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Regional Assessment of Drug Registration and Regulatory Systems in CARICOM Member States and the Dominican Republic

Final Report - Volume I

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Final Report - Volume I

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The Consultant Team
Reet, July 2009

List of abbreviations and acronyms

ACCSQ	ASEAN Consultative Committee for Standards and Quality
ACTD	ASEAN Common Technical Document
AFTA	ASEAN Free Trade Area
AI	Assessment Instrument
ANT	Antigua and Barbuda
APEC	Asia-Pacific Economic Cooperation
ASEAN	Association of Southeast Asian Nations
ATCR	ASEAN Common Technical Requirements
BAH	The Bahamas
BAR	Barbados
BBD	Barbados Dollar
BEL	Belize
BGVS	Drug Supply Company Suriname
BSD	Bahamian Dollar
BZD	Belize Dollar
CAREC	Caribbean Epidemiology Centre
CARICOM	Caribbean Community
CARIPROSUM	Caribbean Regional Network of Procurement and Supply Management Agencies
CARPHA	Caribbean Public Health Agency
CHRC	Caribbean Health Research Council
CMPH	Committee for Medicinal Products for Human Use
COHSOD	Council of Human and Social Development
COMESA	Common Market for Eastern and Southern Africa
CRDTL	Caribbean Regional Drug Testing Laboratory
CSME	CARICOM Single Market and Economy
CTD	Common Technical Document
DOM	Dominica
DOP	Dominican Peso
EAC	East African Community
EC$	East Caribbean Dollar
EFTA	European Free Trade Association
EMEA	European Medicines Agency
EU	European Union
FDA	Food and Drugs Administration

FTA	Free Trade Area
GCC	Gulf Cooperation Council
GCG	Global Cooperation Group
GMP	Good Manufacturing Practices
GRE	Grenada
GUY	Guyana
GYD	Guyanese Dollar
HAI	Haiti
HTG	Haitian Gourde
ICDRA	International Conference of Drug Regulatory Authorities
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
INN	International Non-proprietary Name
JAM	Jamaica
JMD	Jamaican Dollar
MON	Montserrat
NRA	National Regulatory Authority
OECS	Organization of East Caribbean States
OECS/PPS	Organization of East Caribbean States/Pharmaceutical Procurement Services
OTC	Over the Counter
PAHO	Pan American Health Organization
PAHO/CPC	Pan American Health Organization / Caribbean Program Coordination
PANCAP	Pan Caribbean Partnership against HIV/AIDS
PANDRH	Pan American Network for Drug Regulatory Harmonization
PEPFAR	President's Emergency Plan for AIDS Relief
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PPWG	Pharmaceutical Product Working Group
RQCL	Regulatory Quality Control Laboratory
SADC	Southern African Development Community
SEAMRAC	Southern and Eastern African Medicines Regulatory Authorities Conference
SIAMED	Model System for Computer assisted Registration
SKN	St Kitts and Nevis
SLU	St Lucia
SOP	Standard Operating Procedure
SRG	Surinamese Guilder

SVG	St Vincent and the Grenadines
SUR	Suriname
TAG	Technical Advisory Group
TRI	Trinidad and Tobago
TRIPS	Trade Related aspects of Intellectual Property Rights
TTD	Trinidad & Tobago Dollar
UN	United Nations
UNAIDS	United Nations Program for HIV/AIDS
UNICEF	United Nations Children's Fund
USD	United States Dollar
WHO	World Health Organization
XCD	East Caribbean Dollar

Summary

CARICOM countries are faced with an increasing burden of non-communicable chronic diseases for which treatment and care needs to be ensured. This, in addition to scaling up treatment of HIV/AIDS, requires sustained access to adequate quality medicines at affordable prices.

In this context the Technical Advisory Group, established at the 10th CARICOM Council of Human and Social Development, recommended conducting a study on existing medicines regulatory systems in CARICOM countries with a view to establish their adequacy for ensuring the timely supply of safe, effective and quality medicines. Realizing that market, human and financial constraints might pose a potential barrier to effective and efficient medicines regulation in individual member countries the study was also tasked with establishing strategies and an action plan for the development of a harmonized drug regulation system for the region.

Study implementation

All 15 CARICOM member states were included in the study: Antigua & Barbuda, the Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, St Kitts & Nevis, St Lucia, St Vincent & the Grenadines, Suriname, and Trinidad & Tobago. The Dominican Republic had been identified as an additional beneficiary of the study in the Pan Caribbean Partnership against HIV/AIDS (PANCAP)/World Bank agreement.

The study was conducted in two main phases, i.e. data collection phase and consolidation phase. Data collection for the regulatory systems assessment in countries was based on the 'Guide for Data Collection to Assess Drug Regulatory Performance' developed by WHO (Ratanawijitrasin S, Wondemagegnehu E 2002) that was amended to suit the specific purposes of this study. Both, data collection instruments and implementation work plan were approved by the CARICOM Secretariat and the Technical Advisory Group.

Based on the assessment instrument stakeholder interviews were conducted in Barbados, the Dominican Republic, Guyana, Jamaica, St Lucia, Suriname and Trinidad & Tobago during the period 18 January to 15 February 2009. During the same period questionnaires for self-completion were sent out to the remaining study countries. These countries were supported in person by HERA team members of the CARICOM study on Intellectual Property Rights, TRIPS and Access to Medicines that was conducted in parallel, and through telephonic follow-up by the study team leader.

During the consolidation phase responses collected in countries were analyzed and documented in specific reports for each study country (Volume 2), and summarized for the main report. In addition, study countries' medicines legislation was assessed.

Study findings and resulting recommendations for medicines regulatory harmonization strategies presented in the draft report were discussed with the Technical Advisory Group. This Final Report includes the results of these discussions.

Medicines regulation

Medicines are a crucial input to improving and maintaining the health of the population, and considerable funds are being dedicated by governments and individuals to the purchase of medicines. In order to be beneficial, medicines need to be safe, effective and of adequate quality - otherwise funds will be wasted, and the populations' health will be put at risk. However, neither the consumer nor the prescriber has the information and expertise needed to establish whether a particular product complies with these requirements. It is thus in the interest of public health that government intervenes in the medicines market through regulation.

According to international consensus medicines regulation encompasses the following critical functions that need to be provided for in the national medicines legislation:

- Licensing (registration) of pharmaceutical products
- Licensing of pharmaceutical premises (manufacturers, importers, distributors)
- Inspection of distribution channel and good manufacturing inspections
- Quality control laboratory testing

- Adverse drug reaction monitoring
- Control of advertising and promotion
- Control of clinical trials

The National Regulatory Authority (NRA) is the authority empowered by law to carry out medicines regulatory functions and to ensure compliance with the legal requirements.

Study findings

Pharmaceutical sector characteristics define to a great extent the context within which medicines regulatory systems operate. National Medicines Policies provide guidance on governments' goals related to the public and private pharmaceutical sectors, including the commitment to ensure quality, safety and efficacy of the medicines marketed. Out of the 16 study countries, 7 have a National Medicines Policy, and of these 3 have been officially adopted by government.

Seven of the study countries have privately owned pharmaceutical manufacturing plants producing multi-source (generic) products only, in 4 countries also for export. Private sector pharmaceutical importers and/or wholesalers are operating in 14 of the 16 countries, while all study countries have private retail pharmacies (ranging from 1 in Montserrat to 2,812 in the Dominican Republic).

Legislative provisions

All study countries have some type of medicines legislation, including specific acts providing for the control of narcotics and psychotropic substances. However, none of the existing legislations is fully comprehensive. Provisions frequently missing include control of clinical trials, adverse drug reaction monitoring, control of product promotion and advertisement, and specific prohibition of counterfeit medicines. Registration of pharmaceutical products is a requirement by law in 7 of the 16 study countries.

Challenges identified include legislation that is not being updated, provisions in 'old' laws that have not been harmonized with newer legislation, and multiple amendments not consolidated into one revised law. In some countries enforcement of laws is constrained by the lack of regulations. Passing of medicines related bills and draft regulations has been found to be a very lengthy process.

Regulatory framework and institutional capacity

In those study countries with more comprehensive medicines legislation the NRA is set up by law as a public sector entity operating under and/or reporting to the Ministry of Health. Of the 6 countries that have operational medicines registration systems, 2 have a NRA responsible for all regulatory activities. In the remaining 4 countries responsibilities are spread over different Ministry of Health departments, with no dedicated overall responsible body. It was reported that this leads to coordination and communication challenges and is affecting efficiency and effectiveness of regulatory performance.

All study countries reported a shortage of **human resources** assigned to medicines regulatory activities, which was attributed most frequently to low salaries, lack of funds, and bureaucratic delays in approving restructuring proposals. Except for the Pharmacy Council in Jamaica, none of the regulatory authorities have power to recruit or retrench its staff. Human resources capacity is further constrained by the general lack of adequate training activities to build the specific technical expertise required for medicines regulatory functions.

All but 1 study country reported that **financial resources** to carry out medicines regulatory functions were inadequate. Regulatory authorities are generally not aware of their operational budgets. While in 8 countries fees are being collected for e.g. product registration or licensing of premises and persons, only in 1 country can these be used to support NRA activities.

Some deficiencies regarding adequate **infrastructure** for NRAs were reported. These were mainly related to access to transport to carry out inspections, and in a few cases to availability of reliable communication tools (internet and e-mail facilities).

Licensing and inspection

The following pharmaceutical licensing activities were reported to be conducted:

- licensing of manufacturers: 7 countries (all countries with pharmaceutical manufacturing)
- licensing of importers and/or wholesalers/distributors: 9 of 14 countries where these businesses are present
- licensing of retail pharmacies: 11 of 16 countries
- licensing of other retail premises allowed to sell a restricted number of non-prescription medicines: 7 of 16 countries

Six countries that do license all types of pharmaceutical premises were questioned about the existence of unlicensed establishments: four countries were aware of or thought it very likely that unlicensed activities were performed in their countries. The extent was not known.

None of the study countries do as yet license or otherwise control the operation of internet pharmacies.

Import permits are required by all countries for controlled drugs falling under the respective UN conventions. Import permits for other pharmaceutical products need to be obtained from the NRA in 5 countries, while 3 require import permits for antibiotics only.

Distribution channel **inspections** are conducted in 11 of the 16 study countries. However, these are mainly pre-licensing inspections as compared to preventive planned inspections (surveillance). Nevertheless, violations of medicines legislation during the past 3 years were detected by inspectors in 9 countries. These included the sale of medicines in street markets, operation of business without license, sale of unregistered and expired products, and improper storage conditions.

Those 7 countries with pharmaceutical manufacturing do good manufacturing practices (GMP) inspections, mainly in connection with licensing. However, GMP certificates for export are only issued by 3 countries.

Product assessment and registration

In 7 of the 16 study countries pharmaceutical product registration is a legal requirement, which is being implemented in 5 countries. One additional country requires registration of medicines without having an explicit legal provision for this.

All 6 countries with an operational registration system require registration of new drugs and known multi-source (generic) drugs for human use. Some countries also register veterinary drugs, biologicals, herbal products, or medical devices. The number of products registered varied between 2,635 and 12,124. Information on how many of the registered products were actually available on countries' markets was not available from the NRAs.

One country makes the list of registered products publicly available on the department's web site, and 4 countries produce updated lists from time to time which can be obtained on request by interested parties. In one country the newly registered products are published in the official government gazette, but a complete list is not available.

All countries collect registration fees for processing an application for registration. For new drugs these fees varied between USD 10 and USD 128.

Four of the 6 countries have access to external expert committees for the assessment of application dossiers. Reported time needed to process registration applications was acceptable (between 3 and 6 months for new drugs).

While provisions are made for requiring proof of registration with other established NRAs, this was reported not to impact the regulatory assessment process. Likewise, different information requirements for the application of registration of new and known products are not always clearly specified in the legislation. In practice, clinical safety and efficacy studies are usually not required for registration of known (multi-source /

generic) products. Only 1 country has different processes for assessment of applications for registration of new and known products.

Linkages between intellectual property laws and medicines registration were reported by 3 countries, where provisions for data exclusivity exist. Only one country reported to implement this provision.

Regulatory quality control laboratories

Thirteen of the 16 study countries are signatory to the Agreement establishing the Caribbean Regional Drug Testing Laboratory (CRDTL), and 12 countries are using this facility (OECS member states usually submit samples through the OECS/Pharmaceutical Procurement Services). CRDTL also conducts planned quality surveillance of priority pharmaceutical products where samples are to be submitted by individual countries as per established schedule. Out of 640 samples analyzed by the CRDTL during 2006-2008, 89 or 13.9% were found to be of unsatisfactory quality. Because there is inadequate random sample collection and testing, the general level of substandard pharmaceutical products in the CARICOM region is not known.

4 of the 16 study countries have in-country regulatory quality control laboratories that are all operating under the respective Ministry of Health. Sterility and microbial limit tests cannot be performed and are done by the CRDTL. Pyrogen and toxicity testing cannot be done by any of the regulatory quality control laboratories in the region.

Challenges identified by the existing laboratories include inadequate human and financial resources to operate satisfactorily.

Specific quality assurance measures in countries without pharmaceutical product registration

Ten of the study countries do not have an operational registration system for pharmaceutical products that would require pre-marketing assessment of product quality, safety and efficacy. All of these countries do implement quality assurance measures during the processes of pharmaceutical procurement for the public sector, e.g. requiring proof of registration with other specified regulatory authorities, pre-registration of suppliers, or random quality control testing. For OECS member states quality assurance measures instituted by the OECS Pharmaceutical Procurement Services apply. These include use of pre-qualified suppliers, specific tender conditions and quality control testing of samples in-house (qualitative) and at the CRDTL.

For the private sector 2 of the 10 countries require import permits for antibiotics, in 1 country all import documents are being screened, and in 7 countries no specific quality assurance measures are taken. Quality assurance of pharmaceutical products in the private sector is clearly inadequate in the 10 countries.

Discussion of study findings

The assessment found that effectiveness and efficiency of medicines regulation in the study countries is affected by delay in updating and passing legislation, human resources constraints, institutional constraints and inadequate access to fully functional regulatory quality control laboratories. While financial constraints were noted by 15 of the 16 countries, there was no detailed information available to establish the extent of the problem.

The risk of unsafe, ineffective or substandard medicines being sold or dispensed to patients clearly increases when the regulatory functions are being performed only partially or not at all. Only 2 countries provided concrete examples for counterfeit medicines. However, without effective registration and surveillance systems the chances for detecting counterfeit products are low. All study countries reported cases of substandard pharmaceutical products in the public sector, where quality assurance measures are more widely applied. Again, the low level of post-marketing surveillance (including random sample collection and testing) makes it difficult to detect substandard medicines in the private sector.

Recommendations obviously need to consider the different country contexts. For the smaller CARICOM member states it will not be feasible to establish comprehensive medicines regulatory systems taking into account market factors, specific technical expertise requirements, and associated costs. For the larger countries with established medicines registration systems the required extension of regulatory activities to ensure adequate performance of inspection and surveillance systems will be a challenge.

It is suggested that CARICOM countries establish a network for cooperation among NRAs to discuss viable approaches to address the identified common challenges.

Except for 2 countries, policy guidance on the envisaged development of the pharmaceutical sectors, including medicines regulatory systems, is either not available, not updated, or not being implemented. We would therefore recommend that National Medicines Policies be developed / updated and implemented. In addition, the development of an overall CARICOM Regional Medicines Policy would be useful to comprehensively define regional goals, strategies, and commitments.

Harmonization of medicines regulation

Existing harmonization initiatives usually focus on harmonization of medicines registration, with the overall aim of reducing registration processing times due to different country requirements. Harmonization should translate into significant cost savings to the pharmaceutical industry and quicker access to new and improved therapies at more affordable prices. Medicines regulatory harmonization activities have often been triggered by wider regional integration activities aiming at the creation of single or common markets, and there has been an increasing trend towards harmonization globally.

However, the focus on approving new products fast may impact appropriate pre-marketing evaluation. It is thus important to keep the primary objective of medicines regulation - i.e. the protection of public health - in mind when considering harmonization option.

Harmonization initiatives are ongoing in several regions world wide, for example in

- the European Union (EU)

  Harmonization activities started in 1965, and in 1995 the European Medicines Agency was established. To date, 3 different routes exist through which applications for registration can be submitted: the traditional route (application to individual member states' NRA); the decentralized procedure (mutual recognition); and the centralized procedure (simultaneous registration in all EU member states through EMEA).

- the Association of Southeast Asian Nations (ASEAN)

  The concept of pharmaceutical harmonization was endorsed in 1999. Facilitated by the Pharmaceutical Product Working Group established under the ASEAN Consultative Committee for Standards and Quality focus is on development of common technical dossiers and technical requirements for medicines registration. In April 2009 a mutual recognition arrangement for good manufacturing practices inspections was signed.

