2004
Amsterdam, the Netherlands

8:00 Opening & Introduction
Mr. Michael Weinstein, AIDS Healthcare Foundation

8:15 - 12:15 Morning Discussion: "The Scope of the Problem."

8:15 Session 1: Approvals, Patents, and Quality Assurance:
Ms. Marthe Everard & Ms. F. Amolo Okero, World Health Organization

How is scale up of distribution of ARV products in least-developed and middle-income countries impeded by problems with patents and quality assurance and approval mechanisms? (FDA, WHO, EMEA, MCC, etc.)?

9:30 Break

9:45 Session 2: Supply Chain:
Mr. Alain Pierre, Interchurch Medical Assistance

Early scale up of ARV programs has been hampered in many developing countries by supply-chain delays or breakdowns. What are the key issues causing such problems for ARV programs in least-developed and middle-income countries?

11:00 Session 3: Market Factors:
Ms. Helena Walkowiak, Management Sciences for Health

What are the most important market factors (for pharmaceuticals used in the treatment of HIV/AIDS) causing difficulties in scale up for ARV programs in least-developed and middle-income countries?

12:15 Lunch


The afternoon session will mirror the agenda for the morning, except the focus of each presentation and discussion will be to suggest solutions and an action plan.

1:15 Session 1: Patent approvals, Patents, and Quality Assurance, Consensus/ Action
Ms. Marthe Everard & Ms. F Amolo Okero, World Health Organization

2:30: Break
2:45 Session 3: Supply Chain, Consensus/Action
Ms. Bianca Kamps, International Dispensary Association

4:00 Session 4: Market Factors, Consensus/Action
Mr. Robert Dintruff, Abbott Laboratories

5:15 Agreement and Implementation
Mr. Michael Weinstein, AIDS Healthcare Foundation

6:00 Close
Objective of the session:
- To identify the 2–3 most important market factors for pharmaceuticals used in the treatment of HIV/AIDS causing difficulties in scale-up for ARV programs in least-developed and middle-income countries

Outline of the session:
- Market for ARV drugs in least-developed and middle-income countries
- Key market factors impacting ART scale-up: Supply
- Key market factors impacting ART scale-up: Demand
- Supply systems issues
- Discussion

HIV/AIDS Pharmaceuticals: Prevention and Treatment

- Antiretrovirals (ARVs):
  - Post-exposure prophylaxis
  - Prevention of mother-to-child transmission
  - Clinical AIDS
- Anti-infectives (antibacterials, antifungals, and antivirals) for prevention and treatment of opportunistic infections
- Treatment of sexually transmitted infections (STIs)
- Tuberculosis treatment
- Analgesics and palliative care pharmaceuticals
- Anticancer pharmaceuticals
- Pharmaceuticals for noninfectious and other complications:
  - Cardiac
  - Renal
  - Hepatic
  - Neuropathic
  - Dermatologic
  - Hematologic
  - Pulmonary
  - Gastrointestinal/diarrhea
  - Oral and esophageal
  - Psychiatric

HIV/AIDS Health Commodities: Prevention, Diagnosis, Monitoring

- Prevention
  - Condoms
- Diagnosis and Monitoring:
  - HIV test kits
  - Other diagnostic test kits
  - Automated analyzers (ELISA)
  - Other laboratory monitoring equipment
  - Reagents
  - Gloves
  - Needles and syringes
- Diagnosis and Monitoring (cont.):
  - Vials
  - Sharps disposal bins
  - Bleach and other disinfectants
  - Microscopes
  - Precision pipettes
  - Centrifuges
  - Incubators
  - Refrigerators
  - Freezers
Antiretroviral Drugs

- **Product Characteristics**
  - Expensive
  - Often delivered with short shelf life
  - Require secure and often temperature-controlled storage

- **Antiretroviral Therapy**
  - Combinations of 3 or more drugs
  - Clinical and laboratory monitoring
  - Fast development of resistance if adherence < 90%
  - Treatment failure likely if adherence <95%
  - Adverse drug reactions
  - At the moment ART is for life

The Market for ARV Drugs in Least-Developed and Middle-Income Countries

- Imperfect market – supply and demand forces are influenced by factors not usual in a “perfect” competitive environment

