Update on national regulatory development in Africa - vaccines perspective

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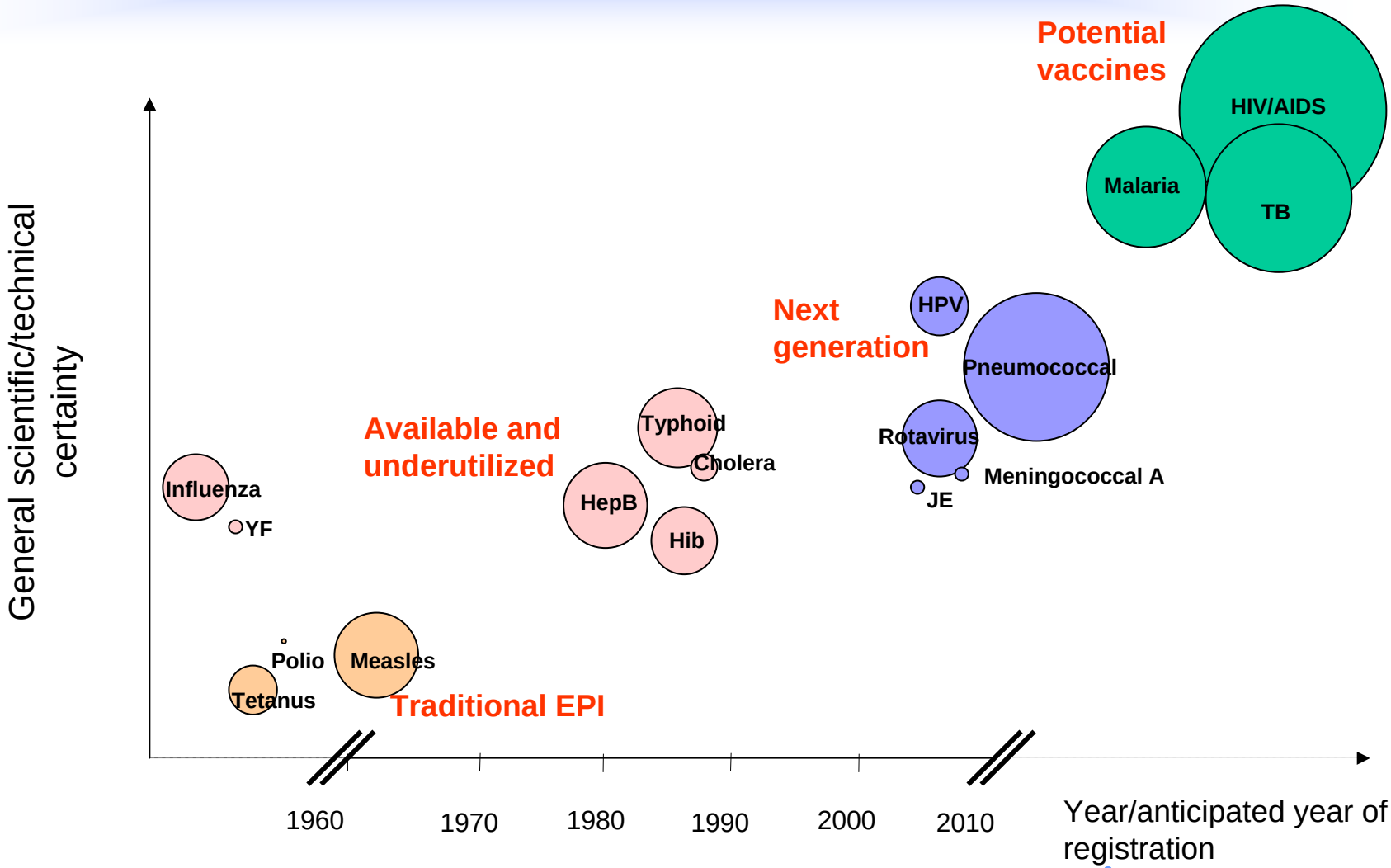
Key messages

- Vaccine development pipeline is buoyant:
  - Complex products are under development
  - Specialist regulatory oversight is needed
- WHO objective:
  - 100% of vaccines used in all national immunization programs are of assured quality
  - NRA strengthening is one strategy to attain this goal.