- the Southern African Development Community (SADC):

  Harmonization activities in the region started in 1995 with the development of technical guidelines. Currently the SADC Directorate of Social & Human Development / health & pharmaceuticals in Botswana coordinates activities. To date 14 guideline documents have been approved by member states. Challenges experienced included varying capacity of pharmaceutical sectors and level of economic development in member countries, language differences, and a rather weak Secretariat.

- the Pan American Region through the Pan American Network for Drug Regulatory Harmonization (PANDRH)

  PANDRH was formally endorsed by the 42nd meeting of the PHAO Directing Council in 2002. It comprises of NRAs of all 35 PAHO member states and representatives of the pharmaceutical industry. The Secretariat is provided by PAHO and 12 working groups have been established to address specific regulatory sub areas. To date 5 conferences were held, were decisions on adoption of harmonized guidelines are being taken. Approved guidelines include those on bioequivalence testing and on the prevention and combat of counterfeit medicines. CARICOM member states' NRAs are members of PANDRH. Challenges regarding active participation, and communicating and implementing PANDRH decisions at national levels have been identified.

In addition there are global harmonization initiatives (e.g. International Conference on Harmonization/ICH), and initiatives supporting national NRA's capacity (e.g. US FDA tentative approval mechanism, EMEA scientific

opinion mechanism, WHO pre-qualification project, the International Conference of Drug Regulatory Authorities).

Harmonization in the CARICOM context

In 2001, CARICOM member states signed the 'Revised Treaty of Chaguaramas Establishing the Caribbean Community including the CARICOM Single Market and Economy (CSME)'. Part 2 of the Treaty addresses consumer protection and provides - amongst others - for member states to enact harmonized legislation.

Respondents in study countries were asked about their general perception regarding harmonization of medicines regulation and any priority areas for harmonization. Those countries that do not yet have registration systems were in favor of a central body for assessing applications for registration. The main reason provided was lack of expertise and human and financial capacity at country level. Respondents that do register medicines were more in favor of enhanced cooperation between NRAs. In addition to assessment of application for registration, priority areas for harmonization included technical support and information sharing, regional quality control, and harmonized norms for inspections. It was also remarked that countries' sovereignty would need to be respected, and that any regional regulatory body should be built on existing structures.

Strategic options for medicines regulatory harmonization in CARICOM

Regarding their medicines regulatory features CARICOM countries can be divided into 3 groups:

- Group 1 comprises of the 5 countries with more comprehensive medicines regulatory systems, including medicines registration. These countries account for approximately 91% of the total population of CARICOM member states.
- Group 2 comprises of 2 countries where registration of medicines is planned to be implemented in the near futures.
- Group 3 comprises of the 8 countries with limited regulatory systems, and where medicines registration is not planned to be instituted soon. Seven of these countries belong to the OECS. Due to limited market size and human and financial capacity constraints, implementation of stand-alone medicines registration systems in each of these countries does not appear to be feasible.

However, public health in **all** countries need to be protected by ensuring that only safe, effective and quality medicines are circulating and made available to patients. We therefore suggest as the overall mission of a CARICOM medicines quality assurance policy and harmonized structure to ensure that in all CARICOM member states adequate pharmaceutical products to address prevalent health conditions are marketed timely, and that these products are of proven safety, efficacy and quality.

Harmonization strategies

The policy principles guiding harmonization efforts and strategy selection are suggested to include the following:

- Member states' governments commit to support all areas of medicines regulation considering this a critical step for protecting public health.
- Only medicines that have been assessed for safety, efficacy, and quality will be allowed to be marketed.
- The assessment process will as far as possible be based on harmonized requirements and guidelines appropriate for the region.
- Existing guidelines developed by PANDRH will be considered.
- There will be distinct requirements for the assessment of products containing new chemical entities and well known multi-source (generic) products.
- There will be procedures to ensure priority assessment of dossiers for application for registration of priority medicines
- Joint support will be provided for member states without a registration system to implement licensing requirements using a phased approach
- Existing resources will be shared between member states.

Seven strategies are recommended for consideration, i.e.

- development of harmonized guidelines for application and assessment

- capacity building of National Regulatory Authorities
- capacity building of the local pharmaceutical industry
- promoting formal cooperation/exchange of information
- resource sharing
- supporting licensing of medicines in countries without registration system, and
- strengthening of quality control capacity

The body of this report provides detailed descriptions for each of the strategies, and summarizes requirements, challenges, and opportunities related to their implementation.

Institutional framework

For a sustainable harmonization effort, it is imperative to have a formal structure that enables effective coordination of issues agreed by member states, where the guiding principle should be to create efficient and effective systems without expensive structures.

Identifying as priority strategies those related to development/adoption of harmonized guidelines and general capacity building it is recommended to start with a small but permanent Secretariat charged with e.g. establishment of relevant databases of guidelines, legislations, experts etc.; communication with countries, relevant regional and international organizations, pharmaceutical industry, and the public; coordination, and organisation of meetings (physical or virtual) as per established business and work plan.

Because of its regional public health responsibility it is recommended to consider establishing the Secretariat under the planned Caribbean Public Health Agency (CARPHA). In case the establishment of CARPHA would be delayed possible options for provisional housing of the Secretariat include PAHO/CPC in Barbados or the CRDTL in Jamaica. This would ensure that none of the member states feel disadvantaged (which might happen if the Secretariat would be established under one of the existing NRAs).

Due to the amount of work that will arise from listing products, and the time needed for establishing the legal requirement for registration for Group 2 and Group 3 countries, it is suggested to handle this as a special project. Within the framework of this project the options for establishing a sub-regional regulatory authority for the OECS could be explored. One option could include linking this authority to the Secretariat in charge of regional harmonization activities. In that case this sub-regional authority could serve as a 'pilot' for a CARICOM medicines regulatory agency that might be envisaged.

Critical steps towards harmonization

The report identifies 5 critical steps for starting up regional medicines regulatory harmonization efforts:

1. Formulation of regional quality assurance policy (to be integrated in a CARICOM Regional Medicines Policy)
2. Adoption of policy by member states
3. Establishment of harmonization Secretariat
4. Development of strategic and annual work plan for policy implementation
5. Securing funding for work plan implementation

Concluding remarks

The report concludes by reiterating the key issues and lessons learnt for harmonization of medicines regulation, i.e. medicines regulation serves the protection and promotion of public health; harmonization takes time; commitment is essential; legal backing while important is not absolutely necessary for all activities; and trust building amongst member states is key.

1. Introduction

The Caribbean Community (CARICOM) evolved from the Caribbean Free Trade Association, and was established in 1973 through the Treaty of Chaguaramas, initially ratified by Barbados, Guyana, Jamaica and Trinidad & Tobago. In 2001 this Treaty was superseded by the 'Revised Treaty of Chaguaramas Establishing the Caribbean Community including the CARICOM Single Market and Economy (CSME)' (CARICOM 2001). The objectives of the revised treaty include improving standards of living and work, accelerated economic integration of member states, improved trade relations with outside nations, and enhanced international competitiveness.

Currently CARICOM has 15 full members, i.e. Antigua & Barbuda, the Bahamas, Barbados, Belize, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, St Kitts & Nevis, St Lucia, St Vincent & the Grenadines, Suriname, and Trinidad & Tobago. The total population is approximately 16.5 million.

The supreme Organ of the Community is the Conference of Heads of Governments that determines and provides policy direction. The Community Council of Ministers, in accordance with the policy directions established by the Conference of Heads of Governments, has primary responsibility for the development of strategic planning and co-ordination in the areas of economic integration, functional co-operation and external relations. The Council of Human and Social Development consists of Ministers designated by the member states, and is responsible for the promotion of human and social development in CARICOM. The principle administrative organ is the CARICOM Secretariat with offices in Guyana[1].

1.1 Study background and context

CARICOM countries are faced with an increasing burden of non-communicable chronic diseases for which treatment and care needs to be ensured. This, in addition to scaling up treatment of HIV/AIDS, requires sustained access to adequate quality medicines at affordable prices. The 10th CARICOM Council of Human and Social Development decided to establish a Technical Advisory Group (TAG) which - in collaboration with the Caribbean Regional Negotiating Machinery - has been mandated to work on access to anti-retroviral medicines and other pharmaceuticals required to address the region's public health needs.

Realizing that efficient and effective medicines regulatory systems are a decisive factor to ensure availability of quality medicines in CARICOM member states the TAG recommended that an assessment of existing regulatory systems be conducted. It was further anticipated that the particular context of CARICOM member states, i.e. small populations and consequently small pharmaceutical markets, could be a disincentive for pharmaceutical companies to invest in registration of their products. In addition, human resources and financial capacity required for operating effective, full-fledged medicines regulatory authorities might be inadequate, especially in the smallest member states. The study was therefore also charged with exploring possibilities for harmonized regional drug regulation that would facilitate access to affordable quality medicines of public health relevance in all member states. The work was to be carried out in conjunction with a regional study on Patents, Trade Related aspects of Intellectual Property Rights (TRIPS) and access to medicines. In December 2008 HERA was contracted to perform both studies.

The **Terms of Reference** for the drug regulation assessment (see Annex 1) define the general objectives of the study as

[1] see: http://www.caricom.org/index.jsp (accessed 29 June 2009)

- To make recommendations on the adequacy of the systems in Member States for regulation of the pharmaceutical market to ensure the timely supply of safe, effective and quality medicines
- To explore the possibilities and identify the requirements and process for establishing a harmonized, pro-public health regional (Caribbean) drug regulation policy (to include generic drugs)[2] and registration system, and
- To identify mechanisms for the development of regional country coalition for joint procurement strategies[3]

The specific outputs are

- an evaluation and assessment of the current status of registration of pharmaceuticals in CARICOM member states and the Dominican Republic, and
- recommendations and a plan of action for establishing a regional drug regulatory system

The Dominican Republic had been identified as an additional beneficiary of the study in the Pan Caribbean Partnership against HIV/AIDS (PANCAP)/World Bank agreement.

The Terms of Reference further specify that four sets of documents are to be delivered, the project work plan and the assessment instruments; an interim report providing feedback on progress; a draft final report for consideration by the TAG; and a final report and related power point presentation. The first 3 sets of documents were delivered to the client. The interim report provided information on how the survey phase was conducted, challenges experienced, and some preliminary findings. The draft final report had been discussed with the TAG and conclusions of these discussions are reflected in the final report, which constitutes this document.

After providing information on the study methodology, and a general section on the rationale and general objectives of medicines regulation the **report presents** the summary findings of the country assessments for the following areas[4]: pharmaceutical sector context, legislative frameworks & set-up and capacity of regulatory systems, licensing and inspection processes, medicines assessment and registration practices, quality control laboratories, and quality assurance in the absence of medicines registration. A brief introduction on concepts and internationally accepted standards precedes the documentation of findings for each of these areas.

We continue by discussing the implications of the assessment results with a focus on possible effects on availability of affordable, safe and effective medicines of public health relevance. The final section of the report is dedicated to the development of strategic options leading to a harmonized regional drug regulatory system. A brief literature review and documentation of experiences with harmonization initiatives in other regions with a special focus on the Pan American Network for Drug Regulatory Harmonization (PANDRH) will be provided, and the perception of countries' stakeholders regarding harmonization options presented. From that strategic options will be developed and discussed.

For practical reasons study countries' names are being abbreviated in the document tables as follows:

[2] We would like not note that any regional drug regulation policy would need to be integrated into a comprehensive regional medicines policy.

[3] In consultation with the CARICOM Secretariat it was agreed to address this objective as a side issue, because the complexities involved would require a comprehensive study on its own. On recommendation of the TAG, options for regional joint procurement strategies for CARICOM are outlined in Annex 3 of this report.

[4] The detailed country reports are included in Volume II of this report. They include assessment results, discussions and recommendations for each of the 16 study countries.

Antigua and Barbuda	ANT	Haiti	HAI
The Bahamas	BAH	Jamaica	JAM
Barbados	BAR	Montserrat	MON
Belize	BEL	St Kitts and Nevis	SKN
Dominica	DOM	St Lucia	SLU
Dominican Republic	DR	St Vincent and the Grenadines	SVG
Grenada	GRE	Suriname	SUR
Guyana	GUY	Trinidad and Tobago	TRI

As study countries' characteristics differ, so does **the context** within which medicines regulatory systems operate. Table 1 provides an overview of demographic, economic and health indicators of the 16 countries included in the study. Population figures and economic and health indicators are sourced from 'Health in the Americas - basic indicators 2008' (PAHO 2008-1). Where data was not available from this publication information as reported by countries was used.

Table 1 - Overview of study countries

Country	Surface Area (km²)	Population (2008 est.)	GNP/capita USD (PPP) in 2006	Official Language	Official Currency	Infant Mortality Rate (year)	Maternal Mortality Rate (year)
ANT	440	70,000	15,130	English	EC $	21.8 (07)	not available
BAH	13,940	335,000	not available	English	BSD	17.6 (07)	68* (08)
BAR	430	295,000	15,150	English	BBD	14.2 (05)	16* (05)
BEL	22,700	294,000	7,080	English	BZD	17.2 (07)	140* (00)
DOM	790	73,000	7,870	English	EC $	13.6* (06)	0* (06)
GRE	344	106,000	8,770	English	EC $	11.0 (07)	not available
GUY	215,000	736,000	3,410	English	GYD	22.0 (05)	161 (05)
HAI	27,700	9,751,000	1,070	French	HTG	57.0 (06)	630 (06)
JAM	11,424	2,728,000	7,050	English	JMD	19.9* (06)	95 (03)
MON*	102	4,875	not available	English	EC $	23.3 (07)	0 (07)
SKN	269	40,000	12,440	English	EC $	16.2 (07)	not available
SLU	616	167,000	8,500	English	EC $	15.0 (05)	not available
SVG	345	121,000	6,220	English	EC $	26.2 (06)	not available
SUR	163,820	461,000	7,720	Dutch	SRG	19.1 (06)	110* (06)
TRI	5,128	1,338,000	16,800	English	TTD	16.5 (04)	39 (01)
DR	48,442	9,904,000	5,500	Spanish	DOP	30.7 (07)	73 (07)

*: data provided by countries

The Bahamian $, the Eastern Caribbean $, the Guyanese $, and the Surinamese $ are pegged to the US$ at fixed exchange rates.

2. Scope and methodology

The scope of the study and the basic methodology are defined in the Terms of Reference. In essence, the task at hand comprised a review of legislation and other relevant documents, and the assessment of how medicines regulation is being implemented in the study countries.

It is noted that on purpose the scope of the regulatory country assessments is less wide than that of the detailed assessments of countries' regulatory systems that had been performed for the 'Effective drug regulation study' (Ratanawijitrasin S, Wondemagegnehu E 2002) or that are being done in the context of the WHO supported assessments of National Regulatory Authorities (NRA). The study was

designed taking into account the objectives and expected outputs of the assignment, and reconciling information requirements with budgetary and time constraints.

In this regard reference is made to the comments on the Terms of Reference provided by HERA in the Technical Proposal (HERA 2007):

> "The title and some other parts of the TOR (e.g. Specific Output i.) refer to drug registration, while other areas in the TOR talk about drug regulation (e.g. Objective a., Specific Output ii, Scope of Work 1.). Obviously drug regulation covers a much wider area, including licensing and inspection of manufacturing, distribution, and retail sale; drug promotion and advertising; and post-marketing surveillance. Considering the special focus on counterfeit medicines in the TOR HERA assumes that regulatory activities related to the distribution chain in countries need to be addressed in addition to drug registration issues. On the other hand it is understood that the remaining regulatory areas are of lesser importance for the purpose of this assignment."

This Technical Proposal further suggested that the assessment will concentrate on medicines registration and control of the distribution chain.

Assessment instruments

For the purpose of the in-country assessments the data collection tool was to be developed based on the 'Guide for Data Collection to Assess Drug Regulatory Performance' (Ratanawijitrasin S, Wondemagegnehu E 2002; Annex 1). In consultation with the client this questionnaire was amended taking into account the study focus and the feasibility of implementation. In addition, the (yet to be published) 'WHO Data Collection Tool for the Review of Medicines Regulatory Systems' (WHO 2008-1) was reviewed and relevant new sections incorporated in the assessment instrument.

Considering that not all study countries are currently having comprehensive medicines regulatory systems, of which registration of medicines is one key component, two sets of questionnaires were developed: one for countries that have an operational registration system, and a less comprehensive one for countries without such a system. After approval by the client the final assessment instruments were submitted together with study work plan as first deliverable under the contract (HERA 2009-1).

Country visits[5]

Due to budgetary constraints not all 16 countries could be visited in person by the study team. On request of the client we amended our original proposal, which foresaw visits to 4 countries with the objective to pilot test the assessment instruments for their suitability for self administration: the comprehensive assessment instrument (Annex 2 to the work plan) was now administered by team members in Barbados, the Dominican Republic, Guyana, Jamaica, Suriname and Trinidad & Tobago. Country visits took place in the period 18 January to 15 February 2009.