Supply Forces

- **Oligopoly**
  - Few manufacturers
  - Impact of prequalification, registration, patents
  - Examples
    - 3TC 150mg tablets – 14¹ (3 prequalified UN/MSF)²
    - EFV 600mg tablets – 4¹ (0 prequalified)² (1 originator)
    - d4T 30mg cap – 12¹ (1 prequalified UN/MSF)²
    - 3TC 10mg/ml liquid – 3¹ (2 prequalified UN/MSF)²
    - NVP 10mg/ml liquid – 3¹ (1 prequalified UN/MSF)²

Capacity of Manufacturers to Meet Demand

- Lead times for ARV products are increasing
- Why?
  - Inaccurate forecasting leading to insufficient production?
  - Lack of flexibility to increase production to meet short-term needs?
  - Increasing lead times in shipping to and release of goods by local agents?
  - Or are manufacturers experiencing problems meeting demand for active ingredients and end products?

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¹ Sources and Prices of Selected Medicines & Diagnostics for People Living with HIV/AIDS (June 2004)
² UNICEF/UNAIDS/WHO/MSF

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(1) Sources and Prices of Selected Medicines & Diagnostics
(2) Access to HIV/AIDS: Drugs and Diagnostics of Acceptable Quality
Demand Forces

- Demand
  - Characterized by extreme uncertainty
  - Financing
    - Major purchasers mainly using donor funding
    - Public and not-for-profit sector demand is increasing relative to private sector demand
  - Variable user “demand” for, prescribing and use of, and response to ART
  - Push for rapid ART scale-up

Coverage and Need for Antiretroviral Treatment (WHO June 2004)

- All WHO Regions
  - Number of people on treatments: 440,000
  - Estimated need: 5,500,000
  - Coverage: 8%

- Africa Region
  - Number of people on treatments: 150,000
  - Estimated need: 3,840,000
  - Coverage: 4%

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  - Coverage: 4%

U.S. President’s Emergency Plan for AIDS Relief

- In July 2004 – directly funding ART for approx. 18,000 people
- Goal by June 2005 – to provide ART to at least 200,000 people

<table>
<thead>
<tr>
<th>Country</th>
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<tr>
<td>Ethiopia</td>
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</tr>
<tr>
<td>Haiti</td>
<td>N/A</td>
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<tr>
<td>Namibia</td>
<td>2,500</td>
<td>4,000</td>
<td>23,000</td>
</tr>
<tr>
<td>Nigeria</td>
<td>500</td>
<td>16,000</td>
<td>250,000</td>
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<tr>
<td>Rwanda</td>
<td>100</td>
<td>4,000</td>
<td>23,000</td>
</tr>
<tr>
<td>South Africa</td>
<td>3,700</td>
<td>20,000</td>
<td>500,000</td>
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<tr>
<td>Tanzania</td>
<td>100</td>
<td>11,000</td>
<td>150,000</td>
</tr>
<tr>
<td>Uganda</td>
<td>7,300</td>
<td>27,000</td>
<td>60,000</td>
</tr>
<tr>
<td>Vietnam</td>
<td>N/A</td>
<td>1,000</td>
<td>22,000</td>
</tr>
<tr>
<td>Zambia</td>
<td>1,500</td>
<td>15,000</td>
<td>120,000</td>
</tr>
</tbody>
</table>

Unpredictability in Product Demand

- Variable use of and response to ART
  - Non-ART treatment naïve clients
  - Need for second-line drugs
- Pediatric issues
  - Selection of regimen, formulation, and dose
  - Product stability and shelf life
- Variable user demand for ART
  - Treatment literacy and preparedness
  - Stigma
- Prevention and treatment of opportunistic infections (OIs)
  - Increasing need for OI drugs
### Constraints to Accurate Forecasting

- Lack of historical (consumption) data
  - New program
  - Inadequacy of management information systems to gather and report data
- Impact of donor financing on procurement
- Unpredictability in scale-up/roll-out of ART services
- Variable user demand for, use of and response to ART
- Products are often short-dated; expensive; require secure and often temperature-controlled storage
- Inflexible procurement mechanisms
  - Long procurement periods with annual delivery
  - Flexibility to adjust delivery schedules and/or quantities not routine

### Affordability of Products and Services

- In developing countries the public sector is likely to continue be the main market for most people
- Donor funding has “created” demand by dampening the issue of affordability for the time being
- GFATM established to address some of the usual concerns about donor financing; however, commitments continue to outstrip disbursements
  - Delays in approval of Global Fund proposals
  - Delays in disbursement of funds

