SCMS Product Integrity Issues

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“Providing Quality Medicines for People Living with and Affected by HIV and AIDS”

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PEPFAR Implementing Partner

Why Counterfeit?
• Why counterfeit?
• What kinds of counterfeit products are out there?
• What technologies are required to detect them?
• How does SCMS protect its supply chains?
• How does SCMS plan to assist client sovereign states to protect the follow-on supply chains?

Tiered Analytical Assessments
• To conserve resources the appropriate technologies should be used to perform the assessments. Tiered levels should be instituted.
• In addition to capital costs maintenance costs are estimated at 10% of capital costs per year
• In addition supply costs are estimated at 5-10% of capital costs per year

Two Pharmaceutical Markets
• Legitimate Market
  o Products registered or formal waiver
  o Routine inspection of imports
  o GMP inspection of local manufacturers
  o Some pedigree control
• Gray Market
  o Unregistered and no waiver
  o No inspection or oversight
  o Unknown pedigrees

Minimum Level Investment - One Off Sales - Local
• Flour in capsules

Higher Level Investment - Return Markets - Internet Sales - Cross Border Trafficking - International
• Impure drugs
• Undeclared therapeutic product substitution
• Sophisticated relabelers and manufacturers

Highest Level Investments - Return Markets - Diversions into Legitimate Supply Chains - International
• Designer Unapproved New Drugs
• Sophisticated relabelers and manufacturers

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Some Counterfeiters Are Sophisticated Business People
Return on Investment?
• Minimum Level Investment - One Off Sales - Local
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• Higher Level Investment - Return Markets - Internet Sales - Cross Border Trafficking - International
  • Impure drugs
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• Highest Level Investments - Return Markets - Diversions into Legitimate Supply Chains - International
  • Designer Unapproved New Drugs
  • Sophisticated relabelers and manufacturers
Implementing Partner Level One Product Quality Assessments

- Technical Resources
  - Thin Layer Chromatography
  - Colorimetric Tests
  - Near Infrared or Raman Spectroscopy
- Personnel Qualifications
  - Basic Laboratory Skills
- Facility Requirements
  - Good ventilation
  - Minimal power requirements
- Capital Investment
  - Tens of thousands USD

Implementing Partner Level Two Product Quality Assessments

- Technical Resources
  - Chromatography systems HPLC, GC, TLC-Densitometry
  - Spectroscopic procedures UV-Visible
- Personnel Qualifications
  - Trained laboratory personnel-GMP levels
- Facility Requirements
  - Controlled temperature space
  - Stable power required
- Capital Investment
  - Tens to hundreds of thousands USD

Implementing Partner Level Three Product Quality Assessment

- Technical Resources-Forensic Levels
  - Chromatography coupled Mass Spectrometry
  - Near Infrared or Raman Spectroscopy
- Personnel Qualifications
  - Highly trained personnel
  - Ph.D. with experience
- Facility Requirements
  - Controlled temperature
  - Stable power supplies
- Capital Investment
  - Hundreds of thousands to millions USD

Overview SCMS Supply Chain Product Integrity

- SCMS Support for Client Requirements
  - Procurement
    - Contracts
  - Warehousing and Customs
    - Distribution to Client Sites in Sovereign States
      - Central Medical Stores—Most
      - District Level—Few
  - Sovereign States
    - Ministry of Health
    - Regulatory Authority
    - Internal Distribution System
    - Health Care Delivery Workers

The Need for Rapid Scale-up

Number of people in low- and middle-income countries on antiretroviral therapy (in millions)

- ARVs (including FDA tentatively approved generics)
- Rapid HIV test kits
- Laboratory equipment [e.g., Enzyme ImmunoAssay (EIA), CD4, Nucleic Acid Amplification Testing (NAT)]
- Drugs for Opportunistic Infections
- Drugs for Sexually Transmitted Infections
- Drugs for home care and palliative care
- Drugs for Tuberculosis
- Medical supplies
- Miscellaneous (e.g., vehicles)
SCMS has established routine and with-cause sampling and testing procedures to pose a credible threat of detection to unscrupulous suppliers.

- Routine sampling is conducted at SCMS Regional Distribution Centers
- With-cause sampling is performed for complaints or any deviation in processes.