The questionnaire for countries without an operational medicines registration system (Annex 3 to the work plan) was distributed by e-mail to the remaining countries[6]. These countries were supported in person by HERA team members of the CARICOM study on Intellectual Property Rights, TRIPS and Access to Medicines that was conducted in parallel, and through telephonic follow-up by the study team leader.

[5] Reference is made to the interim report (HERA 2009-2) providing a detailed account of country visits.

[6] Haiti does have an operational registration system but had not been included in the client's list of countries to be visited. Unfortunately budget constraints did not allow our team to visit Haiti in addition to the agreed upon countries.

For member states of the Organization of East Caribbean States the Pharmaceutical Procurement Services (OECS/PPS) has been mandated "to undertake and manage on behalf of Participating States a range of quality assurance activities respecting pharmaceutics and medical supplies" (ECDS 1990). In addition to the study countries listed above, OECS/PPS in St Lucia was therefore also visited and meetings held with the Managing Director.

For a list of all stakeholders interviewed reference is made to Annex 4.

Literature review

Background documents relevant for the study were sourced from the internet and individual consultants' databases. These include studies/reports on harmonization of drug regulation, documents related to the International Conference of Drug Regulatory Authorities (ICDRA), documents published by the Pan American Network for Drug Regulatory Harmonization (PANDRH), and papers related to the PAHO Strategic Fund. Additional studies and reports were collected from Ministries of Health, local PAHO offices, and the OECS/PPS during the country visits. The list of references is attached as Annex 5.

Medicines legislation, regulations and forms were sourced from the internet - mainly from official government web pages and the CARICOM Law Virtual Library. Countries were then contacted with the request to confirm that the obtained legislation is up-to-date and currently being applied. In those cases were laws could not be sourced electronically these were collected as hard copies during the country visits. National Medicines Policies and Essential Medicines List were collected during country visits.

Data analysis

Comparative analysis of the existing legal framework in the study countries was done using a matrix approach. Legal provisions considered essential for appropriate regulation of the pharmaceutical market were identified, and each country's legislation was checked to determine whether these provisions are covered in the current legislative framework.

Countries' responses on the questions contained in the assessment instruments were documented for each country in specific country reports (Volume 2 of this report), and tabulated and summarized for this main report. Countries were given the possibility to provide feedback on the correctness of data reported in the draft documents, and information was updated accordingly.

Limitations

The study findings reflect the situation found as per April 2009, but systems are evolving. For example, Suriname and Haiti are in the process of substantially revising medicines legislation and organization of the National Regulatory Authority (NRA); the Bahamas have just passed a Pharmacy Act (April 2009) that for the first time provides for a more comprehensive regulation of the pharmaceutical sector and a regulatory authority in form of the Pharmacy Council. While we tried as far as possible to take recent changes into account, the report should still be interpreted by considering the actual timing of data collection.

Terminology

In the existing medicines regulation literature a variety of terms are being used describing essentially the same, e.g. drug or medicine, pharmaceutical or medicinal product, national regulatory agency or drug regulatory agency. Likewise in national legislation terms and definitions differ within and between countries. We are aware of efforts within PANDRH to develop a common glossary, and

WHO established a database of the various terms and their (different) definitions used in official WHO publications[7]. For the purpose of this report we will apply the following:

- The terms 'product licensing', 'registration', and 'marketing authorization' are used interchangeably.
- The terms 'drug' or 'controlled drug' is used in relation to substances defined in the Schedules to the United Nations (UN) Conventions on narcotic and psychotropic substances; in all other cases we apply the term 'medicine'.
- The term 'multi-source (generic)' is used to describe products not manufactured and marketed under the original branded name by the originator company.

Where necessary, further clarification of terms will be provided in the specific sections.

3. Medicines regulation - rationale & basic principles

Medicines are a crucial input to improving and maintaining the health of the population, and considerable funds are being dedicated by governments and individuals to the purchase of medicines. In order to be beneficial medicines need to be safe, effective and of adequate quality. If these attributes are not complied with funds will be wasted, and the populations' health will be put at risk, as evidenced by several incidents that occurred during the past decades[8]. However, neither the consumer nor the prescriber has the information and expertise needed to establish whether a particular product complies with the requirements. It is thus in the interest of public health that government intervenes in the medicines market through regulation. Implementation of medicines regulation is the responsibility of the National Regulatory Authority (NRA) as established by law.

The necessity for every country to have a NRA is generally recognized and there is consensus regarding the authority's overall objective and resulting critical functions (e.g. WHO 1990, WHO 1999-2, WHO 1999-3, WHO 2003-1, WHO 2003-2):

What is medicines regulation?

"Drug regulation is a public policy that restricts private-sector activities in order to attain social goals set by the State. Drug regulation is the totality of all measures — legal, administrative and technical — which governments take to ensure the safety, efficacy and quality of drugs, as well as the relevance and accuracy of product information. Public health and safety concerns have obliged governments to intervene in the activities of the pharmaceutical sector." (Ratanawijitrasin S, Wondemagegnehu E 2002)

- The **overall objective** of the NRA is to ensure that all pharmaceutical products (as defined in the national legislation) are safe, effective and of assured quality. Ensuring that products are accompanied by appropriate information to promote their adequate use is often included in the general objective.
- In order to achieve its objective the NRA must exercise the following **critical functions**:
    - Licensing of products following assessment of safety, efficacy and quality
    - Licensing of premises (manufacturers, importers and distributors)
    - Good Manufacturing Practice (GMP) and distribution channel inspections
    - Quality control laboratory testing
    - Adverse drug reaction monitoring
    - Control of advertising and promotion
    - Control of clinical trials

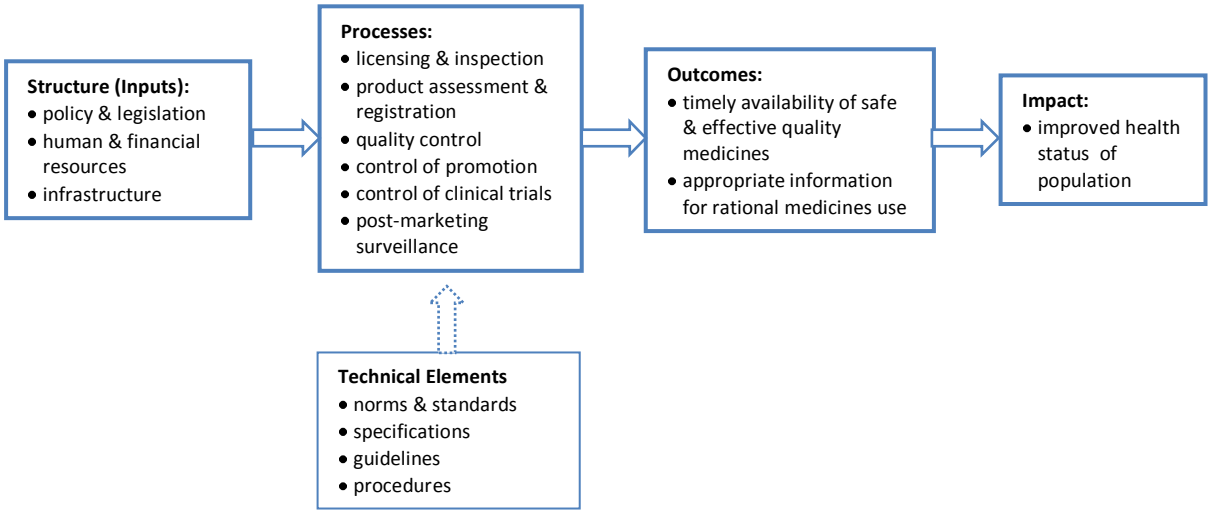
[7] Available at: www.who.int/medicines/areas/quality_safety/quality_assurance/en/

[8] E.g. birth defects in many countries caused by Thalidomide in the 1960s (Abraham J & Lewis G 2000); deaths related to contamination of Paracetamol syrups with diethylene glycol in Haiti and Bangladesh (CDC 1996, Hanif M 1995).

It has been noted, however, that while most countries have a NRA, in less than 17% of WHO members states medicines regulation is well developed, and 30% have no or very little medicines regulatory capacity (WHO 2004-1).

General factors that contribute to the effectiveness of NRAs are a clear mission, adequate legal power and legislative framework, appropriate organizational structure and management, adequate human resources (numbers and technical capacity), and sustainable financing. Political commitment by governments to safeguarding public health through effective medicines regulation is key for NRAs to achieve their general objective. Figure 1 provides an overview of structures, processes and outcomes are related.

Figure 1 - Medicines regulation: inputs, processes and outcomes



4. Study findings

This section provides a summary of study findings on pharmaceutical sector contexts, and for each of the regulatory areas addressed in the assessment instruments. In addition, it draws on the review of countries' medicines legislation. The detailed study findings for each country are documented in the individual country reports contained in Volume 2 of this report.

4.1 Pharmaceutical sector context

National Medicines Policies express and prioritize "the medium- to long-term goals set by the government for the pharmaceutical sector", and identify "the main strategies for attaining them" (WHO 2001). Objectives and strategies cover all sub-sectors, i.e. public, private for-profit and private not-for-profit. Following WHO recommendations National Medicines Policies usually include the following components: selection of essential medicines, affordability, medicines financing, supply systems including local manufacture, regulation and quality assurance, rational use, research, human resources, and monitoring and evaluation.

What are the general objectives of a National Medicines Policy?

1. Access (equitable availability & affordability of essential medicines
2. Quality (quality, safety & efficacy of all medicines)
3. Rational use (promotion of therapeutically sound and cost-effective use of drugs by health professionals & consumers) (WHO 2001)

In the context of medicines regulation National Medicine Policies express the formal commitment of government to ensure quality, efficacy, and safety of medicines reaching their

populations. The selected strategies provide guidance on how this is supposed to be achieved.

National Medicines Policies therefore provide an important foundation for the establishment and/or further development of national regulatory systems including the framework for legislative reform. This would also contain guidance on regional harmonization of drug regulation.

Out of the 16 study countries, 7 have a National Medicines Policy, and of these 3 are officially adopted by government. A Model Policy was also developed for the CARICOM region. Table 2 provides an overview of the existing regional and national medicines policies.

Table 2 - National Medicines Policies overview

NMP Characteristics	BARs	DOM	DR	GUY	HAI	SUR	TRI	CARICOM
Year published	2005	1999	2005	2008	1997	2005	1998	2001
Officially approved	No	No (draft)	Yes	No	No	Yes	Yes	No
Implementation Plan	No	No	Yes	Yes	Yes (2-year log frame)	Yes	No	No
Government responsibility to regulate medicines	not explicitly stated	Yes	Yes (implied - MOH is responsible lead agency for NMP)	Indirectly (NMP Committee to oversee)	Yes	Yes	Yes (MOH and Customs & Excise)	Yes
Harmonization/ Cooperation addressed	No	Yes	No	Yes	No	Yes	No	Yes
Other comments	under revision		Includes section on TRIPS/IP	Includes section on TRIPS/IP	under revision			

The existing Caribbean Community Model National Drug Policy dated February 2001 is available at the OECS/PPS office. The majority of interviewees in other countries were not aware of the CARICOM model policy. The policy prescribes that all medicines are to be registered, and identifies government, through the Ministry of Health, as responsible for drug medicines regulation. The policy does not have an implementation plan, which is understandable considering that its purpose is to serve as a model for national policy development. OECS/PPS, however, reported to implement part of the provisions stated in the model policy.

The number of pharmaceutical businesses operating in a country provides an indication for the size of the **private sector pharmaceutical market**, and for the regulatory capacity required to regulate the market through licensing and inspection activities. Table 3 provides information on the number of pharmaceutical manufacturers, importers, distributors, and retail businesses where they could be provided. The numbers refer to those businesses that are authorized to operate. Often importers operate at the same time as wholesaler/distributor and vice versa, and separate licenses are not always required / provided for. In most countries respondents noted that there might be establishments operating without required authorization, but could not provide further estimates.

Table 3 - Private sector pharmaceutical markets overview

Country	# of manufacturers	# of importers	# of wholesalers/ distributors	# of retail pharmacies	# of other private sector establishments
ANT	0	10 (also wholesalers)	-	?	none mentioned
BAH	0	-	11	57	none mentioned
BAR	1	-	8 (also importers)	83	none mentioned
BEL	0	30 (also wholesalers)	-	75	none mentioned
DOM	0	?	?	12	none mentioned
DR[1]	160	490 (also distributors	364	2,812	none mentioned
GRE	0	1	8	40	
GUY	2	27 (also wholesalers)	29	100	300 'patent shops'
HAI	3	-	38 (also importers)	181	21 warehouses
JAM	7	-	29 (also importers)	394	none mentioned
MON	0	0	0	1	0
SKN[2]	0	0	0	5	none mentioned
SLU	0		5 (also importers)	25	none mentioned
SVG	0	?	?	15	none mentioned
SUR	3	26 (also wholesalers)	-	28	? (drug stores)
TRI	2	?	?	232	? (retail outlets)

1: Except for pharmacies, registered businesses also include businesses dealing in personal & domestic hygiene products, which need to be licensed by the NRA as per Medicines Regulations (Dec. 246-06)
2: Retail pharmacies import directly & sell OTC medicines to shops; the number of retail pharmacies is for St Kitts only
?: data was not provided by respondents.

None of the study countries has a researched based pharmaceutical industry. All pharmaceutical manufacturers exclusively produce multi-source (generic) products that are marketed either as branded generics or under their International Nonproprietary Name. Trinidad & Tobago has 10-12 small manufacturing units in addition to the 2 main manufacturing businesses.

Manufacturers in Barbados, the Dominican Republic, Guyana, and Trinidad & Tobago export medicines within the Caribbean region, but on a rather small scale.

4.2 Regulatory systems' frameworks and institutional capacity

The regulatory framework consists of legislation regulating the medicines market and of the administrative structures that are provided for and have been established to implement and enforce the legislative provisions.

4.2.1 Legislative provisions

Medicines legislation should provide for establishment of a NRA, define its responsibilities and powers, provide for the mandatory licensing of pharmaceutical products and premises, and for a surveillance system to ensure that medicines are safe, effective and of adequate quality up to the time they are used. The law needs to make provision for regulations to be made that will give further details on implementation of the main law. Finally, regulations need to be passed for the law to become enforceable (WHO 1999-2).

All study countries have some type of legislation that regulates pharmaceutical products and/or the pharmacy profession. However, legislation is not always updated, provisions in 'old' laws have not

been appropriately harmonized with newer legislation (e.g. laws originating in the 1940/50s dealing specifically with antibiotics co-exist with newer Food and Drug legislation), or amendments published over many years are not consolidated in one revised law. Annex 2 provides a list of medicines legislation per country.

Table 4 provides an overview of which of the key regulatory functions are provided for in the legislation of the individual study countries. For the following countries legislation could not be examined in detail:

- The Bahamas: The new Pharmacy Act has just been passed with amendments (April 2009) and the final official document was not yet available. Information in the table is derived from the questionnaire that was completed based on the new act. Information that was not available is indicated by a question mark. Respondents expect marketing authorization to be included as a requirement in the yet to be drafted regulations to the Pharmacy Act.
- Dominica: The Medical Act of 1938 could not be made available to us; we only have a copy of the Pharmacist Professions Bill 2007 that was not considered.
- Montserrat: Respondents were not aware of existing medicines related legislation
- St Kitts & Nevis: Has an old Medical Act and a draft Pharmacy Bill - none of the two was available to us.

Dominica, Montserrat and St Kitts & Nevis are therefore not included in Table 4.

Table 4 - Regulatory functions covered by legislation

Key regulatory function expected to be covered by legislation	Functions that are covered in legislation in:												
	ANT	BAH	BAR	BEL	DR	GRE	GUY	HAI	JAM	SLU	SVG	SUR	TRI
Licensing of													
Manufacturers	X	?	X	X	X	X	X	X	X		X	X	X
Importers	X	X	X	X	X	X	X	X	X		X	X	X
Wholesaler/Distributor	X	X	X	X	x	X	X	X	X		X	X	X
Retailers/dispensing outlets	X	X	X	X	X	X	X	X	X	X	X	X	X
Market Authorization					X	X		X	X		X	X	X
Inspection of premises	X	X	X	X	X	X	X	X	X	X	X	X	X
Establishment of Regulatory Quality Control Laboratory	X				X		X						X
Control of clinical trials		?											
Prohibition of counterfeit medicines		X			X	X	X		X		X		X
Adverse drug reaction monitoring		?			X								
Control of product promotion and advertisement*		?			X		X	X	X			X	X
Provision for medicines distribution schedules/categories other than controlled drugs	X	?	X	X	X	X	X	X	X	X	X	X	X
Generic substitution (dispensing)		X			X	X			X	X			
Scope of regulated products defined	X	?	X	X	X	X	X	X	X	X	X	X	X
Administrative and legal sanctions e.g. suspension or revocation of licenses or fines/imprisonment	X	X	X	X	X	X	X	X	X	X	X	X	X
Power to make regulations	X	?	X	X	X	X	X		X	X	X	?	X
Regulations made under the Act (D: draft only)	D		X	X	X	X	X	D	X	X	D	X	X

* only marked if this goes beyond the prohibition of advertising of controlled drugs

Having core provisions addressed in existing acts and regulations does not always imply that these are being implemented. The following sections, and in particular the country reports in Volume 2 provide more detailed information on this aspect.