### Capacity of the Market to Absorb Supply

- Lack of capacity of systems to effectively manage the expected and sudden influx of supplies is perhaps the biggest barrier to scale-up

### Constraints to Scaling Up ART Service Delivery (1)

#### Limited Capacity of Health Care Systems (1)

- Human resources – staffing levels, motivation, and training
- Infrastructure – functioning laboratory, secure storage
- Treatment guidelines and clinical procedures/protocols
- Systems to provide comprehensive health services for HIV/AIDS care and prevention, as well as continuity of care
Constraints to Scaling Up ART Service Delivery (2)

Limited Capacity of Health Care Systems (2)
- Functional and responsive procurement and supply chain for drugs and supplies
- Systems to monitor and support adherence to treatment
- Management information systems
- Monitoring and supervision – quality of services and long-term patient outcomes

Constraints in Supply System Capacity
- Most existing public supply systems are not adequately structured or staffed to cope with expected massive supply
- Private sector is also often stretched to capacity already
- System strengthening takes time and sustained investments

Example: Getting the Product to the Service Delivery Point (1)
- Tanzania
  - Medical Stores Department distributes about $30 million (about 30% of pharmaceutical market)\(^1\) – can it cope and do more?
- Kenya
  - Kenya Medical Supplies Agency (KEMSA) is experiencing considerable challenges
  - Mission for Essential Drugs and Supplies (MEDS)\(^2\) has sales of $6 million (probably <10% of pharmaceutical market) but lacks capacity and know-how to procure drugs under USG regulations

Example: Getting the Product to the Service Delivery Point (2)
- Uganda
  - National Medical Store (NMS) purchases $11 million (probably 15–20% of market)\(^1\), but having problems; could be privatized
  - Space and numbers of pallets needed per month and per year will have to be expanded greatly
  - Joint Medical Stores (JMS) has sales of $7 million\(^2\) (<10% of pharmaceutical market but JMS still stretched to the limit)

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\(^1\) Strategies for Enhancing Access to Medicines (SEAM) Assessment. MSH (2001)
Summary (1)

- Imperfect market – supply and demand forces are influenced by factors not usual in a “perfect” competitive environment
- Demand characterized by extreme uncertainty
- Supply characterized by oligopoly
- Lack of capacity of systems to effectively manage the expected and sudden influx of supplies limit the capacity of the market to absorb supply

Summary (2)

- Key market factors influencing ART scale-up include:
  - Constraints to accurate forecasting
  - Variable user demand for, use of, and response to ART
  - Capacity of the health care system to deliver ART services
  - Capacity of supply system to deliver products to the service delivery point
  - Others??

Discussion Objective

- To identify the 2–3 most important market factors for pharmaceuticals used in the treatment of HIV/AIDS causing difficulties in scale-up for ARV programs in least-developed and middle-income countries
Annex 3. Quality assurance and approval mechanisms: Challenges for scaling up of antiretrovirals: Ms. Marthe Everard World Health Organization
Quality assurance and approval mechanisms: challenges for scaling up of antiretrovirals

"Unclogging the ARV drug pipeline"
20 January 2004

Marthe Everard, Technical Officer
WHO/Medicines Policy and Standards
Geneva, Switzerland

Introduction: antiretrovirals

- HAART improves considerably morbidity and mortality in developed and developing countries;
- Improving access to ARVs in the developing countries through numerous treatment programmes including WHO’s "3 by 5";
- Improved funding for ARVs through GFATM, PEPFAR, WB and other funding agencies etc.;
- Simplification of treatment protocols important to help rapid scale-up of treatment programmes;
- Use of FDC’s crucial for simplifying treatment.