The Vaccine Pipeline



Size of circle indicates number of deaths (400,000 deaths, 2002 data) Left side of circle aligned with expected introduction date

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WHO's Goals

Ensure that **"100%"** of vaccines used in all national immunization programmes are of assured quality

- ✓ **Definition of "Assured quality vaccines":**
  - ✓ National Regulatory Authority (NRA) independent from vaccine manufacturer
  - ✓ NRA functional *(system + 6 regulatory functions)*

Guided by Expert Committee on Standardization of Biologicals (ECBS) recommendations on safety, efficacy and quality issued in WHO Technical Report Series (TRS)

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New challenges

- **Responsibility for regulation of new vaccines: :**
  - Now more on Developing Countries using vaccines
  - Less on Industrialized Countries producing vaccines
  - Countries have insufficient expertise and experience to assess data and dossiers

  ☞ **NRAs must acquire new skills**

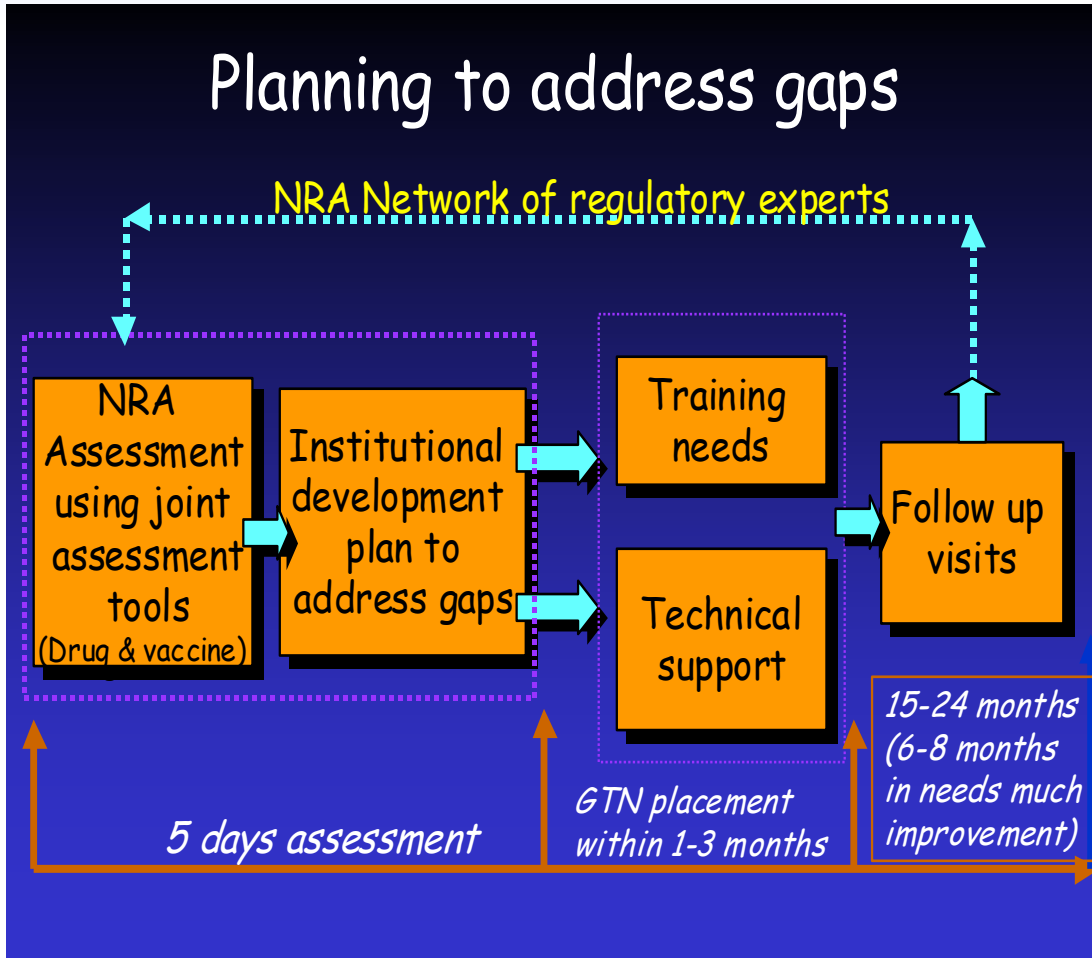
- **Clinical trials for new vaccines**
  - Are being run in ANY country, no matter the expertise/strength of their NRA