Table 4 clearly shows that there are 2 areas that are inadequately addressed in most countries' legislation, i.e. control of clinical trials, and adverse drug reaction monitoring (post-marketing surveillance).

All study countries have specific acts providing for the control of narcotics and psychotropic substances. All countries are signatory to the 1961 UN Single Convention on narcotic drugs and subsequent treaties.

Medicines Acts need to clearly define the **scope of products** being regulated. WHO recommends that these include pharmaceuticals, biological products, and herbal products for human and for animal use, as well as other products intended for therapeutic use. It must further be specified whether related products (e.g. diagnostic materials, medical devices, or cosmetics) are included (WHO 1999-2). Table 5 provides an overview of the type of medicinal products being regulated in the study countries. As some countries do not have a specific Medicines Act relevant information provided in the Pharmacy Acts has been included.

Table 5 - Scope of regulated products

Country	Scope of regulated products
ANT	Antibiotics & therapeutics substances as per schedule (Antibiotics & Therapeutics Substances Act 1951) Drugs and poisons for human and animal use (Pharmacy Act 1995)
BAH	Drugs and poisons for human and animal use, glandula products, toxoids, serum, vaccines or bacterin for human use, veterinary biologicals, devices (in old Pharmacy Act of 1962)
BAR	Drugs and poisons for human and animal use (Pharmacy Act 1986)) Drugs and therapeutic substances as per schedule (Therapeutic Substances Act 1950)
BEL	Drugs for internal and external use (Food & Drugs Act 1953) Drugs, poisons, patent and proprietary medicines (Chemist & Druggist Act 1940)) Antibiotics as gazetted (Antibiotics Act 1948)
DR	Medicines, cosmetics, personal hygiene products and domestic hygiene products, pharmaceuticals of natural origins as well as all materials used for manufacture (General Health Act 2002 & Medicines Regulations 2006)
GRE	Medicinal products for human and food-producing animal use (Medical Products Act) Drugs and poisons (Pharmacy Act 1987)
GUY	Food, drugs & devices for human and animal use, cosmetics(Food & Drugs Act 1971) Antibiotics (Antibiotics Act 1952) Medicines & poisons (Pharmacy and Poisons Ordinance 1956)
HAI	Human and veterinary drugs, medicated dressings, drains and sterilized sutures (Act of 1955)
JAM	Food, drugs and devices for human and animal use, devices (Food and Drugs Act 1975) Drugs for human and animal use & poisons (Pharmacy Act 1975)
SLU	Drugs for human and animal use & poisons (Pharmacy Act 2003)
SVG	Drugs for human and animal use & poisons (Pharmacy Act 2002)
SUR	Medicines for human use; narcotic and psychotropic substances raw materials
TRI	Food, drugs for human and animal use, cosmetics and devices (Food and Drugs Act 1965) Antibiotics as defined in the schedule (Antibiotics Act 1948) Drugs and poisons (Pharmacy Board Act 1961)

Regarding the control and prohibition of **counterfeit medicines** some of the existing Acts while not referring explicitly to 'counterfeit' products do have provisions that address the issue, although not fully in line with current international recommendations. For example, the Grenada Medical Products Act in Article 17 e) prohibits medicinal products that have been 'labeled, packaged or promoted in a manner that is false, misleading, deceptive or likely to create an erroneous impression regarding its source, character, value, quality, composition, potency merit or safety'. Similarly, the Trinidad & Tobago Food and Drugs Act states in Article 10 (1): ' Any person who labels, packages, treats, processes, sells or advertises any drug in a manner that is false, misleading, or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety, is guilty of an offence'. The Dominican Republic has a specific law dealing with counterfeit medicines and food products (Act 22-06), which gives powers to the Ministry of Health to temporarily of indefinitely close any establishment where counterfeit medicines are found, and to confiscate and destroy these products. This is in addition to other fines that apply under the Medicines Regulations. Reference is made to Section 5 where this subject is being discussed further.

Regarding the establishment of a **regulatory quality control laboratory**, 12 of the study countries are signatory to the 1974 'Agreement establishing the Caribbean regional drug testing laboratory' (CRDTL) (Antigua, Barbados, Bahamas, Belize, Dominica, Grenada, Guyana, Jamaica, Montserrat, St Lucia, St Vincent, Trinidad)(CARICOM 1974). The agreement foresees that it is the responsibility of signatory governments to ensure that analytical reports provided by the CRDTL will be accepted as admissible evidence in court. We could not establish whether this has been complied with. Countries where legislation does not explicitly provide for a regulatory quality control laboratory but are signatory to the CRDTL agreement are identified in Table 4 by a lighter shading of the respective field. In Suriname a quality control laboratory is to be set up under the act establishing the Drug Supply Company Suriname (BGVS). This laboratory is, however, not explicitly assigned to regulatory quality control.

In some countries enforcement of laws is constrained by the lack of regulations. The process of officializing available draft regulations can take years. Other study countries are in the process of reviewing their medicines related legislation (e.g. Dominica, Haiti, St Kitts & Nevis, Suriname), which in cases has also be ongoing for years.

4.2.2 National regulatory authorities

Ensuring that medicines legislation is complied with is the responsibility of departments or agencies as assigned in the legislation, i.e. the NRA. NRA has been defined differently. For the purpose of this report we apply a slightly amended version of the definition provided in "Marketing authorization of pharmaceutical products with special reference to multisouce (generic) Products" (WHO 1999-3):

National Regulatory Authority (NRA) means the network that administers the spectrum of medicines regulatory activities implemented in the country. Ideally at least the following functions are covered by the NRA:

- Marketing authorization for new products and variations
- Quality control laboratory testing
- Licensing of manufacturers, wholesalers and other distribution channel premises
- GMP and distribution channel inspections
- Adverse drug reaction monitoring (post marketing pharmacovigilance)
- Enforcement operations

This takes account of the situations found in some study countries, where either responsibility is spread over different departments/agencies (whose work should ideally be overseen and coordinated by one central body), or regulatory activities are performed but at a very limited scale.

Table 6 provides an overview of the key characteristics of regulatory authorities in the study countries. Where no overall regulatory authority exists the different agencies are listed instead.

Dominica, Montserrat and St Kitts & Nevis do not have any medicines regulatory structure (control of narcotics/psychotropics is done as per international conventions) and are therefore not included in the Table.

Table 6 - Aspects of regulatory authorities

Country	Main regulatory authority	(Legal) status	Reports to	Power to hire/fire personnel	Financial independence	Regulatory functions currently performed
ANT	Pharmacy Council	not specified in Act	Minister of Health	No	No	Distribution channel inspections (valid licenses cannot be issued - only draft regulations)
BAH	Pharmacy Council (to be established)	? Act not yet available	?	No	No	none: Council yet to be established; (import control of narcotics done by Bahamas National Drug Agency)
	Up to now: Health Professions Council	Body corporate	Minister of Health	Yes	Yes	Registration and licensing of pharmacists and pharmacy technicians
BAR	in practice: Barbados Drug Service (BDS) (not specified in law)	public sector entity	Minister of Health	No	No	Licensing of premises (excl. pharmacies); licensing of imports; inspection of premises including pharmacies (on behalf of pharmacy council)
BEL	Drug Inspectorate Unit	Ministry of Health department	Director of Health Services	No	No	Licensing of pharmacies; import permits for antibiotics & controlled drugs; distribution channel inspections
DR	Drugs and Pharmacy Directorate (DGDF)	MOH department	Under Secretary Public Health	No	No	marketing authorization; licensing of premises all types; GMP inspections; distribution channel inspections
GRE	Pharmacy Council	not specified in Act ('body')	Minister of Health	No	No	licensing of all type of premises; distribution channel inspections
GUY	Food & Drug Department and Office of Chief Pharmacist	MOH departments	Chief Medical Officer	No	No	marketing authorization; licensing of premises; GMP inspections; other inspections; quality control
HAI	Directorate for Pharmacy, Medicines & Traditional Medicines	MOH department	?	No	No	marketing authorization; licensing of premises all types; inspections
JAM	Pharmacy Council	semi-autonomous body	Minister of Health	Yes	partly (fees & government subsidies)	licensing of premises all types; inspection of distribution channel
	Pharmaceutical & Regulatory Affairs Branch under the Standards & Regulations Division	MOH department	Chief Medical Officer	No	No	marketing authorization; GMP inspections; import permits
SLU	Pharmacy Council	not specified in Ac	Minister of Health	No	? - partially retains fees	registration of pharmacists and pharmacies

Country	Main regulatory authority	(Legal) status	Reports to	Power to hire/fire personnel	Financial independence	Regulatory functions currently performed
SVG	Pharmacy Council	not specified in Act ('body')	Minister of Health	No	? - fees are provided for	registration of pharmacy owners, professionals, students; licensing of premises
	Drug Inspector MOH	MOH department	Minister of Health	No	No	distribution channel inspections
SUR	Registration Commission	independent commission	Director of Health	No	No	marketing authorization
	Pharmaceutical Inspection	MOH department	Director of Health	No	No	licensing of premises all types; distribution channel inspections; import permits
TRI	Drug Inspectorate Division (+ advisory committees)	MOH department	Chief Medical Officer	No	No	marketing authorization, import permits, licensing of premises, inspections - all for antibiotics and narcotics
	Chemistry, Food & Drugs Division (+ advisory committee)	MOH department	Chief Medical Officer	No	No	marketing authorization, licensing of premises, inspections - for controlled & other drugs; quality control

Spreading of regulatory responsibilities over various agencies/departments needs good communication and coordination mechanisms. Respondents in Suriname and Trinidad & Tobago noted that communication between the two existing structures was unsatisfactory and impacted on efficiency and efficacy of regulatory actions.

The agency to which regulatory functions have been delegated in Barbados does perform additional functions such as public sector procurement and supply management, formulary development, and operation of pharmacies. A clear separation of regulatory functions and procurement & supply functions is required to avoid any conflict of interest impacting on regulatory performance.

4.2.3 Human resources

An adequate number of human resources with specialized training are a precondition for effectively conducting the core regulatory functions. Competitive staff salaries and career structures need to be provided to attract and retain competent personnel.

All of the study countries perceived that there are inadequate numbers of technical and administrative staff to effectively and efficiently fulfill drug regulatory activities. Details of staff complements involved in medicines regulatory activities within the study countries are outlined in Table 7.

Table 7 - Number and type of medicines regulatory staff[9]

Country	# Technical Full time	# Technical Part time	# Administrative Full time	# Administrative Part time	Remarks
ANT	1	7	-	-	7 part time are Pharmacy Council members, with 3 acting as inspectors
BAH	-	?	-	-	7 Pharmacy Council members to be appointed in the near future. 1 Full time Registrar to be appointed.
BAR	6	-	3	-	
BEL	2	-	-	-	
DOM	-	-	-	-	Medicines regulatory activities practically non-existent
DR	53		?	-	Staff establishment needed for implementation of new law not yet finalized
GRE	2	-	-	-	
GUY	12	-	4	-	
HAI	5	-	-	-	
JAM	21	-	12	-	
MON	-	-	-	-	Medicines regulatory activities practically non-existent
SKN	-	-	-	-	Medicines regulatory activities practically non-existent
SLU	-	4	-	-	4 part time are Pharmacy Council members
SUR	3	1	2	2	1 technical part time is the acting head of the Registration Bureau
SVG	1	5	-	-	5 part time are Pharmacy Council members
TRI	33	-	4	-	Chemistry, Food & Drugs Division 20 technical; Drug Inspectorate Division 13 technical
TOTAL	**117**	**22**	**23**	**2**	

? = Data not provided

[9] Members of external commissions or advisory boards are not included

The technical staff is comprised mainly of pharmacists and quality control analysts. As an indication of the level of shortage, the Dominican Republic reported that plans were being made to recruit an additional 50 pharmacists.

In addition to the staff members employed by the Ministries of Health, the Dominican Republic, Jamaica, Trinidad & Tobago and Suriname have external expert committees to assess applications for registration.

Eight of the study countries provided reasons for the shortage of staff, which include:

- Bureaucratic delays in approving restructuring proposals (3)
- Failure to keep pace with increased level of activity and responsibility
- Low salary (3)
- Lack of funds (3)
- Lack of qualified candidates
- Inadequate/inappropriate structure (2)

There were 7 study countries where it was perceived that the salaries of medicines regulation personnel were significantly lower than private sector counterparts. Two countries did not respond on this matter and it was not applicable for 5 countries (Bahamas, Dominica, Montserrat, St Kitts & Nevis, and St. Lucia). Despite the negative perception regarding low salaries, staff turnover was reported to be low.

As most of the units involved in medicines regulation fall under central government the managers have no power to hire and fire staff. The sole exception is the Pharmacy Council in Jamaica, which is a semi-autonomous body whose legislation vests it with such power.

Job descriptions were reported to be available for medicines regulation personnel in 4 of the study countries (Barbados, Guyana, Jamaica and Suriname). Guyana's job descriptions are, however, in need of review and in Suriname only the staff of Registration Bureau has job descriptions; there are none for the Pharmaceutical Inspectorate staff. The remaining 10 study countries gave no information on job descriptions.

Two of the study countries (Barbados and Jamaica) agreed that the basis for the appointment of technical staff was level of education and experience. Additional criteria reported by Barbados were years of service and seniority. Trinidad & Tobago reported that the sole determinant for appointment of staff with managerial responsibility is seniority. The remaining study countries provided no information.

Wherever staff development planning exists, it takes place at the central level, usually as part of an overall Ministry of Health plan or central government manpower plan. This was so for 3 of the 5 study countries that provided information (Barbados, Guyana and Jamaica). Suriname and the Dominican Republic have no staff development planning for medicines regulation staff. Of the 6 countries visited, only the Food and Drug Department in Guyana has a small training budget. Only 4 of the 12 study countries had staff who had received training in any aspect of drug regulation during the past 3 years. Details are provided in Table 8. Training in Trinidad & Tobago took the form of on the job training of inspectors and laboratory technicians. Training of medicines regulatory staff in the Dominican Republic was said either not to be specific to medicines regulation or not at the required technical level. Sources of funding for training included the government's budget, PAHO, pharmaceutical companies, and other donors.

Table 8 - Summary of medicines regulatory training (past 3 years)

Area of Training	BAR	GUY	HAI	JAM*	Remarks
NRA administration & management	2				
Product assessment & registration	7	3	6		Barbados in preparation for implementation of drug registration system
Quality assurance		2	6		
GMP inspection		4	6	12	Jamaica – 5 years ago
Distribution channel inspection		4	6		
Quality control of drugs		6			
Pharmacovigilance	7				
Identification of illicit drugs				3	

* Jamaica's training was restricted to staff of the Pharmaceutical and Regulatory Affairs Branch; there was no training of Pharmacy Council staff.

Based on reports from 8 of the study countries, the main effects resulting from shortage of staff and lack of adequate training include:

- Activities take longer and have to be rushed or neglected (2)
- Staff cannot be released for training
- Ineffective medicines registration (2)
- Unable to implement medicines registration system
- Insufficient pharmacovigilance (2)
- Inadequate import control (3)
- Inadequate level of inspection (3)
- Delay in implementing registration of herbal remedies
- Delay in implementing regulation of internet pharmacies
- Insufficient monitoring of unregistered dispensers/sellers of medicines
- Slow revision of legislation to incorporate pharmacy technicians
- Have to miss important meetings
- Generally weak regulatory unit (2)
- Staff have to multi-task (8)

This is an indication that a critical strategy to strengthen medicines regulation activities throughout the region will be recruitment and retention of adequately trained technical and administrative staff.

4.2.4 Financial resources and infrastructure

Sustainable and adequate financing of NRA operations is crucial for implementation of medicines regulatory activities. If the NRA is a government entity (as in all study countries) a dedicated budget allocated to the authority would provide a certain security that funds will be made available.

All agencies are government funded, but respondents - except for Barbados - were not aware of a specific budget allocated to their activities, implying that there is limited active management of available funds. Only for Suriname could information of expenditure of the regulatory agencies be obtained. The Pharmacy Council in Jamaica has a dedicated budget but this is not the case for the Ministry of Health Pharmaceutical & Regulatory Affairs Branch.