Where We Work

Botswana  Côte d’Ivoire  Ethiopia  Guyana  Haiti  Kenya  Mozambique  Namibia  Nigeria  Rwanda  South Africa  Tanzania  Uganda  Vietnam  Zambia  Zimbabwe

Regional Consolidation Centers

- SCMS is establishing Regional Consolidation Centers in India
- Rapid access to Indian generic products afforded by the Tentative FDA-Approval process
- Inspection and sampling at RCCs prior to consolidation and shipping.
- Chain of custody
- Controlled packing of shipments at the RCC and unloading them at the RDC
- Customs inspections under SCMS observation
- Visibility of any in-transit security breaches (RFID seals)

To protect their sovereign markets the National Drug Regulatory Authorities (NDRA) must have in place the basic regulatory functions including: product registration, product and premises inspection, product testing, stringent laws and regulation for standards enforcement.
• Defines what products may be legally marketed in the country
• WHO prequalification Q&A states: “quality assessment is product and manufacturing site specific”
• Registration is product, manufacturer, and site specific

Registered 5.6%
Not Registered 23.6%

• Product testing shows that registered products (5.6% substandard) are much less likely to be substandard than unregistered products (23.6% substandard).

Registered 5.6%
Not Registered 23.6%

• Product testing is the most expensive tool in the regulatory process.
• Product testing is the only way to prove that a product is substandard or is counterfeit.
• Product testing results may be contested in courts, so chain-of-custody and rigorous adherence to good practices and legal standards are essential.

394 ARV samples collected from seven African countries
• 1 failed appearance (NPQ)
• 2 failed labeling (NPQ)
• 1 failed disintegration (NPQ)
• 2 failed dissolution (1 NPQ, 1 PQ)
• 1 failed assay (PQ)
  1.8% failure rate with no serious failures
  84% of the products were registered in the country
  60% were WHO pre-qualified
• No samples were collected from unofficial sources or remote sites
• Non-registered products primarily from the private sector

Products not legally imported or marketed were rejected or seized and not screened
• 1,257 samples of the targeted drugs were screened; ca. 500 per annum
• 3.7% or 46 of the samples tested failed screening tests.
  • 4 sulfa products failed dissolution—all locally manufactured
  • 5 samples failed screening test—wrong drug or markedly sub-potent
    o 3 samples of quinine tablets
    o 2 samples of erythromycin tablets.

Tanzania FDA Data in press
• TZ surveillance focused on legal products which had passed the registration requirements and were stored in approved premises
• Upstream compliance activities: registration, record inspection and physical examination are reflected in improved quality of marketed products
• This overall regulatory activity provides a significant deterrent.
• Therefore legitimate conscientious manufacturers and distributors can compete.

The following five slides concerning detection of illegal Erectile Dysfunction (ED) drugs are taken from a presentation by the US FDA Forensic Chemistry Center in Cincinnati, Ohio.

SCMS does not distribute ED drugs and these slides are intended only to illustrate the level to which some unscrupulous manufacturers will go to sell products.

### FDA FCC Materials

- The three approved products for ED treatment are:
  - Sildenafil Citrate (VIAGRA®) FDA approval - 1998
  - Tadalafil (CIALIS®) FDA approval - 2003
  - Vardenafil HCl (LEVITRA®) FDA approval - 2003

### VIAGRA Summary

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### Unapproved Products

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### Cialis Summary

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### Levitra Summary

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One sample was bulk powder declared as "sodium pyruvate" contained 82% pure vardenafil.
The presence of ED drugs and numerous analogs is widespread among herbal products, supplements and dosage forms.

Screening procedures that target only approved APIs are inadequate.

Preliminary results suggest that polymorphs may also be a factor for this class of compounds.

Those who produce and market these illegal products are becoming more clever. Those trying to prevent it must adjust accordingly.

Establish a strong well-publicized regulatory posture including enforcement.

Purchase products which are approved AND marketed in ICH or PIC/S countries or WHO prequalified products.

Watch the pedigrees of incoming products.

Level One
- Product and premises compliance to standards

Level Two
- GMP inspection of manufacturers
- GLP inspection of testing laboratories

Level Three
- Sterile operations
  - Terminal sterilization
  - Sterile filling
  - Lyophilized products

Strengthen level one drug product and premises regulation-registration, inspection.

Strengthen level one assessment technologies.

Technical assistance to strengthen level two assessment technologies.

Assist in regional coordination of efforts to strengthen level three assessment resources.

Technical assistance to strengthen regional and international communications and alerts.
• Report immediately issues relating to the quality, safety, and/or efficacy of products to the SCMS quality team. Your quick reporting will help ensure the quality of products procured and distributed by SCMS.

• Access Form on SCMS Intranet to report issues, incidents, or complaints relating to product quality.

Product Quality

Please immediately quarantine the product sample and any unopened containers of product with the same lot number if available and alert the SCMS quality team.

Product Information

* Product Name, Strength, and Dosage Form
* Batch/Lot No.
* Manufacturer
* Manufacturer Location
* ASIN (If Known)
* Detailed description of product condition, event or incident
* Date Discovered
* Discovered By
* Location/Date Discovered
Any immediate actions taken
Any suggested corrective actions

Questions?

Thank You!!

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