Before and after HAART

Traditional HAART

- Pill burden, difficult schedules, potential low compliance and difficult supply management
Challenges identified

♦ What are the challenges?
  – ARVs are complex chemical molecules
  – Quality assurance: counterfeit ARVs
  – Safety and efficacy: various formulations
  – Market approval: public health perspective
  – Post-marketing surveillance

ARVs are complex molecules

♦ More than 20 generic manufacturers worldwide have started to produce ARVs;
♦ Generic ARV formulations including FDCs, but……
♦ Few meet international criteria for quality, safety and efficacy……

Quality assurance: Counterfeit ARVs

♦ WHO distributed in 2003 Rapid Alert about Ginovir 3D which was found not to contain the three active ingredients on label in amounts suggested

Safety and efficacy: various formulations (1)

♦ FDCs
  - most likely one size does NOT fit all but may fit most in mass treatment programmes;
  - need for availability of various individual medicines and formulations.
Safety and efficacy: various formulations (2)

- Need for multiple formulations for paediatrics:
  - weight-based dosing needed for most ARVs until adolescence – linear proportional decrease of doses of all components may not be always the case;
  - very limited paediatric PK studies;
  - lack of studies with combinations in paediatric populations;
  - need for liquid formulations for infants;

Market approval

- Public health perspective:
  - proven comparative efficacy, safety and cost-effectiveness;
  - on the National Essential Drugs List;
  - included in the national treatment guidelines or protocols;
  - procured in right quantities, of assured quality for prices that the government can afford.

National List of Essential Medicines

- All the drugs in the world
- Registered medicines
- National list of essential medicines
- Levels of use
- Supplementary specialist medicines
- CHW
- Dispensary
- Hospital
- Referral hospital
- Private sector

Post-marketing surveillance

- Pharmacovigilance:
  - data available from industrialized countries
  - limited data available from developing countries
What is WHO doing to ensure quality, safety and efficacy of ARVs?

♦ On-going activities
  – UN pre-qualification scheme
  – Training on GMP
  – Workshops for DRAs
  – Guidelines for Model Quality Assurance System (MQAS) for procurement agencies

UN pre-qualification scheme

♦ Partners:
  – UNAIDS
  – UNICEF
  – UNFPA
  – WHO
  – With the support of the World Bank

♦ WHO role:
  – Technical assistance based on WHO norms and standards, plus ICH and other standards, where applicable

Pre-qualification: basic principles

♦ Voluntary for participating manufacturers;
♦ Open to both innovators and multisource / generic manufacturers:
♦ Legitimate - General procedure and standards approved through WHO Expert Committee mechanism;
♦ Widely discussed in many fora;
♦ Transparent (all information available on web site http://www.who.int/medicines/);
♦ No cost for applicants so far.

Pre-qualification: quality generics or not?

FDA requirements for generic drugs (www.fda.gov/odc/gd)

Generic drugs must:
1. contain same active ingredients as the innovator drugs
2. be identical in strength, dosage form, and route of administration
3. have same use indications
4. be bio-equivalent
5. meet same batch requirements for identity, strength, purity and quality
6. be manufactured under same strict standards of GMP required for innovator products.
Pre-qualification: how is it done?

♦ By competent national regulators and inspectors exactly as the best regulatory agencies do it:
  – Thorough assessment of documentation provided for quality, safety and efficacy
  – Inspections of all manufacturing sites
  – Inspection of API manufacturers (if not inspected by others like EU inspectors or US FDA) planned
  – Inspections of CROs where BE studies are done
  – Quality Control lab testing
  – Follow-up surveillance of supplies

Pre-qualified HIV/AIDS-related products

♦ Till date pre-qualified:
  – 86 HIV/AIDS-related medicines
    • 48 single-drug ARVs
    • 5 two-drug ARVs
    • 2 triple-drug ARVs
    • 31 medicines for OIs

Training on GMP

♦ Workshops on GMP and Quality assurance
  ♦ ......................

Workshops for DRAs

♦ Prequalification of finished pharmaceutical products (FPPs) used in the treatment of HIV/AIDS, Malaria and Tuberculosis
  – Training course for African Drug Regulators, June 2002
  – Training course for Pan American Health Drug Regulators, 2002
♦ Pharmacovigilance
  – First training workshop to introduce monitoring of safety and efficacy of ARVs in Africa, September 2004
Guidelines

♦ Model Quality Assurance System (MQAS) for procurement agencies:
  - Document will contain norms and standards and model documentation that can be used by procurement agencies.
  - Document will focus on recommending standards for procurement agencies involved in prequalification, purchasing, storage and distribution of pharmaceutical products.

What is the current situation?

♦ Several countries scaling up their treatment programmes;
♦ Removal of some products from pre-qualified list;
♦ WHO draft guideline for FDCs developed;
♦ Good progress but still huge unfinished agenda.

Where to find more information?