Eight of the study countries collect fees for medicines regulatory services; however, with the exception of the Directorate of Pharmacy, Medicines & Traditional Medicines in Haiti and the

Pharmacy Council in Jamaica, fees are not accessible to the regulatory bodies to defray expenses but are deposited to the national treasury.

Guyana was the only study country that reported that medicines regulation operations are adequately funded. All other study countries involved in medicines regulation felt that such operations were not financially sustainable.

Fees for regulatory services are published in Barbados, Jamaica, St Lucia, Trinidad & Tobago and Suriname but not in Guyana. The remaining study countries did not provide information on the publication of fees.

Infrastructure

The status of infrastructure, which is critical for the efficient delivery of medicines regulatory services, is deficient in a number of the study countries. Details are outlined in Table 9.

Table 9 - Infrastructure available to medicines regulatory authorities

Country	Dedicated Office Space	Dedicated computers & printers	Dedicated internet & e-mail access	Adequate transport facilities	Remarks
ANT	No	No	No	No	
BAH	n/a	n/a	n/a	n/a	Pharmacy Council just being established
BAR	Yes	Yes	Yes	Yes	In process of relocating due to dilapidated building
BEL	Yes	Yes	Yes	No	
DOM	n/a	n/a	n/a	n/a	no established regulatory authority
DR	Yes	Yes	Yes	No	Office space limited; e-mail contact through web page not working
GRE	Yes	Yes	Yes	No	Office space inadequate
GUY	Yes	Yes - FDD; No - PPB	No	No	FDD's recent relocation has left it without internet access for 2 months
HAI	Yes	Yes	Yes	No	
JAM	Yes	Yes	Yes	Yes	PRAB requires more storage space; PCJ has no funds to refurbish following relocation.
MON	n/a	n/a	n/a	n/a	no established regulatory authority
SKN	n/a	n/a	n/a	n/a	no established regulatory authority
SLU	n/a	n/a	n/a	n/a	does registration of pharmacists and pharmacies by the Pharmacy Council only
SUR	Yes	Yes	Yes	No	
SVG	No	Yes	Yes	Yes	
TRI	Yes – CFDD No - DI	Yes – DI; No - CFDD	No	Yes	Unreliable internet access

n/a = not applicable; FDD – Food & Drug Department; PPB – Pharmacy & Poisons Board; CFDD – Chemistry, Food & Drug Division; DI – Drug Inspectorate; PRAB – Pharmaceutical and Regulatory Affairs Branch; PCJ – Pharmacy Council of Jamaica.

The Dominican Republic reported that the inadequacy of transport facilities has a negative impact on inspection activities.

4.3 Licensing and inspection

Licensing and inspection of manufacturing processes, and distribution and retail activities are important regulatory activities ensuring that the standards required to assure and maintain quality and appropriate use of pharmaceutical products are adhered to. Inspections are done to establish whether licensing requirements are met (pre-licensing inspections), whether they are being

maintained, and whether any unlicensed establishments operate or products are marketed (planned preventive inspections, surveillance). Inspections are also conducted as a response to complaints.

4.3.1 Licensing of premises

Most of the smaller study countries do not have a NRA performing all critical regulatory functions (for example Antigua, Belize, Dominica, Grenada, Montserrat, St Kitts & Nevis, St. Lucia, St. Vincent & the Grenadines). Hence, regulatory activity including licensing and inspection is limited, if it exists at all. Montserrat, St Kitts & Nevis and Dominica are the only study countries that have no authority that issues licenses for operation of pharmaceutical establishments[10] - only business licenses are required for the operation of pharmaceutical wholesale and retail establishments.

Barbados, the Dominican Republic, Guyana, Jamaica, St Lucia, and Trinidad & Tobago publish conditions for licensing so that they are known by applicants. In addition, Barbados, Guyana and Jamaica make guidelines for licensing based on WHO documents available.

As noted in Table 3, pharmaceutical manufacturing is absent in most of the study countries. Consequently, licensing of manufacturers is the least prevalent licensing activity throughout the region. The types of licensing of premises activity being conducted by the study countries is outlined in Table 10.

Table 10 - Licensing of premises

Country	Manufacturers	Importers	Wholesalers/ distributors	Retail pharmacies	Other establishments
ANT	n/a	No	No	No	No
BAH	n/a	to be implemented under new act	to be implemented under new act	to be implemented under new act	?
BAR	Yes	Yes	Yes	Yes	Authorized sellers of poisons
BEL	n/a	No	No	Yes	No
DOM	n/a	No	No	No	No
DR	Yes	Yes	Yes	Yes	
GRE	n/a	Yes	Yes	Yes	
GUY	Yes	Yes	Yes	Yes	Patent shops
HAI	Yes	Yes	Yes	Yes	Pharmaceutical depots
JAM	Yes	Same as wholesalers/ distributors	Yes	Yes	Authorized sellers of poisons
MON	n/a	n/a	n/a	No	No
SKN	n/a	n/a	n/a	No	No
SLU	n/a	No	No	Yes	Authorized sellers of poisons
SVG	n/a	Yes	Yes	Yes	No
SUR	Yes	Yes	same as importer	Yes	Drug Stores
TRI	Yes	Yes§	Yes§	Yes	Retail outlets

n/a = not applicable, type of establishment does not exist
§ only businesses dealing with narcotics, antibiotics & controlled drugs
? information not available

Some of the countries do not differentiate between wholesalers/distributors and importers as they advised that all wholesalers/distributors are importers of medicines. In addition to issuing licenses to

[10] It is not known what the current practice is in The Bahamas, as the Pharmacy Council that will have licensing responsibilities is yet to be established.

operate retail pharmacies, Guyana and Jamaica also issue special licenses to licensed retail pharmacies for the sale of narcotics and Guyana for medical devices.

Guyana, Suriname and Trinidad & Tobago also issue licenses to establishments desiring to sell non pharmacy-only over-the-counter (OTC) medicines (i.e. 'patent shops', 'drug stores' and retail outlets respectively). In Suriname and Trinidad & Tobago these licenses are issued by the relevant local authority but only if recommended by the Pharmaceutical Inspectorate or Pharmacy Council respectively. Barbados, Jamaica, and St Lucia license 'authorized sellers of poisons', where poisons are specified in Schedules to the relevant act/regulations. In St Lucia medicines specified as OTC in the pharmacy regulations can be legally sold by shops without a license from the Pharmacy Council.

None of the study countries has legal provisions for licensing or otherwise regulating internet pharmacies or retailers. However, some of the draft legislation available to us to provides for this. There are also no provisions in place to regulate the sale of herbal or alternative remedies. Jamaica advised that it was in the process of revising its legislation to allow for stricter monitoring of the sale of herbal remedies.

For the 6 countries visited, an inspection report is required for the issuing of a license for a pharmaceutical business as well as the renewal of that license. However, Suriname advised that sometimes the inspection is done but no report is forthcoming and Jamaica indicated that there are times when the inspection is not conducted for renewal of license. In the case of Jamaica, this appears to be due to a shortage of staff.

The Dominican Republic and Jamaica publish lists of licensed pharmaceutical establishments, while Guyana makes such lists available upon request. Lists of revoked licenses are also published in Jamaica but none of the study countries publishes lists of applicants not granted licenses.

On the matter of unlicensed establishments being involved in the manufacture, wholesale/distribution or retail of medicines and illegal retail of medicines outside of pharmacy establishments, 4 countries provided responses for all type of establishments, i.e. Barbados, Dominican Republic, Guyana and Jamaica. Suriname provided a response on unlicensed manufacturing and illegal retail of medicines. Barbados and Jamaica reported being unaware of unlicensed establishments manufacturing medicines, while Guyana and Suriname were aware of establishments manufacturing herbal medicines and home remedies, respectively. Barbados and Jamaica were also unaware of unlicensed wholesaler/distributor activity but Guyana felt it was highly probable that such activity was taking place in that country. The Dominican Republic reported that unlicensed establishments of all types operate. All four countries indicated awareness of the sale of medicines by unlicensed retailers and all, including Suriname, were aware of the illegal retail of medicines outside of pharmacy establishments. None of the four countries was aware of the extent of these unlicensed and illegal activities. Where establishments or individuals were discovered to be conducting such activities the Dominican Republic, Guyanese and Jamaican authorities conduct product seizure and destruction operations.

4.3.2 Licensing of persons

Eleven study countries register their pharmacists with the relevant professional body. Dominica and Montserrat do not have this provision. The Dominican Republic, Grenada, and Haiti did not indicate whether they do or do not. Grenada was unable to report on the number of practicing pharmacists in the island therefore it is unlikely that a register of pharmacists is being maintained.

In addition to issuing licenses to practice pharmacy, Jamaica and St. Vincent maintain registers of pharmacy students and pharmacy owners. St. Vincent also maintains a register of pharmacy assistants.

Ten of the 16 study countries have pharmacy schools, where either diploma, associate of sciences or bachelor's degrees are awarded[11]. Individual countries have their specific requirements for registration of pharmacists. This was not further assessed by the study.

4.3.3 Import Permits

With the exception of Trinidad & Tobago, the countries with medicines registration systems – the Dominican Republic, Guyana, Haiti, Jamaica and Suriname – require import permits involving the NRA for all registered products. These countries will also issue import permits for the importation of unregistered products in the case of a national emergency or to satisfy the emergency needs of an individual patient and for investigational products, where relevant. In these instances, the issuing of the import permit is subject to waiver approval from the Chief Medical Officer or a senior officer in medicines regulation. Trinidad & Tobago only requires importers to acquire import permits for registered antibiotics, narcotics and controlled drugs, and will only facilitate the issuing of import permits for unregistered products if these are samples being submitted for registration or investigational products.

Those study countries without medicines registration systems, issue import permits to monitor the entry of narcotics and/or controlled drugs through the ports of entry. In addition, Barbados and Belize issue import permits for the importation of antibiotics. In Antigua import permits for non-controlled pharmaceutical products are issued by the Ministry of Trade subject to approval by the Chief Pharmacist.

In addition to import permits, only Trinidad & Tobago and Haiti reported having other mechanisms in place to prevent illegal importation/smuggling of medicines into the country. Trinidad & Tobago has inspectors posted at the country's 8 import stations and Haiti has a strong system of collaboration between its Registration Department and the Customs Department to ensure that only registered products are imported. The Bahamas, Belize, Dominican Republic, Guyana, Jamaica, and Haiti indicated awareness that their countries have a problem with illegal importation of medicines, while Barbados stated that there is a possibility that such a problem exists in that country. In Haiti, even licensed importers were noted to be importing medicines without import permits.

It can be concluded from the foregoing that there is significant need throughout the region for mechanisms to be implemented to reduce the occurrence of illegal imports of medicines and where mechanisms exist to make these more stringent. This is particularly critical in light of the global threat of counterfeit and substandard products.

4.3.4 Inspection

Haiti, the Dominican Republic, Suriname and Trinidad & Tobago indicated having a dedicated inspectorate with responsibility for Good Manufacturing Practices (GMP) and/or distribution channel inspections. Antigua reported that it has a dedicated inspectorate established under the Pharmacy Council that conducts distribution channel inspections only.

[11] It is important to take note of the wide variation in professional qualification of pharmacists throughout the region**.** The Caribbean Association of Pharmacists has been actively lobbying for there to be standardization in this area across the region with the minimum qualification being a bachelor's degree.

GMP inspection is only relevant for those countries with local pharmaceutical manufacturing establishments, i.e. Barbados, the Dominican Republic, Guyana, Haiti, Jamaica, Suriname, and Trinidad & Tobago. In Suriname inspections are done by the Pharmaceutical Inspectorate but GMP certificates are not being issued. In the case of Trinidad & Tobago, the Chemistry, Food and Drugs Division conducts GMP inspection of manufacturers, but certificates issued are not official GMP certificates for use in the WHO certification scheme (for export purposes free sale certificates are provided). Barbados, the Dominican Republic, Guyana, Haiti and Jamaica do GMP inspections (not more frequently than once each year). Planned 'preventive' GMP inspections are non-existent.

Barbados has no written national GMP guidelines and Trinidad & Tobago follows guidelines outlined in the 1964 Regulations to the Food and Drugs Act (last amended in 1985), which were said to be according to WHO standards. Haiti is using the GMP guidelines produced within the framework of the Pan American Network for Drug Regulatory Harmonization. None of the countries that conduct GMP inspections has manuals or standard operating procedures (SOPs) to guide GMP inspectors. Jamaica has manuals but these are outdated. The Dominican Republic reported that GMP inspection manuals and SOPs are being developed.

Barbados, Guyana and the Dominican Republic issue GMP certificates, which are required for local manufacturers to obtain export licenses. Jamaica indicated that it does not issue GMP certificates as none of its local pharmaceutical manufacturers is involved in export of medicines.

None of the countries that conduct GMP inspection had found any violations during the past two years. Guyana's GMP inspectors are the only ones that collect samples sometimes and Jamaica was the only study country that conducted GMP inspections outside the country, although this was admittedly on a limited basis.

All 16 study countries, except Dominica, Montserrat, St Kitts and St. Lucia conduct **distribution channel inspections**.

Barbados, Haiti, and Jamaica have written guidelines for Good Distribution Practice and in the Dominican Republic guidelines are being developed. Barbados has inspection guidelines or SOPs for inspectors; the inspectors in Suriname and Antigua are provided with checklists. Planned 'preventive' inspections are conducted in Jamaica and Antigua. Suriname's deficiency in this area was reportedly due to a shortage of staff and there are plans to rectify this. Other countries conduct at least one inspection for each establishment annually for renewal of license and inspect in response to complaints. There appears to be little, if any, collection of samples during distribution channel inspections, with Antigua being the only country reporting this practice.

Details of violations detected in the last two years and measures taken against violators are outlined in Table 11. Only 2 of the 16 study countries provided concrete examples for counterfeit medicines – the Dominican Republic (anti-tetanus gamma globulin) and Haiti (anti-tetanus serum, pentazocin). Bahamas reported that its challenge with counterfeit medicines results from the Bahamas being used for transshipment of these medicines to other jurisdictions. Guyana and Grenada felt that their countries are at high risk related to counterfeit medicines. The remaining countries expressed no specific concern about counterfeit medicines but also noted that there might be cases where the regulatory authority is not aware of. Trinidad & Tobago felt a high level of confidence that there is no problem with counterfeit medicines in that country due to the stringent inspection activities at the ports of entry.

Table 11 - Violations detected during distribution channel inspections (last 2 years)

Country	# of violations	Types of violations	Measures taken against violators
ANT	?	sale of medicines in the street market	?
BAH	16 in 2 cases	1 related to dangerous drugs	referred to court
BAR	0		
BEL	?	?	?
DR	Unknown	No license; expired licenses; pharmacist not present; unregistered products; expired drugs; unauthorized sale	Illegal medicines confiscated; closure of business.
GRE	0		
GUY	4	Substandard products; improper storage conditions	Seizure of products; violation notices; withhold license.
HAI	10	illegal operation of pharmacies and importers; sale of unregistered medicines; street sale of medicines; counterfeits	Seizure of products; closure of premises.
JAM	Unknown	Sale of expired drugs; expired licenses; improper storage conditions.	Seizure of products; violation warning notice; closure of premises
SVG	3	Substandard product (Nelfinavir)	Fine or up to 1 year in jail; warning letters; product recall.
SUR	0		Confiscation of medicines; closure of premises; prosecution.
TRI	4 (Drug Inspectorate Division only)	Inadequate documentation of prescriptions and receipt of stock; storage of unregistered antibiotics.	?

? = information not available

4.4 Product assessment and registration

The purpose of product assessment and registration (or marketing authorization, licensing) is to ensure that pharmaceutical products reaching the consumer have been adequately tested and evaluated for safety, efficacy and quality. In addition, the information provided by the manufacturer needs to be accurate.

Licensing of products is a prerequisite for being able to define and distinguish between the legal and illegal pharmaceutical market.

The required processes include assessment of data submitted by the applicant, deciding on whether to approve or reject the application for registration, and issuing of a registration certificate. Data and other formal requirements for applications need to be established and made public.

4.4.1 General provisions and processes

In 7 of the 16 study countries registration of pharmaceutical products is a legal requirement (Dominican Republic, Haiti, Grenada, Jamaica, St Vincent & the Grenadines, Suriname, and Trinidad & Tobago). Except for Grenada and St Vincent all these countries do have operational registration systems. In addition, Guyana requires registration of pharmaceutical products with the Food & Drugs Department without an explicit legal provision.

The type of products where assessment and registration is currently being performed by the medicines regulatory authority varies between countries. Table 12 provides an overview.