  ☞ **Quality of the trials must be guaranteed**

Process to strengthen NRAs

The five step capacity building program

1. **Benchmarking**
2. **NRA assessment**
3. **Planning to address gaps (IDP)**
4. **Implementation of plan, including technical inputs (GTN)**
5. **Monitoring and evaluation**



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National Regulatory Functions

Regulatory functions

Regulatory functions	Source of vaccines: UN agency	Procure	Produce
Regulatory system	✓	✓	✓
Marketing Autorization & Licensing activities	✓	✓	✓
Postmarketing: AEFI	✓	✓	✓
Lot release		✓	✓
Laboratory access		✓	✓
Regulatory inspections			✓
Authorization & monitoring of CTs	✓	✓	✓

For countries conducting Clinical Trials

CTs : Clinical trials, UN: United Nations, AEFI: Adverse Events Following Immunization

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Country Status: 86 NRA assessments conducted (Oct.1998-Dec 2006) using a network of 350 regulatory experts

Country status : NRA assessment conducted & planned

- NRA assessment conducted*
- Not yet conducted
- Planned

* Assessment conducted in AFR were organised through NRA planning workshop except for 5 countries were country visite were conducted

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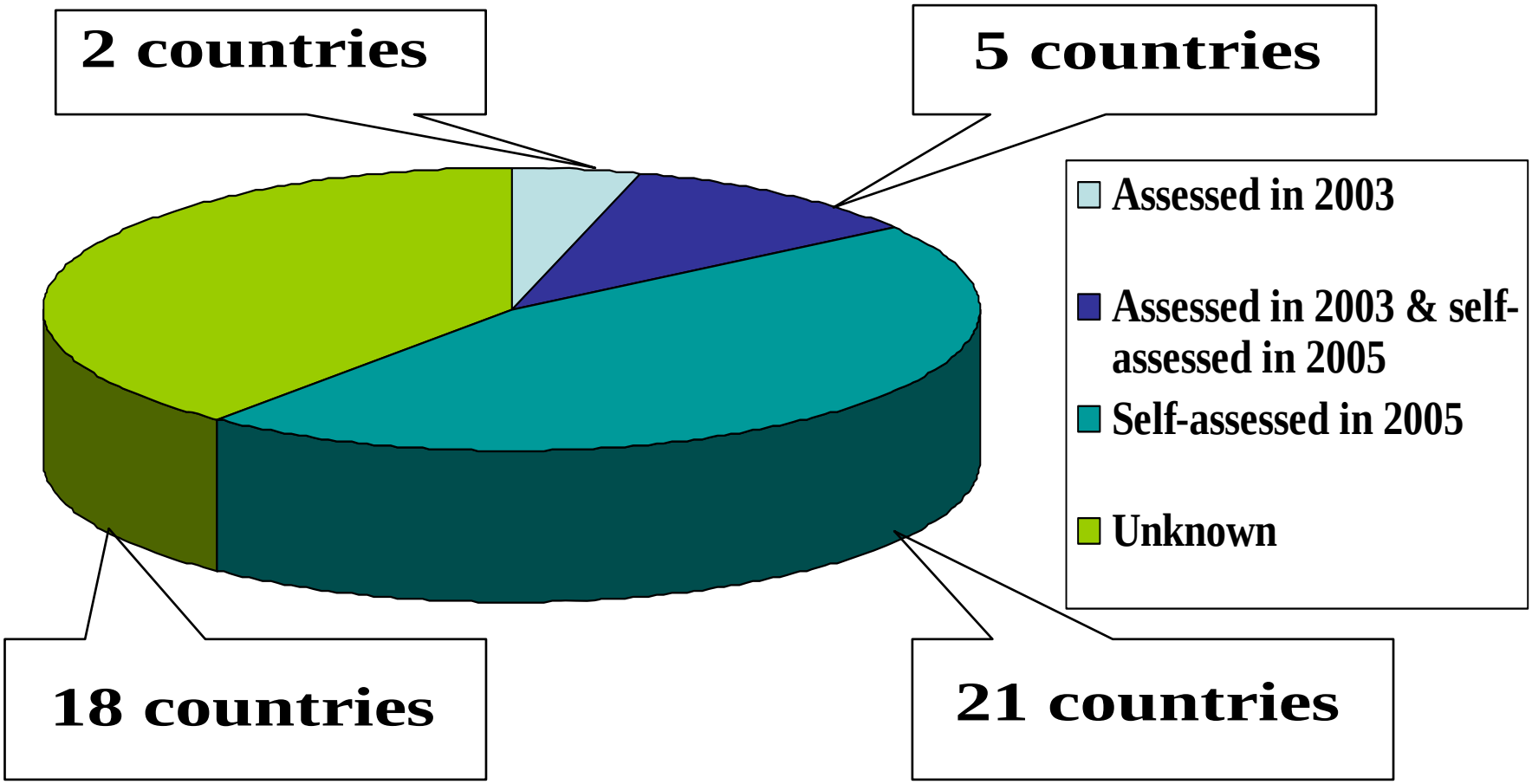
7 NRAs assessed in the AFR by 2003
26 NRAs self-assessed during planning workshops