♦ Web site:
  - http://www.who.int/medicines
  - http://mednet3.who.int/prequal/

♦ Department:
  - Dr Lembit Rágo, Coordinator
    Quality Assurance and Safety: Medicines
    Department of Medicines Policy and Standards
    WHO Geneva
Annex 4. Patents and access to ARVs: Ms. F. Amolo Okero, World Health Organization
Patents and access to ARVs

F AMOLO OKERO, WHO (Geneva)

TRIPS Agreement, Doha Declaration, Cancun meeting

- WTO Ministerial Conference, Nov. 2001
- Patent and prices debate
- Clarification of TRIPS provisions
- Para 4: TRIPS “can and should be interpreted and implemented in a manner supportive of WTO Members’ right to protect public health and in particular, to promote access to medicines for all”
- August 2003 decision: waiver of obligations on
  - limitation to export
  - in relation to Para 6 – export within Regional Trade Areas
  - compensation

Patent situation of ARV’s

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<td>ATV</td>
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Patent and treatment access

- Patents restrict choice for buyers
- Reliability of supply can be impacted by single source
- Patents can lead to higher price
- Patents may/not impede the production of some ARVs by Indian manufacturers
Country action on patents

- KENYA – IP Act 2001; expansive interpretation of the principle of international exhaustion of IPR
- CAMBODIA – patent law first enforced 2003; pharma products excluded from patent protection until 2016 (Doha)
- UGANDA – patents for at least 6/13 possible ARVs – no obvious action on violation by patent holder
- MALAYSIA – Govt use authorisation; importation of FDC from India for supply to govt (public) hospitals (also Cameroon)

Country action (cont.)

- MALAWI – letter invoking para 7 of Doha to expedite purchase of generic FDC’s using GFATM funds by UNICEF
- ZIMBABWE – Period of Emergency declaration; under section thirty-four allows the power to make, use, exercise and vend the invention for any purpose which appears to the Minister necessary or expedient to the life/well-being of the community
- MOZAMBIQUE - Compulsory licence to Pharco Mocambique Lda for local manufacture of FDC – royalty to patent owner not to exceed 2% of total turnover

Actions patent holders have taken

- Voluntary licenses
  - GSK: ZDV, 3TC (South Africa, Kenya, Ethiopia)
  - BMS: d4T, ddI (South Africa)
  - Merck: EFV (South Africa)
  - BI: NVP (South Africa)

  ...BUT NET EFFECTS YET TO BE FELT

Patents not the only hurdle..

- Tenofovir – little patent protection in LDC’s, low price but access very limited - very limited availability?
- Lopinavir/r – limited patent protection, low price, access still limited
Possible solutions..

- Make drugs available at affordable prices
- Don't patent in developing countries (but patent in high-income)
- Voluntary license

Acknowledgements to Cecilia Oh (WHO/EDM), J Perriens, P Graaff (WHO/HIV)
Annex 5. Supply Chain Challenges to ARV Scale Up: Mr. Alain Pierre, Interchurch Medical Assistance
Supply Chain: Challenges to ARV Scale Up

Presented by
Alain Pierre
Interchurch Medical Assistance, Inc.
Pharmaceutical Consultant

Prepared by
Interchurch Medical Assistance, Inc.
Procurement and Pharmaceutical Management Teams

AIDSRelief

Five Organization Faith-Based Consortium
- Catholic Medical Mission Board
- Catholic Relief Services
- The Futures Group
- Institute of Human Virology
- Interchurch Medical Assistance

Funded by the President’s Emergency Plan For AIDS Relief

AIDSRelief: Year 1

- 9 Focal Countries - Guyana, Haiti, Kenya, Nigeria, Rwanda, South Africa, Tanzania, Uganda and Zambia
- 17,500 people
- 59 Points of Service
- ARV purchase over $5 Million
ARV Production Issues

- Some manufacturers not adequately prepared for increased demand
- Lack of adequate forecasting
- Closure of some manufacturing plants for extended periods of time
- Some manufacturer ARV production schedule unknown

Consolidation challenges

- Some manufacturers not historically or currently linked with consolidators on warehousing or shipment of ARV’s, resulting in multiple warehouses and shipments of program ARV’s
- Proforma quantities not held for sufficient time to submit confirmation of an order. Thus, out of stock ARV’s must be replaced before shipment can be made, resulting in delays.
- Some consolidator’s up-front fees restrict procurement funds from being utilized for further ARV purchases