Table 12 - Type of products being assessed and registered

Country	Type of Products
Dominican Republic	New drugs, multi-source (generic) drugs, biologicals*, natural products
Guyana	New drugs; multi-source (generic) products
Haiti	New drugs; multi-source (generic) products
Jamaica	New drugs; multi-source (generic) products, biologicals, herbal products, veterinary drug products, medical devices
Suriname	New drugs, multi-source (generic) products, herbal medicines
Trinidad & Tobago	New drugs; multi-source (generic) products, biologicals, herbal products, veterinary drug products

*: for biologicals: only document assessment - no testing

The **definition of new drugs** varies. In Jamaica and Trinidad & Tobago's food & drugs regulations new drugs are defined as those that contain a substance, whether as active or inactive ingredient, that has not been imported for use as a drug before or that is a new drug in the country of manufacture; combinations of drugs that have not been imported before (including new combination of strengths); and drugs for which new claims are made (including related to dosage and treatment duration). In the Dominican Republic a new drug is a product that does not contain a chemical entity which has previously been approved in the territory of the Dominican Republic. Chemical entity does not mean an inactive ingredient which might be contained in the new pharmaceutical product (Decreto 625-06).

Products imported for investigational or single patient use and samples for submission of application for registration are usually exempt from registration requirements but do require an import authorization or inspection. The Dominican Republic, Guyana and Haiti do not register donated medicines. In Suriname donations and other products that may urgently be required may be granted exemption by the Director Health. In Guyana a temporary registration (usually within 7 days) is issued in cases of urgency.

The standard assessment and registration processes are documented in Table 13.

Table 13 - Standard assessment and registration processes

	DR	GUY	HAI	JAM	SUR	TRI
Standard application form	Yes	Yes	Yes	Yes	Yes	Yes
SOPs for staff	Yes	No	Yes	Draft	No	No
External expert/ committee support	Yes (for new drugs)	No	No	Yes	Yes (RC*)	Yes
Final decision-maker	Head Reg. Dept.	Dir. Food & Drug Dept.	Dir. Pharmacy	Dir. Stand. & Regul. Dept.	RC	Minister of Health
Document of approval issued	Yes	Yes	Yes	Yes	Yes	Yes
Registration number to be printed on package	Yes	No	No[#]	No	No	No
Restriction on registration validity	5 years	No	5 years	No	No	No
Formal fast-track registration procedure	For priority medicines	No	For vaccines	For priority diseases	No	No
Fees	Yes	Yes	Yes	Yes	Yes	Yes
Months taken to assess new drugs (max allowed)	4-5 (3)	4 (6)	4-6	4 (4)	? (6)	3 (4)
Months taken to assess generic drugs (max allowed)	4-5 (3)	4 (6)	4-6	3 (3)	1 (6)	3 (4)

* RC = Registration Committee

#: Haiti does not issue registration numbers

The average time taken to process an application for registration was based on the assumption that applications are complete and no further communication with the applicant is required. However, respondents also noted other factors that do extend the time beyond the officially set limits. These include delays in obtaining laboratory test results, and inadequate capacity related to (external) assessors (not enough for the number of applications to be assessed).

Five countries could provide information on the number of applications for medicinal products (new and known drugs) received and processed during 2008, which is summarized in Table 14:

Table 14 - Level of activities (assessment & registration)

	DR	HAI	JAM	SUR	TRI (for antibiotics only)
No. of applications received	2,166	287	342	245	36
No. processed	531	17	408 (including some pending from 2007)		36
No. approved	499	17		app. 75%	28
No. rejected	32	0	40		

The Dominican Republic uses the WHO developed Model System for Computer assisted Registration (SIAMED) for managing registration data, Suriname uses a tailor made Microsoft Access database and Guyana just started with a Microsoft Excel program while deciding on a more comprehensive software. Jamaica and Trinidad & Tobago use mainly paper based systems - attempts to automate

systems have started very recently and on a low scale. Information on **number of registered pharmaceutical products** could be provided by 5 of the six countries:

- Dominican Republic 10,410 (database still to be updated/ app. 1 year backlog)
- Jamaica 12,124
- Haiti 3,926 (app 10% are unbranded generics)
- Suriname 2,635
- Trinidad & Tobago 2,377 (antibiotics only - ever registered since 1969)

Regulatory authorities could not provide information on how many of the registered products were actually available on the markets in the respective countries.

All countries collect **registration fees**, which only in Haiti are retained by the regulatory authority. In the other countries these fees revert back to the general Ministry of Health or Treasury account and cannot be used by the regulatory authorities to support their work. Fees charged for application for registration for a new drug are as follows (converted from local currencies to USD):

- Dominican Republic USD 197
- Guyana USD 10
- Haiti USD 128
- Jamaica USD 58 (to be increased to USD 348)
- Suriname USD 18
- Trinidad & Tobago USD 123

In Haiti the fee for registration of multi-source (generic) products is reduced by 50%.

The **technical information and documentation** required by countries to be submitted with the application for registration of a new drug are usually prescribed by law. The information actually required as per application forms is summarized in Table 15:

Table 15 - Information requirements for application for registration - New drugs

	DR	GUY	HAI	JAM	SUR	TRI
Product characteristics & label	√	√	√	√	√	√
Chemical/ pharmaceutical information	√	√	√		√	√
Clinical data	√	√	√	√		√
Pharmacological / toxicological data	√	√	√	√		√
GMP certificate	√					
WHO product certificate (for imports)		√		√	√	√ (or free sale certificate)
Manufacturing process	√	√	√		√	√
Quality certificate raw material						
Bioavailability data	√	√	√	√		√
Stability data	√	√	√		√	√
Applicant information	√	√	√	√	√	√
Samples finished product	√	√	√	√	√	√
Samples reference standards	√			√		√

For Suriname some of the information requirements might be implied by the general statement that "all reports, publications and other scientific data on results of all tests and all observations with regard to substance or combination known to the applicant and being important for the estimation of the application" need to be submitted in addition to the information specified on the application

form. The Jamaican form makes provision for 'any other relevant information'. This might cover those areas that are not ticked in Table 15 above.

The medicines legislation is not always clear regarding differences in **registration requirements for** new and **known (well known multi-source) products**. In practice and according to the application forms the following differences are made: In the Dominican Republic pharmacological & toxicological documentation and clinical studies are not required for known products and applications are being assessed by the in-house standing technical medicines committee. In Suriname 'all other information' does not need to be submitted for application of known products. Jamaica and Trinidad & Tobago only have a form for 'new drugs'. According to respondents in Trinidad & Tobago and in Haiti, data requirements for new and known drugs are the same, while in Jamaica applications for registration of multi-source (generic) drugs where an equivalent has been marketed before in the country do not need necessarily to be accompanied by clinical safety and efficacy studies. In vivo bio-equivalence studies are explicitly required for all multi-source products in Jamaica and Trinidad & Tobago.

Information on **registration with other national medicines regulatory authorities** should be provided with applications in Jamaica and Guyana (United States, Australia, Canada, European Medicines Agency (EMEA), United Kingdom, Trinidad, Jamaica); Trinidad & Tobago requests proof of registration with the regulatory authorities of Australia, Belgium, Canada, Denmark, France, Netherlands, Sweden, United Kingdom, United States or other countries; the laws of Suriname provide for simplified registration procedure if products are registered in Netherlands, France, Belgium, Switzerland, England, West Germany, Sweden, Norway, Denmark, Canada and the United States of America. However, according tor respondents in practice registration with another recognized regulatory authority is only providing 'added confidence' and does not impact otherwise on information requirements and the assessment process. The same applies for products that are pre-qualified by the WHO.

Except for controlled drugs, most countries do not have up-to-date lists of active ingredients categorized according to the common **distribution schedules** that are established in the legislation (e.g. controlled drugs, prescription only, OTC-pharmacy only, OTC-other shops)[12]. Decision were said to be made during the registration process according to the literature, US Food and Drugs Administration (FDA) practices, or own experts' advice. In the Dominican Republic criteria for 'free sale' medicines are documented in the Medicines Regulations (Article 212). In Jamaica reference is made on the application form to List 1 and List 2 drugs established by the Pharmacy Council List Committee. List 1 and 2 drugs are OTC - pharmacy only and OTC- other shops.
Applicants do state on the application form under which distribution category the product should fall.

There are no **independent appellate bodies** where applicants can lodge complaints related to registration processes or decisions. Complaints can be directed to the administrative supervisors in the Dominican Republic, Guyana and Suriname, and to the bodies in charge of registration in Jamaica and Trinidad & Tobago. Respondents noted that the number of official complaints received is very low.

Most countries reported that they issue updated **lists of registered products** regularly, but do not distribute them widely. Table 16 provides and overview.

[12] St Lucia has lists for 'pharmacist assisted drugs' and 'prescription only drugs' as well as a list of conditions that can be treated with OTC medicines (Pharmacy Regulations 2007)

Table 16 - Access to information on registration status

Dominican Republic	updated list not produced, but information available through DGDF website
Guyana	updated list produced and distributed internally; photocopies made available on request to interested parties
Haiti	not publicly available
Jamaica	updated list produced but not distributed; copies available on request to interested parties
Trinidad & Tobago	no list produced; newly registered products are published in the official gazette
Suriname	updated list can be made available from database; no active distribution; interested parties can buy copy

4.4.2 Linkages with patents and intellectual property laws[13]

Examples for linkages between drug registration and pharmaceutical patents are requirements or practices to notify the patent holder about an application for registration for a patented product from a different (generic) manufacturer, the provision of data exclusivity rights to the first applicant for registration of a pharmaceutical product, or provisions for 'early working'/regulatory review exception ('Bolar' exception) of pharmaceutical patents.

> **Data exclusivity** grants to the first applicant a temporary exclusive right to the submitted information, so that the DRA cannot rely on this information (e.g. clinical studies for safety and efficacy) for the approval of products of other companies, making an abbreviated registration procedure of generic products impossible for this period. *N.B.: this is not required in order to be TRIPS compliant.*
>
> **Early working provisions** allow that an application for registration for a multi-source product can be processed by the regulatory authority before the patent of the originator product has expired. This facilitates that the multi-source (generic) product can be issued with a marketing authorization and be marketed immediately upon expiry of the originator's patent. *N.B.: this is allowed under TRIPS flexibilities.*

In the Dominican Republic data exclusivity and early working provisions are regulated in Article 32 of the Act 424-06 - Implementation of the Dominican Republic-Central America Free Trade Agreement (DR-CAFTA). A data exclusivity period of 5 years for non-disclosed information is provided for pharmaceutical products (subject to solicitation by the applicant), and early working is allowed in which case the regulatory authority is obliged not to issue the final marketing authorization before patent expiry of the originator product. The patent holder has to inform the regulatory authority about any existing patent when submitting the application for a new drug. In turn the regulatory authority is required to inform the patent holder about any application for marketing authorization by a third party during the validity period or the patent.
In practice, notification of a known patent holder is the only provision currently being implemented by the Ministry of Health. Any further action is seen as the responsibility of the patent holder. The regulatory authority continues to process the application and grants marketing approval if warranted.

[13] The impact of intellectual property laws on access to medicines is also addressed in the report of the study 'Regional assessment of patent and related issues and access to medicines' implemented by HERA in parallel to this study.

In Trinidad & Tobago there is provision for at least 5 years of data exclusivity in the Protection Against Unfair Competition Act 1996 (Act No. 27 of 1996). The Food & Drugs Department, however, reported that patents and data exclusivity are not being considered during the registration process.

Jamaica stated to have provisions for data exclusivity that are being followed. In addition, applicants for registration of multi-source (generic) products need to state the expiry date of the patent of the originator product on the application form, but this apparently does not affect the registration process.

Haiti as the only Least Developed Country in CARICOM is not yet obliged to be TRIPS compliant (grace period until 2016).

NRA respondents in all study countries reported that they were not aware of any formal collaboration with the patent office, and that they do not consciously take intellectual property rights into account during the process of medicines registration.

In those countries where parallel import is not restricted (Dominican Republic, Suriname) there were no specific requirements for these products by the national medicines regulatory authority. However, importers need to provide an authorization letter by the manufacturer as is the case with all pharmaceutical products. It should be noted that the concept of parallel import was not well understood by regulatory staff[14].

4.5 Regulatory quality control laboratories (RQCL)[15]

The medicines quality testing status of the study countries is outlined in Table 17. It should be noted that Haiti is the only study country that is neither doing nor accessing some level of drug quality control testing. Only 4 countries have regulatory quality control laboratories owned by the NRA and/or the Ministry of Health (RQCL). Except for the Bahamas, Grenada, Haiti, Suriname and the Dominican Republic all study countries access some level of quality control testing services from the CRDTL. OECS member states usually submit samples through OECS/PPS.

Table 17 - Regulatory quality control laboratories overview

Country	Legal provision for RQCL	MOH RQCL established in country	NRA/MOH RQCL has adequate facilities, materials & resources	Other in-country QCL used	External QCL used
ANT	Yes	No		No	CRDTL
BAH	No	No		No	FDA (USA); PIS, Vienna
BAR	No	No		No	CRDTL; Eurofin, UK
BEL	Yes	No		No	CRDTL
DOM	No	No		No	CRDTL
DR	Yes	Yes	No°	No	No
GRE	Yes	No		No	No
GUY	Yes*	Yes	Yes	Yes – MMU minilab	CRDTL
HAI	No	No		No	No
JAM	No*	Yes	No	Yes – CRDTL	No
MON	?	No		No	CRDTL

[14] Parallel import "refers to the import and resale in a country, without the consent of the patent holder, of a patented product that has been legitimately put on the market of the exporting country." (WHO 2004-2) The sale in the exporting country is deemed to 'exhaust' the patent holder's right in the importing country. The importing country needs to have provisions for regional or international exhaustion of patent rights in the national patent legislation.

[15] Due to time constraints the RQCL in the Dominican Republic could not be visited. Less detailed information is therefore available for this institution.

Country	Legal provision for RQCL	MOH RQCL established in country	NRA/MOH RQCL has adequate facilities, materials & resources	Other in-country QCL used	External QCL used
SKN	No	No		No	CRDTL
SLU	No	No		Yes – OECS/PPS minilab	CRDTL
SVG	No	No		No	CRDTL
SUR	No	No		Yes – BGVS QCL	No
TRI	Yes§	Yes	?		CRDTL

MMU – Materials Management Unit; QCL = Quality Control Laboratory; PIS = Pharmaceutical Security Institute.
* Has legislation with provisions for the appointment of analysts, and allowing RQCL to perform quality testing of pharmaceutical products and issue official results of testing.
§ Has legislative provision for the appointment of analysts.
° Information provided by the Head of the Technical Medicines Commission
? Information not provided

The 4 countries with in-country RQCL conduct testing of non-biological pharmaceuticals for drug registration. None of the RQCLs has the capability to test biological products. None of the RQCLs is involved in inspection of industry quality control laboratories or the training of analysts. The RQCL in Guyana allows limited use of its facilities by students from the University of Guyana to support research. The tests and assays that can be performed by the RQCLs in Guyana, Jamaica, Trinidad & Tobago and the CRDTL are outlined in Table 18. The 3 countries send samples to the CRDTL for sterility testing and microbiological testing. The region has no capability in pyrogen testing or toxicity testing. Only Guyana and Trinidad & Tobago have the capacity to do polarimetry. Trinidad & Tobago reported not being able to conduct thin-layer chromatography due to the inability to source the required coating material. In addition to the lack of equipment, the RQCLs and the CRDTL reported other challenges contributing to some samples not being tested, including lack of reference materials, lack of required procedures, inadequate training, poor calibration of instruments, high staff turnover, insufficient funds, and lack of notice by persons submitting samples for testing. Only the CRDTL and the RQCL in Guyana participate in the WHO proficiency scheme. Trinidad & Tobago evaluate the performance of its RQCL via retesting of samples and cross analysis by the CRDTL. The RQCL in the Dominican Republic is actively involved in training and evaluation activities related to implementation of WHO Good Laboratory Practices supported by PANDRH.

Table 18 - Test / Assay capability of RQCLs

Test/Assays	Guyana	Jamaica	Trinidad & Tobago	CRDTL
Chemical tests and assays	Y	Y	Y	Y
Infra-red spectrophotometry	Y	Y	N	Y
Thin layer chromatography (TLC)	Y	Y	N	Y
UV-visible spectrophotometry	Y	Y	Y	Y
Polarimetry	Y	N	Y	N
High-performance liquid chromatography (HPLC)	Y	Y	Y	Y
Atomic absorption spectrophotometry	Y	N	Y	N
Disintegration test	Y	N	Y	Y
Dissolution test	Y	N	Y	Y
Microbial limit test	N	N	N	Y
Pyrogen test, LAL or rabbit method	N	N	N	N
Sterility testing	N	N	N	Y
Toxicity testing	N	N	N	N

Only Guyana and Trinidad & Tobago collect samples for testing as part of local planned quality surveillance. Guyana targets anti-malarials and antiretrovirals, while Trinidad & Tobago targets drugs under its chronic disease assistance program as well as tuberculostatic drugs. In addition, the CARICOM member states, except Grenada, collect samples as part of the CRDTL's planned quality

surveillance. The schedules for testing of the priority samples for surveillance for 2007/08 and 2008/09 published by the CRDTL are outlined in Table 19.