Assessed in 2003:

- **Functional**: Algeria, South Africa, Nigeria, Zimbabwe, Senegal
- **Non-functional**: Uganda, Côte d'Ivoire

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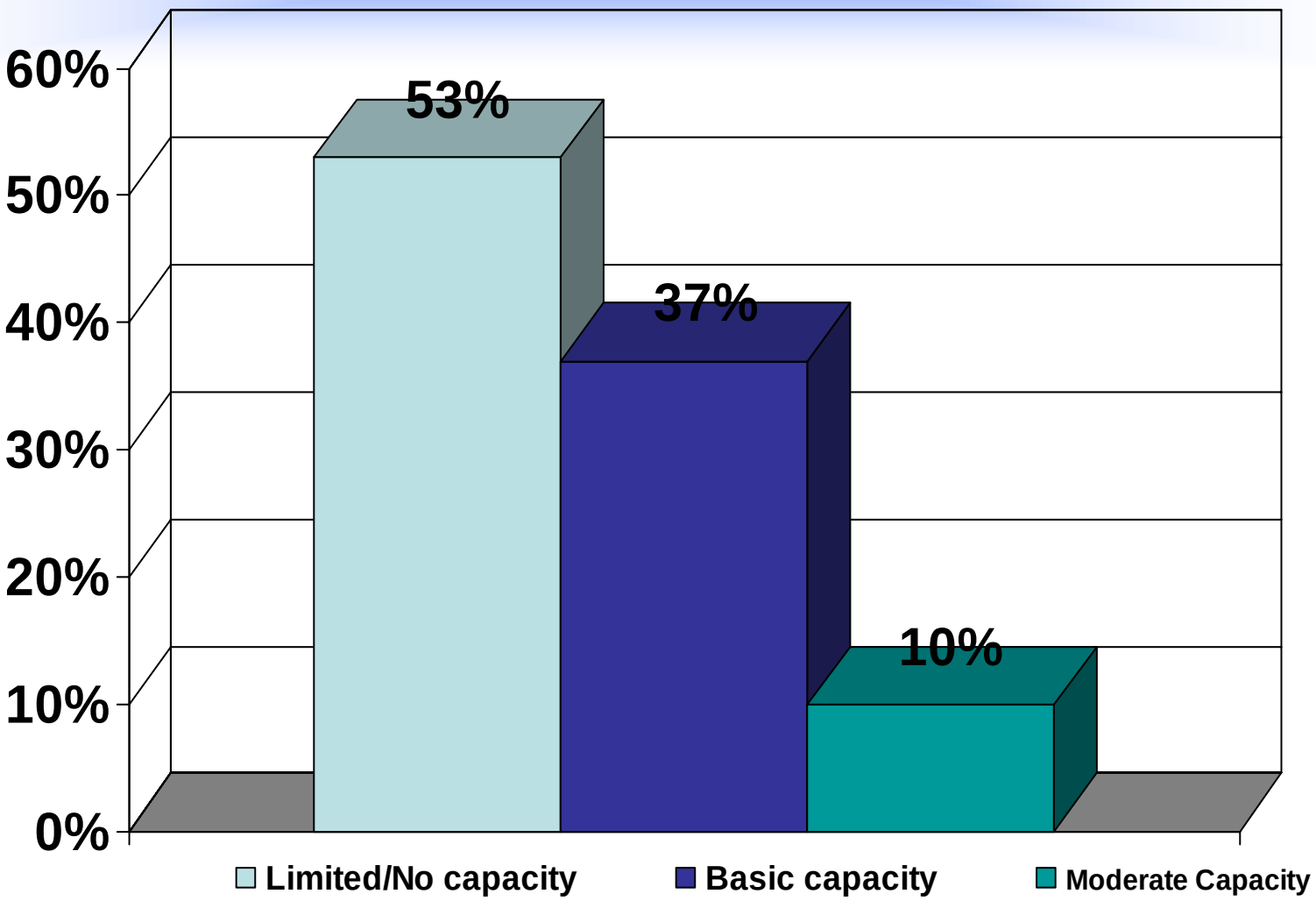
Status of medicine regulation in Africa*