In-country ARV supply agencies

- Several countries where AIDSRelief is working have no in-country mechanism to supply ARV’s. As a result, ARV’s must be procured and shipped into the country, as opposed to placing orders directly with an entity that has stock or would handle the procurement function
- In some circumstances, existing in-country supply agencies are not able to supply the necessary ARV’s

In-Country Management of ARV’s

- In-country program staff need to have warehousing resources to process ARV’s through country specific customs procedures
- Without proper resources potential for delay of ARV’s at airport resulting in elevated expenses and improper storage of drugs. For example, delays can break the cold chain and because of this there is a risk of having to limit the amount of pediatric drug available to children
Country-specific ARV policies

- Only non-branded and/or Fixed Dose Combination ARV’s, for the first line regimens, are permitted in some countries.
- Certain countries allow FDA approved ARV’s to be used only in 2nd line treatment protocols.
- Some ARV’s that AIDSRelief would like to utilize for treatment are not on National Formularies.

Basket Funding

- Certain countries want funding for all in-country ART programs to be consolidated into one centralized fund for procurement.
- Program participation is sometimes delayed by efforts to streamline procurement via a large national system with multiple partners.

Conditions hampering importation and delivery

- Payment of duties/taxes on ARV’s
- Warehousing
- Maintaining the cold chain

Challenges often result in hindering the number of patients being enrolled in ARV programs.

Lessons Learned

- Forecasting needs to be done anywhere from 6 months to one year in advance, and updated regularly according to consumption stats.
- Constant assessment and analysis of present and future patient load is necessary.
- Gather ARV utilization data at each facility/health institution on a regular basis (i.e. every 2 weeks)

Mua Methodist Hospital in Kenya meets with Glen of the I.M.A. Pharmaceutical Management Team.
Lessons Learned Con’t

- The data collection system must be comprehensively designed to ensure proper reporting of consumption and forecasting of ARV’s from Point of Service to Headquarters to Global Distributor. This is particularly important in the current circumstances of ARV drug needs increasing and challenging companies in their ability to meet the demands.
- Work with consolidators who give timelines of how long they will hold ARV’s for confirmation of purchase.

Lessons Learned Con’t

- Partner with in-country organizations who have a institutional history, extensive relationships/networks, and a working knowledge of the context of pharmaceutical management.
- Where necessary, facilitate in-country partners in their efforts to strengthen their own capacities, thereby enabling the orgs to better serve their countries and your efforts.

Establishing a Global ARV order allows for the shifting of ARV’s where and as needed amongst the different countries.
- Many non-FDA approved companies are not seeking FDA approval. Thus, in keeping with PEPFAR regulations, we need to be sure to verify the approvals that are in place for the products we procure.

THANK YOU

For More Information Contact:
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- Patty Pickett pattypickett@interchurch.org
- Erika Pearl erikapearl@interchurch.org

ALL CAN BE REACHED AT 410-635-8720
Annex 6. Solutions to Supply Chain Delays or Breakdown: Ms. Bianca Kamps, International Dispensary Association
IDA ARV BV

Jan 1st 2004 IDA ARV Procurement Services BV was established as a legally independent organisation. It is a 100% IDA Foundation affiliate.

GOAL IDA ARV BV: To sell high quality essential Antiretroviral medicines and medical supplies at the lowest possible price to the not-for-profit sector in low and medium income countries.


ARV SUPPLIES 2004

- ARV’s supplied to 25 countries under Global Fund, World Bank, USAID, bilateral & government funded programs
- For all 2004-IDA ARV orders, 70% of worth where Research Based Antiretroviral drugs
- On average 30% of the products in an order come from the generic industry
- For 2005 IDA ARV BV intends to buy around US$ 30 Mio in branded ARV’s

TODAY’S REALITY

- Different funds, different guidelines
- Unexpected ARV shortages (e.g. WHO QSM withdrawals)
- Challenge of worldwide forecasting
- Long decision making processes in-country
- Lack of supply chain management experience in-country
- Complex logistics

Resulting in ‘last minute’ ordering and emergency requests

SOLUTIONS TO:
SUPPLY CHAIN DELAYS OR BREAKDOWN

Bianca Kamps
Director IDA ARV Procurement Services BV
January 20th 2005
WHAT CAN BE DONE?