Table 19 - CRDTL schedule for testing of priority drugs for surveillance

Month	2007/08	2008/09
January	Tetracycline	Ranitidine Tablets
February	Metronidazole	Carbimazole Tablets
March	Carbamazepine	Carbamazepine Tablets (Immediate-Release)
April	Phenytoin	Prednisolone Tablets (Immediate-Release)
May	Phenytoin	Chlorpromazine Tablets
June	Erythromycin & Chlorpropamide	Methyldopa Tablets
July	Furosemide	Ibuprofen Tablets
August	Amoxicillin and Penicillin	Zidovudine Capsules
September	Isoniazid and Mebendazole	Phenytoin Prompt-Release Solid Dosage Forms
October	Digoxin	Doxycycline Capsules
November	Fluphenazine decanoate	Hydrochlorothiazide Tablets
December	Warfarin	Verapamil Hydrochloride Tablets

Over the past 2 years 250 samples were submitted to the RQCL in Jamaica. The samples submitted came from the drug regulatory authority (59), manufacturers (139), and the MOH in furtherance of police investigations (52). The samples submitted to the Trinidad & Tobago RQCL were from government drug inspectors (59), the NRA (126), the public procurement agency (23), and hospitals/clinics as a result of complaints (8). During the past 2 years the CRDTL received 801 samples from countries in the CARICOM region, as outlined in Table 20.

In 2006, the RQCL in Guyana tested 125 samples of which 55 products failed. Over the past 2 years, Jamaica's RQCL tested 240 samples of which 25 failed. The Trinidad & Tobago RQCL analyzed 216 samples in 2007 and reported a 1% failure rate for samples tested in-country. For 2006/07 and 2007/08, the CRDTL tested 640 samples and 89 were found to be unsatisfactory. Details by country are provided in Table 20.

Table 20 - Summary of samples received & analyzed by CRDTL (2006-2008)

submitted by	# of samples received	# of samples analyzed	Satisfactory	Unsatisfactory	% Unsatisfactory
BAR	80	68	60	8	11.7
BEL	13	9	8	1	11.1
DOM	1	2	1	1	50.0
GUY	127	137*	107	30	21.9
HAI#	12	12	12	-	0.0
JAM	355	211	180	31	14.7
OECS/PPS	128	139*	128	11	7.9
TRI	82	62	55	7	11.3
WHO/PAHO	3				
TOTAL	**801**	**640**	**551**	**89**	**13.9**

* Includes samples submitted in the prior year 2005/06

These were samples of a specific donation submitted by PAHO/Haiti

Some countries complained about the lengthy turnaround time to receive results from the CRDTL. For OECS/PPS the average lead time for receiving analysis results stood at 83 days during the period July 2007 to June 2008 (maximum 167, minimum 50 days) (OECS/PPS 2008). However, the Director, OECS/PPS reported that there had been significant improvement in recent times. The CRDTL noted that the international protocol regarding communication prior to submitting samples to allow for agreement on the submission date was largely ignored by the participating countries. This resulted

in overloading of the CRDTL's limited capacity at times. In addition, there are many instances when countries fail to send sufficient reference standards or required procedures to facilitate testing of samples, particularly those samples being submitted for drug registration.

The general level of substandard products in the CARICOM region is unknown. The Director CRDTL attributes this lack of knowledge to inadequate random sample testing throughout the region.

4.6 Specific quality assurance measures in countries without product registration

Registration of pharmaceutical products is necessary to determine whether medicines are marketed legally. Being legally on the market implies that an assessment of product efficacy, safety and quality has been done - either through the NRA or another approved authority.

Ten of the study countries do not have an operational registration system for pharmaceutical products. Out of these, 7 belong to the OECS and participate in pooled procurement for public sector medicines conducted by OECS/PPS. Respondents were asked what specific methods, if any, are applied to assure safety, efficacy and quality of medicines being imported. Table 21 provides a summary of replies received. Issuing of import permits in compliance with UN conventions on narcotics and psychotropics are not considered.

Table 21 - Quality assurance (QA) in the absence of registration systems

	QA measures for public sector	QA measures for private sector
ANT	Procurement through OECS/PPS	screening of import documents
BAH	Proof of registration with recognized NRAs required (e.g. FDA, EU countries)	none (to be instituted with establishment of Pharmacy Council)
BAR	Pre-registration of suppliers; proof of registration with other NRAs (FDA, Canada, EU); random QC testing	import permits for antibiotics only; partly using same products as contracted by Barbados Drug Service
BEL	Tender procedures (proof of registration in other countries including Jamaica & Costa Rica; WHO pre-qualification); visual inspection	import permits for antibiotics
DOM	Procurement through OECS/PPS	none
GRE	Procurement through OECS/PPS	none
MON	Procurement through OECS/PPS	none
SKN	Procurement through OECS/PPS	none
SLU	Procurement through OECS/PPS	none
SVG	Procurement through OECS/PPS	none

It becomes clear that the quality of pharmaceutical products available in the private sector is not being assured adequately. In addition, while all 10 countries are using essential medicines lists for the public sector, which provides for some sort of screening for efficacy and safety of active ingredients, this does not apply for products marketed in the private sector. In Barbados, retail pharmacies that are associated with the Special Benefit Service do partially buy and dispense the same products that were contracted through the Barbados Drug Service.

Assessment of the quality assurance methods applied by public sector procurement agencies was beyond the scope of this study. However, during our visit to OECS/PPS we had the opportunity to discuss the quality assurance measures that are being applied by this organization. These include

- restricted international tender (pre-qualified suppliers only; procedure includes pre-qualification of manufacturers; 51 suppliers are pre-qualified for 2008-2010)
- tender conditions (e.g. requirement for GMP certificates)
- Global Fund quality assurance criteria for products procured with Global Fund money
- testing of samples of new suppliers and new products (CRDTL)
- qualitative quality analysis in-house (mini lab)
- routine testing of products prone to quality/stability problems

Submission of a WHO Certificate for Pharmaceutical Products Moving in International Commerce is not yet a requirement (neither at tendering nor at contracting stage), neither are suppliers required to submit authorization letters of manufacturers.

OECS/PPS has a quality assurance policy. However, when we visited, the responsible quality control officer had just resigned and the position was vacant. During 2007/2008, 32 samples were submitted for testing to the CRDTL, mainly 'pre-tender' samples. Out of those, 8 (25%) failed (5 assay, 2 dissolution, 1 pH)(OECS/PPS 2008). Member states are provided with a 'product complaint form' for submission of samples of products suspected to be substandard.

OECS/PPS is the sub-regional focal point to combat counterfeit medicines and acts as regional pharmacovigilance center for OECS member states. Countries can report any adverse drug reactions on an Adverse Drug Reaction Form.

5. Discussion of study findings

Out of the 16 study countries, 6 have an operational medicines registration system and do licensing and inspection of premises and personnel. An additional 4 do licensing and inspection of all or some categories of premises where pharmaceuticals are manufactured, imported, stored, and/or sold.

Asked about the challenges in medicines regulation respondents noted the following:

Table 22 - Common challenges in medicines regulation

Regulatory Function	Challenges & number of responses	
Product assessment & registration	Staff (number and competency)	5
	Lack of experts	1
	Lack of legislation	1
	Peer review delay & conflicting responses	1
	No fully automated system	1
	Fragmented approach & lack of communication	2
	Workload assessing dossiers	1
Licensing of persons & premises	Weak regulations	1
	Regulations not yet passed	1
	Inadequate number of inspectors	4
	Too many inspections by different bodies	1
Inspection of manufacturers & distribution channel	Staff (number and competency)	10
	Weak regulations	1
	Fragmented approach & lack of information sharing	1
	Inadequate transport	2
Quality control	No QC laboratory in country	4
	Lack of reference standards	3
	Long lead times	2
	Staff (number and competency)	1
	Is very expensive	1

In addition, general challenges for medicines regulation were identified as inadequate regulations (3x), lack of funding (2x), lack of policies and guidelines (1x), lack of enforcement mechanisms (1x), and inadequate infrastructure (1x).

Respondents were also very aware about the weak areas, including the fact that planned preventive inspections are hardly being carried out, and that post-marketing surveillance/pharmacovigilance is yet to be implemented. The majority of countries noted as strength the motivation, and - in many cases - the competence of existing staff.

In summary, effectiveness of medicines regulation in the study countries is affected by

- **Delay in updating and passing legislation** (acts and regulations)
  Professionals in quite a few of the smaller and some of the larger countries need to be commended for having drafted medicines related bills and regulations. However, in most cases processing of these legislations has been going on for years, causing delay in implementation of even the more basic regulatory activities.
- **Human resources constraints**
  Inadequate number of staff but also inadequately qualified staff to perform tasks that require very specific technical skills (e.g. GMP inspection, distribution channel inspection, assessment of highly technical product dossiers). Comprehensive training plans and specific training opportunities to upgrade staff competency are not available.
  Members of external expert committees are not always able to cope with the number of document reviews assigned to them within the officially foreseen time frames, which - in addition to submission of incomplete documentation by applicants - is the main reason for delays in processing applications for registration.
- **Institutional constraints**
  In some countries responsibility for medicines regulatory functions are spread over separate entities, sometimes duplicating functions (e.g. registration of antibiotics by one body, and registration of other medicines by another body). A main coordinating body and effective communication channels are missing. This situation is the result of outdated or insufficiently harmonized legislation.
  The use of clear written guidelines and standard procedures for all aspects of medicines regulation is not yet very common. This also applies to fast track registration procedures for priority products and to differences in documentation requirements for registration of either new or well known multi-source products.
  Data management is inadequate in the majority of countries. Regulatory information (e.g. on registered products, licensed premises, inspection results) is mostly not easily accessible, neither for regulatory staff nor for interested parties outside the NRA.
- Inadequate access to fully functional regulatory quality control laboratories

While all but one country mentioned inadequate funds as a challenge, there was no detailed financial information available to establish the extent of the problem.

There are some obvious consequences of the constraints mentioned above, for example very little medicines regulatory activities in some countries, or restriction of inspection and surveillance activities to those required for licensing purposes. It seems safe to state that the risk of unsafe, ineffective or substandard medicines being sold or dispensed to patients increases when the regulatory functions are being performed only partially or not at all. However, it was beyond the scope of this study to establish the concrete impact on efficacy, safety, and quality of medicines

available on the market in study countries. This would require a more detailed market survey including collection and analysis of samples.

5.1 Access to medicines

The objective of NRA's is to ensure the **timely** availability of effective, safe, quality medicines. Long processing times have been noted as one factor negatively impacting access to medicines by the population. However, the average time noted by respondents for reaching a decision on whether or not to approve an application for registration was relatively short (1 to 6 months - see Table 13). For comparison, processing times for Japan, Canada, and Australia were reported as being 24, 17.5 and 17 months respectively (WHO 2004-1). Another study on medicines regulatory systems in 13 countries found that the average time taken to register a new product ranged from 6 to 19 months, from 2 to 18 months for multi-source (generic) products, and from 2 to six months for fast-track products (Ratanawijitrasin S, Wondemagegnehu E 2002).

Only for the Dominican Republic it was stated that the legally provided maximum period of 3 months is usually being exceeded by 1 to 2 months. It has to be noted that responses where usually based on NRA's estimates because adequate data systems for easy evaluation of processing times were not available.

Although evaluation of applications for new medicines are expected to be more comprehensive and time consuming only Jamaica has a provision allowing more time for processing an application for a new product than for a known multi-source product.

Part of the assessment instrument was a basket of 29 basic medicines usually included in essential medicines lists for the treatment of common diseases such as infections (including HIV/AIDS), and chronic non-communicable diseases. Respondents were requested to indicate for each item the actual products legally marketed in their country. Up to three alternatives should be listed including the originator product if applicable. The purpose was to get an indication for the effectiveness and efficiency of NRAs to ensure availability of an adequate number of alternatives of the same product and thereby market competition and affordability.

Out of the 6 countries that require marketing authorization 5 could provide the requested information, which is summarized in Table 23.

Table 23 - Availability of registered product alternatives

	DR	GUY	HAI	JAM	SUR
Number of basket medicines with 3 alternative products registered	16	4	13	23	15
Number of basket medicines with 2 alternative products registered	0	5	4	1	2
Number of basket medicines with 1 product registered	6	15	3	5	7
Number of basket medicines where only the originator brand is registered	0	5	2	4	1
Number of basket medicines with no registered product	6	5*	9	0	5
Total number of basket medicines	**29**				

* For 5 items no information was provided - it is not clear whether this means that there are no registered alternatives; it was also not clear whether the respondent only considered items that were available at the Central Medical Stores at the time of the survey rather than those included in the register.

Except for Jamaica the number of items without any registered product is relatively high (on average around 20%)[16]. These items included specialist medicines that might not be used in all countries (e.g. Levofloxin or Valganciclovir), but also several standard anti-retrovirals. In Jamaica, two out of 4 items where only the originator product is registered were anti-retrovirals.

Reasons for limited availability of registered alternatives might include lack of interest by applicants (expected market too small; expected profits too low; registration requirements for multi-source products too high), or lack of prioritization of key multi-source products by NRAs. The latter assumption is supported by the finding that there are medicines for which an abundance of multi-source products is registered.

It would thus be beneficial if NRAs instituted policies and monitoring mechanisms to ensure that a reasonable number of registered products for essential medicines will be available on their markets. This should include clear differentiation for documentation requirements for new and known products. In the context of high volume and/or high value essential medicines, speedy registration of generic equivalents can translate into substantial savings for governments and the population.

5.2 The risk of counterfeit and substandard medicines

Counterfeit and substandard medicines circulating in countries are a potential health risk for the population.

> **Counterfeit medicine** is a medicine, which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging (WHO 1999-4).
>
> **Substandard medicines** are genuine pharmaceutical products which do not meet quality specifications set for them.

Please refer to foot note[17].

Except for the Dominican Republic and Haiti, countries did not provide concrete examples for counterfeit medicines. However, one of the general weaknesses of medicines regulation identified in study countries is the area of inspection and surveillance. Without active preventive inspection activities covering the formal and informal pharmaceutical sectors it will be difficult to detect counterfeit medicines. Effective surveillance not only requires an adequate number of human and financial resources but also specifically trained inspectors, and clear guidelines and procedures, both still missing in most countries.

While some countries have provisions in their legislation that might be interpreted as dealing with counterfeit medicines, only the Dominican Republic has an explicit legal provision prohibiting acts involving counterfeit medicines (see Section 4.2.1). Countries are therefore encouraged to update their medicines legislation accordingly. This should include the provision of adequate penal sanctions.

[16] We recognize that the sample size of 29 items is not big enough to draw final conclusions.

[17] This definition for counterfeit medicines has recently been amended (WHO 2007-2); however, as there were concerns by WHO member states and several NGOs that the revised definition could be linked to intellectual property rights and negatively affect access to quality generic medicines we maintain the original definition.

Within the framework of PANDRH the establishment of national and regional networks for the fight against counterfeit medical products is being suggested and possible working procedures are outlined (PAHO 2008-6). This provides a useful model for study countries to address the possible health risks associated with counterfeit medicines. The Working Group for prevention and combat of counterfeit medicines has further been tasked with developing specific strategies for small countries with limited medicines regulatory systems (PAHO 2008-2).

Finally, we would like to point out that in addition to well functioning regulatory systems the market for counterfeit medicines will be further restricted if adequate quantities of affordable quality pharmaceutical products are accessible to patients (WHO 1999-4).

With regard to substandard medicines all countries noted cases where substandard medicines were detected amongst products supplied through the public sector. Again, the low level of post-marketing surveillance, including random sample collection and testing, makes it difficult to detect substandard medicines in the private sector. This is exacerbated by the insufficient quality control laboratory capacity in the region. In addition, in countries without medicines registration pre-marketing assessment of adherence to quality standards is not done, and it is therefore not easy to establish whether a product is legally substandard.

Globally the focus has recently been on counterfeit products. It is, however, important to note that also substandard medicines can have serious negative effects on the health of patients. For developing countries it has been suggested that substandard products are spread more widely than counterfeit medicines (Wondemagegnehu E 1999). Implementation of measures to detect and withdraw substandard pharmaceutical products from the public and private markets is therefore important.

5.3 Final remarks on study findings

Inadequate legislative frameworks and human capacity constraints are common factors that impact on medicines regulation in study countries. The main assets are the individual staff members working under difficult circumstances. Politically, medicines regulation does not always receive the attention it deserves.

Except for two countries, official policy guidance on the envisaged development of the pharmaceutical sectors, including medicines regulatory systems, is either not available, not updated, or not being implemented. We would therefore recommend that National Medicines Policies be developed / updated and implemented. For the smaller (OECS) countries this could be done through a sub-regional approach.