Source: WHO/AFRO and TCM/HQ, Survey on DRAs in Africa, 2005

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What are the problems?

- Inadequate legislation and regulation:
  - Outdated, not comprehensive and in some countries lacking
- Inadequate staff: number, training, professional diversity, etc.
- Inadequate & non sustainable funding
- Lack of access to independent and objective information.

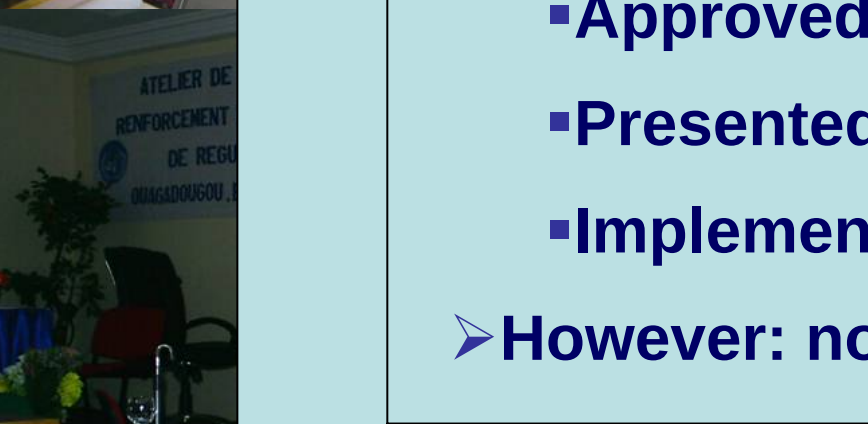
Regional Reaction: High Level Decisions

- The 12th & 13th Meetings of the **Task Force on Immunization in Africa (TFI)** held in 2004 & 2006:
  - Recommendations to strengthen DRAs thru networking & implementation of IDPs.
- Status presented to the 56th Meeting of the **Regional Committee (all Ministers of Health)** held in Addis Ababa, Ethiopia, from 28 Aug. – 1st Sept. 2006:
  - Resolution adopted to strengthen DRAs.

Regional Reaction: Promotion of the “Regional Approach"

- Planning workshops to strengthen NRAs
- Development of (harmonized) procedures for regulation of vaccines
- Joint review of CT applications/discussion of regulatory challenges
- Joint monitoring of clinical trials
- Identification of regional needs for training on regulation of vaccines
- Exchange of expertise and networking.

3 planning workshops for NRA strengthening held for 26 countries



Addis (January 2005)

26 NRA Institutional Development Plans (IDPs) were drafted:

- **18 IDPS were finalized at country level**
- **10 IDPs were assessed by end 2006:**
  - **Approved by MoHs: 7**
  - **Presented to ICCs: 6**
  - **Implementation started: 8**
- **However: no specific funding for IDPs!**

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a,

Zambia and Zimbabwe

African Vaccine Regulators Forum (AVAREF)

- Initiated in 2006 to support NRAs & National Ethics Committees (NECs) in the evaluation of vaccines
- Consists of plenary meetings (Accra 2006 & Ouagadougou 2007) plus support activities between meetings
- 19 countries involved; NRA and NEC representatives.