1. FIRM DELIVERY DATES
   - Proforma quantities resulting in confirmed stock
   - Confirmed delivery dates to be realised on time
   - Avoid rescheduled deliveries when unexpected events occur

AND.....(1)

2. SMOOTHENING PAPERWORK
   - Provide docs required for USAID funded program waivers well in time
   - Provide docs needed for deliveries well in advance
   - Simplify docs for getting access to AAI pricing
   - Proactive supply of registration information

AND.....(2)

2. UNIFORM WORKING METHODS
   - Centralized point of contact at manufacturers’ side
   - Uniform T&C, procedures and contracts per manufacturer

AND.....(3)

3. CONSOLIDATION
   - Consolidation of shipments resulting in less:
     - paperwork
     - mistakes
     - delays at customs
     - supply chain interruptions
   - IDA Foundation is well-equipped to realise consolidation including:
     - tracking & tracing
     - keeping cost to a minimum
     - double checks
4. EMERGENCY STOCK

- Many small emergency requests
- Little variation in throughput time orders
- Centralized emergency stock needed (also for AAI products!)

SUMMARY OF SOLUTIONS

- FIRM Delivery dates
- Smoothening Paperwork
- Uniform working methods
- Consolidation
- Emergency stock

MORE PATIENTS ON ARV TREATMENT
Annex 7: Unclogging the Antiretroviral Drug Pipeline: Market Factors:
Mr. Robert Dintruff, Abbott Laboratories
Scale-up Requirements
“The Challenge of Scale-up in Environments with Limited Infrastructure”

Funding

Products

Knowledge

Organization

ARV Treatment Programs

-Funding

-Products

-Knowledge

-Organization

-ARV Treatment Programs

-Products

-Knowledge

-Organization

10X - 100X
Global Care Initiatives
Abbott Access
Program Fundamentals

Define the offering and geography, register products, establish pricing, create a program structure, set up a request process, remodel the financial system, etc.

Seek to...

Provide product responsibly

Ensure that it goes to those for whom it was intended

**Key Product Offerings**

- Therapeutics
- Diagnostics

$500 per patient year

$.80/test

**Geographic Definition**

Least Developed Countries (U.N.-defined)

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**Shipment Tracking**

Therapeutics (Kaletra and Norvir)

Countries that receive shipments from multiple sources are shown in red.
Ensuring Delivery and Distribution

In-Country Distribution

DISTRIBUTION
Primary Focus:
- Create awareness
- Encourage adoption
- Get product to the country
- Ensure satisfaction

LOCAL DELIVERY
Expertise needed:
- Clear customs
- Manage inventories
- Maintain storage environment

HIV/AIDS Treatment Scale-up
Requirements and Roles

- Funding
- Products
- Knowledge
- Organization

We do what we do best
- Invent, develop, manufacture and market products

What else needs to be done and by whom?
- Create the organizations to:
  - Distribute beyond the port of entry
  - Track usage and manage demand
  - Treat
- Establish the knowledge base to
  - Utilize products responsibly
  - Monitor their use

Symposia Completed: 29 To Date
Market Factors Linked to Scale up

**Key issues:**
1. Need for simplified therapies
2. Moving and tracking product beyond the main warehouse
   - Is it reaching those for whom it is intended?
   - Is it used rationally?
   - Is inventory managed appropriately?
3. Importance of therapy monitoring

**Price**
- Funding is more broadly available and products are generally offered at no profit in developing nations

**Product**
- Regimen simplification
- Therapy monitoring

**Promotion**
- Creating awareness
- Encouraging adoption
- Customer service
- Product-specific education

**Distribution**
- Coordination beyond the central warehouse

Ensuring Delivery and Distribution

**Products can get to key destinations**

**Local delivery and utilization issues:**
- Older procurement processes prevail
- Product flow to local programs and patients can be slow
- Its ultimate destination is not known to suppliers

**Unmet needs:**
- Product tracking (barcode inventory management systems?)
  - To what level?
  - Usage monitoring
  - To know the impact
  - Ensure rational use of product
  - Forecasting systems
  - Streamlining the exchange of product and payment

Solutions Framework

**Having the right products**
- Simpler therapies; convenient formulations
- Preparedness to deal with resistance (2nd and 3rd line)
- Therapy monitoring

**Management of product usage**
- Streamline procurement
- Encourage tracking systems to monitor usage and improve forecasting

**Education and training on use of products**