AVAREF Objectives

- To provide information to regulators of countries that are target for clinical trials
- To promote communication/collaboration:
  - Between NRAs and Ethics committees,
  - Among regulators of the Region and others
- To provide a resource of expert advise to regulators
- To identify needs for expert support to NRAs

Training Workshops

- "Evaluation of clinical trials", Pretoria, March 2005
- Regulatory Procedures [illegible] Sept. 2005)
- Regulatory forum on [illegible]ies (Botswana Dec. 2005)
- Joint review of CTA of [illegible]e (Banjul Jun 2006)
- "Vaccine Regulation" [illegible]arch 2006
- "Surveillance of AEFIs [illegible], Tunis (2007)*
- "Surveillance of AEFIs [illegible]SA), 2006
- "Authorization & Inspe[illegible]h in Ouidah in December 2006, and [illegible]7
- "Good Clinical Practic[illegible]2007
- Joint Inspection of Me[illegible]ali, Jan. 2007**

- In addition, Africa[illegible]N courses on lot relase in Lyon, Fra[illegible]

About 200 trainees from all over the African Region!

* Postponed until Nov. 2007

** Used as a training opportunity

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Joint Inspections of CTs

Inspectors & Facilitators in front of WHO Office, Bamako, Mali, 19 Jan 2007

An historical moment : For 1st time in the African Region, regulators and ethics committee members from Burkina Faso, The Gambia, Ghana, Ethiopia and Mali conducted an inspection of GCP of phase II observer-blind, randomized, active controlled clinical trial of meningococcal a conjugate vaccine at the Centre for Vaccine Development (CVD), Bamako, Mali; January, 2007*

* The real inspectors were from NRA & EC of Mali; others were trainees!

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Template Regulatory Procedures

- 4 template were produced on:
  - Submission of Clinical Trial Applications
  - Clinical Trial Application Review
  - Importation & Release of Investigational Materials
  - Storage & Export of Human Samples from CTs
- Templates translated in French
- Templates shared with all countries for adaptation and adoption:
  - Already used by a few countries: Ethiopia, Cameroon, Malawi, etc.

Technical Support to Countries

- Bi-annual monitoring visits to Senegal ANR in GMP, laboratory access, lot release and post-marketing surveillance of AEFIs:
  - Part of pre-qualification process of YF vaccine
  - Done by WHO staff & consultants
  - Seeks to promote consultants from the AFR
- National stakeholder sensitization workshop in Uganda (2006) to support IDP implementation:
  - Requests for similar workshops received from DRC & Cameroon, expected from Burkina Faso.

A journey of 1,000 miles starts with a 1st step … forward!

- **Previously in most countries in Africa:**
  - IRBs were the only ones reviewing protocols: no CT trial application was sent to NRAs until recently
  - Except for RSA, no GCP inspections were conducted
  - DRAs were not involved in vaccine regulation
  - Regulators were feeling isolated & powerless.
- **Since 2006:**
  - NRAs & NECs of Gambia, Mali, Ethiopia, Ghana, Burkina Faso and Senegal jointly reviewed CT applications and participated in joint GCP inspections
  - DRAs accept vaccine regulation as part of their responsibilities and are building capacity
  - Thru the “regional approach”, regulators feel empowered: no longer alone & knowing where to seek advice & support.

Perspectives: the remaining 999 steps

- Promotion of confidentiality agreements and memoranda of understanding among countries
- Harmonization of regulatory procedures:
  - Seven countries have agreed to accept one CT Application format (Ghana, Burkina, Mozambique, Gabon, Tanzania, Kenya, Malawi).
  - To be extended to other areas of vaccine regulation.
- Training for NRAs in pharmacovigilance for PMS & oversight of CTs:
  - This was limited to surveillance of AEFIs & left to EPI
- Advocacy with National Governments for more support (staff & funds) for NRAs
- Advocacy with Regional Political Organizations to support harmonization: SADC, ECOWAS, AU, etc.
- Advocacy with NRAs of Developed Countries for increased technical support.

Acknowledgement

- Collaboration & support of African Gov-ts through their NRAs & NECs
- Financial support was received from:
  - EDCTP
  - MVP / PATH
  - AAVP
  - Others
- Technical support was received from:
  - EMEA
  - USFDA
  - Health Canada
  - Others

Merci de votre attention!

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