Recommendations obviously need to consider the different country contexts. For the smaller CARICOM member states it will not be feasible to establish comprehensive medicines regulatory systems taking into account market factors, specific technical expertise requirements, and associated costs. For the larger countries with established medicines registration systems the required extension of regulatory activities to ensure adequate performance of inspection and surveillance systems will be a challenge.

It is suggested that CARICOM countries establish a network for cooperation among NRAs to discuss viable approaches to address the identified common challenges. For example, guidelines for inspections or certain standard operating procedures are not necessarily country specific and could be established in a joint effort using existing WHO or PANDRH documents even before any formal harmonization structures might be decided on. Together and seeking assistance from

PAHO/Caribbean Program Coordination (CPC), training opportunities for regulatory staff should be identified.

By commissioning this study country governments have acknowledged the important contribution of medicines regulation to public health. We hope that this will further translate in concrete government efforts to address the identified challenges.

6. Harmonization of medicines regulation - background, experiences and context

Harmonization can be defined as t*he process and/or results of adjusting differences or inconsistencies to bring significant features into agreement*[18]. In the context of medicines regulation harmonization has been seen as a means of 'streamlining regulatory approaches to ensure quality, safety and efficacy while reducing trade barriers and facilitating world wide trade' (Awang D 2003). The term harmonization has been used in its broadest sense to indicate communication, collaboration and standardization leading ultimately to joint evaluations and/or GMP inspections, mutual recognition of registered products and / or centralized procedures for registration of products.

The primary aim of harmonization has been to reduce registration times including the lead-time associated with meeting different country requirements. If well implemented this should translate into significant cost savings to the pharmaceutical industry and quicker access to new and improved therapies at more affordable prices. Such products may be more effective in treating an indication, easier or more convenient to use or more suited to local storage conditions all of which are important factors in patient adherence and therefore in public health.

Moreover, harmonization would lead to more streamlined medicines registration procedures which are less burdensome to the industry and enable NRA staff to spend more time on other areas of medicines regulation. Medicines regulatory harmonization activities have often been triggered by wider regional integration activities aiming at the creation of single or common markets, and there has been an increasing trend towards harmonization globally.

On the other hand it has been argued that the focus on approving new products fast may negatively affect appropriate pre-marketing assessment of safety with implications on public health (Abraham J, Lewis G 2000). Caution has also been expressed towards accepting the International Conference on Harmonization (ICH) standards too easily, as this will increase costs to local industries, and might negatively affect access to especially interchangeable multi-source (generic) products (Gray 2004; WHO 2002). Applying current WHO standards and guidelines instead (sometimes being criticized by the multi-national pharmaceutical industry) has so far not shown to be less effective in ensuring safety, efficacy and quality (Hill S, Johnson K 2004).

It is thus important to keep the primary objective of medicines regulation - the protection of public health - in mind when considering harmonization options. Medicines regulation should be seen as a critical input for ensuring access to effective and safe medicines rather than an obstacle.

6.1 Review of existing regional and global harmonization efforts

The European Union (EU) with its centralized and mutual recognition procedures is the longest established harmonization initiative. The other main model is the International Conference on

[18] see http://www.answers.com/topic/harmonization (accessed 5 July 2009)

Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), which aims to harmonize technical requirements and dossier formats across the US, EU and Japan. Beyond these two initiatives, there are five main sub-regional initiatives established in the framework of the Asia-Pacific Economic Cooperation (APEC), the Association of Southeast Asian Nations (ASEAN), the Gulf Cooperation Countries (GCC), Pan American Network on Drug Regulatory Harmonization (PANDRH) and the Southern African Development Community (SADC). In addition, the East African Community (EAC) initiated a medicines regulation harmonization initiative early this decade but this is still in its infancy stage.

6.1.1 European Union (EU)

The European Community was established in 1957 by 6 Member States under the Treaty of Rome which came into force on 1 January 1958. There has been progressive harmonization of medicines regulation since 1965 (Directive 65/65/EEC) but only in the 1990s were effective processes put in place. Directive 65/65/EEC set the primary objective of any medicines regulation as safeguarding public health, but also stated that this should not hinder pharmaceutical development or trade within the community. The activation of the Maastricht Treaty in November 1993 transformed the European Community into the European Union, with subsequent introduction of a new medicines registration system that allows manufacturers to gain marketing authorization in one of three ways:

- **Traditional Route**: Individual applications to each Member State
- **Mutual Recognition or Decentralized Procedure**: A mechanism which enables manufacturers to seek simultaneous marketing authorization in two or more Member States (known as Concerned Member States), provided that they have an existing marketing authorization in at least one Member State (known as the Reference Member State).
- **Centralized Procedure**: A mechanism which enables manufacturers to seek simultaneous marketing authorization in all EU and EEA-EFTA Member States (Iceland, Liechtenstein and Norway). Under the centralized procedure, the EMEA, established on the 1st January 1995, is responsible for the scientific evaluation of applications for European marketing authorization for medicinal products. It bases its decisions on the advice of two Member States (the Rapporteur and Co-Rapporteur), which are selected to perform the product evaluation on the EMEA's behalf.

All medicinal products for human use derived from biotechnology and other high technology processes and those medicines intended for the treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions, and viral diseases, as well as all designated orphan medicines intended for the treatment of rare diseases must currently be approved via the centralized procedure.

EMEA is established and mandated to undertake evaluation and supervision activities. It is also responsible for centralized procedure for evaluation and marketing authorization, Scientific committees (and working groups), Management and coordination of the EU Network and provision of scientific advice to companies for the development of new products, and publishing guidelines on quality, safety and efficacy.

There are over 40 National Medicines Agencies responsible for human and veterinary medicinal products in 30 EU and EEA-EFTA countries with a good networking structure between the national agencies, the EMEA and over 4,500 European experts.

See: http://www.emea.europa.eu/home.htm

6.1.2 International Conference on Harmonization (ICH)

The ICH initiative is comprised of the medicines regulatory authorities of the European Union (EMEA), Japan (Ministry of Health and Welfare) and the United States (FDA), and representatives of the researched based pharmaceutical industry in these countries (European Federation of Pharmaceutical Industries and Associations, Japan Pharmaceutical Manufacturers Association, Pharmaceutical Research and Manufacturers of America). WHO, EFTA and Canada are observers, and the Secretariat is provided by the International Federation of Pharmaceutical Manufacturers.

The overall objective, set out in 1990, is to harmonize technical guidelines and requirements for medicinal product registration, with the aim of removing redundancy and duplication in the development and review process, and creating a single set of data to demonstrate the quality, safety and efficacy of a new medicinal product across all three regions. In addition to the successful harmonization of technical requirements, the long-term goal of developing a harmonized format has led to the creation of the ICH Guideline M4, The Common Technical Document (CTD), which provides a harmonized format and content for new product applications. Further, an Electronic Common Technical Document (eCTD) has been developed to allow for the electronic submission of the CTD from applicant to regulator, which is currently being implemented across ICH partner and observer regions.

In recognition of the need to expand communication and dissemination of information with non-ICH parties, the ICH Steering Committee has established a Global Cooperation Group (GCG), whose terms of reference include the provision of information on ICH, its activities and guidelines to any country or regulatory authority that requests it. Thus the groups aim is to disseminate finalized ICH guidelines in order to encourage their acceptance and adoption in non-ICH countries. In that context it should be noted that ICH guidelines represent the high technological level of participating countries and can be considered 'state of the art'. With a focus on new medicinal products these guidelines are note necessarily appropriate for countries with a less developed industry (see also WHO 2002 for a more detailed discussion).

> "The public health implications of the application of guidelines of greater technical complexity in developing countries may be far-reaching. In many countries, essential drugs required for the prevention and treatment of locally endemic conditions are not supplied by the major multinationals, but by local industry or by generic manufacturers. If these suppliers are unable to meet what may be unsubstantiated quality standards, the adverse impact of the withdrawal of these drugs on the health of the population might well be far more dramatic than that of any hypothetical risk posed by failing to achieve the ICH standards." (WHO 2002)

The five main regional harmonization initiatives, APEC, ASEAN, GCC, PANDRH and SADC, all have permanent representation on the GCG.

See: http://www.ich.org/

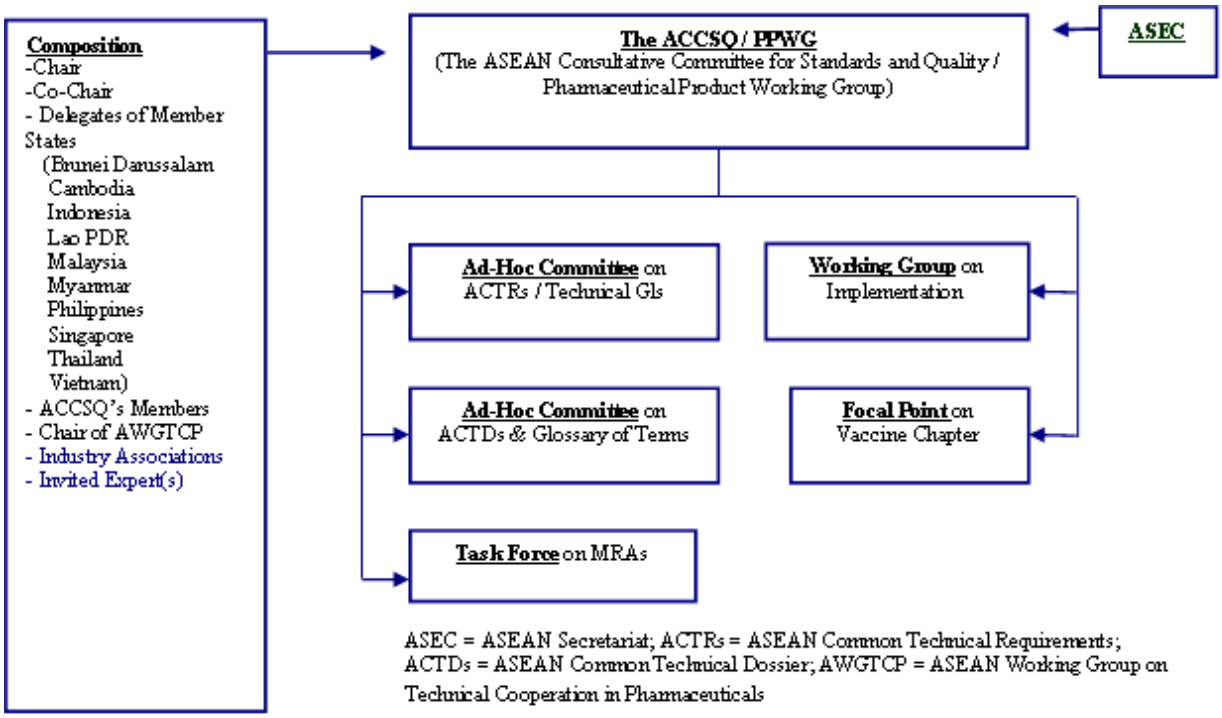
6.1.3 The Association of Southeast Asian Nations (ASEAN)

ASEAN comprises of 10 member states i.e. Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam. It has a total population of 520 million.

Three major cooperation areas under ASEAN include economic, political and security, and social-cultural cooperation. The ultimate goal is to have the ASEAN Economic Community (AEC) established by 2015 and by 2020 ASEAN plans to have a single market and single production base with free flow of goods, services, investment, capital and skilled labour.

The ASEAN Consultative Committee for Standards and Quality (ACCSQ) was established in 1992 to facilitate achieving the objectives of the ASEAN Free Trade Area (AFTA). ACCSQ has Implementation Working Groups and Product Working Groups, including the Pharmaceutical Product Working Group (PPWG). In 1999 the concept of pharmaceutical harmonization was endorsed by the Senior Economic Officials Meeting and the PPWG started to function. Between 2003 and 2005, the ACCSQ had endorsed the 2nd and 3rd term of the PPWG under the same Chair and Co-Chair countries. Figure 2 provides an overview of the organisational structure of the PPWG.

Figure 2 - ASEAN PPWG Organogram



Source: http://www.ich.org/cache/compo/276-254-1.html (accessed 24 May 2009)

The overall objective of the PPWG is to develop harmonization schemes of pharmaceutical regulations of the ASEAN member countries to complement and facilitate the objective of AFTA, particularly the elimination of technical barriers to trade posed by regulations, however without compromising product quality, efficacy and safety. Harmonization activities were focused on pharmaceutical registration with the expected output to have ASEAN harmonized products in four areas, the ASEAN Common Technical Dossier (ACTD), ASEAN Common Technical Requirements (ACTR), Glossary of Terms, and Guidelines. The PPWG was meeting 15 times between September 1999 and July 2008. The current focus is on monitoring implementation of developed documents and guidelines, establishment of sectoral mutual recognition agreements for GMP and bioavailability/bioequivalence studies, and training schemes.

For the development of technical documents Ad-Hoc Committees are being established under the lead of the NRA of one of the ASEAN member states.

The ACTD, covering administrative data, quality, safety and efficacy and the ACTRs, covering quality, safety and efficacy have been developed. The ACTD is the part of the marketing authorization application dossier that is common to all ASEAN member countries, while the ATCR is the set of written materials, intended to guide applicant(s) to prepare application dossiers in a way that is consistent with the expectations of all ASEAN medicines regulatory authorities.

The scope of products for harmonization includes generic, modified release, new chemical entity, and biological products. A harmonization strategy was developed with a clear road map to implement the ACTD by 2002 under a trial arrangement (actual start: 2003), and full implementation by December 2008.

In April 2009, the ASEAN economic ministers signed a' Sectoral Mutual Recognition Arrangement for Good Manufacturing Practice inspections of Manufacturers of Medicinal Products' aimed at ensuring the safety, quality, efficacy and affordability of pharmaceutical products being sold in the region[19].

The PPWG is financed through contributions by member states (for meetings, and in terms of human resources/staff time for participation in ad-hoc committees). Cooperation partners also support selected activities (e.g. WHO, EU).

6.1.4 The Southern African Development Community (SADC)[20]

The Southern African Development Co-ordination Conference, SADCC, the forerunner of the Southern Africa Development Community (SADC), was established in April 1980 by Governments of the nine Southern African countries of Angola, Botswana, Lesotho, Malawi, Mozambique, Swaziland, Tanzania, Zambia and Zimbabwe. Currently SADC consists of 15 Member States, i.e. Angola, Botswana, the Democratic Republic of Congo, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Swaziland, United Republic of Tanzania, Zambia and Zimbabwe. The total population stands at around 248 million.

For achieving the objective of economic cooperation and integration, SADC has adopted milestones to establish the SADC Free Trade Area (FTA) by 2008, the Customs Union (CU) by 2010, the Common Market (CM) by 2015, Monetary Union (MU) by 2016 and the Single Currency by 2018. The Free Trade Area (FTA) was launched on August 17, 2008 during the 28th Summit of SADC Heads of State and Government. In October 2008, the African FTA was launched including COMESA, EAC and SADC Member States (26 countries).

A SADC Health Sector was established in August 1997 in line with the then prevailing decentralized Sectoral Coordination institutional arrangements following which a Sectoral Committee of SADC Heath Ministers was created. The overall coordinating role was allocated to the Government of South Africa and a Sector Coordinating Unit was established to serve as a Secretariat for the Health Sector. With regard to policy development, the region developed and adopted a SADC Health Sector Policy Framework in 2000. The overall goal of this policy is to promote the attainment of an acceptable standard of health for all citizens by promoting, coordinating and supporting the individual and collective efforts of Member States.

The Protocol on Health - a legally binding instrument - was developed and adopted in 1999. Following its ratification by two thirds of member states, this instrument came into force in August 2004. In June 2007 the Draft Implementation Plan for the Protocol on Health 2007–2013 and SADC Pharmaceutical Business Plan 2007-2013 were published simultaneously.

The history of harmonization of medicines regulation under SADC dates back to 1995 when SADC medicines regulatory authorities which formed part of the Southern and Eastern African Medicines Regulatory Authorities Conference (SEAMRAC) initiated the process. The initial drivers were the

[19] http://www.aseansec.org/22481.pdf (accessed 14 June 2009)

[20] A continent-wide initiative was undertaken through the African Drug Regulatory Agencies Network (AFDRAN). However, AFDRAN did not succeed developing harmonized guidelines; language and communication barriers were identified as problems.

South African Pharmaceutical Manufacturers Association, Medicines Control Council of South Africa, Medicines Control Agency of Zimbabwe and the Pharmaceutical Manufacturers' Association of Zimbabwe. Lead teams had been established for coordination of specific activities in response to identified problems. The SEAMRAC group is currently inactive. Under SEAMRAC, various guidelines including application for registration of pharmaceutical products were developed. Following SADC restructuring, all the activities were moved to Botswana with subsequent transfer of coordination of medicines regulation harmonization activities to SADC Health Desk.

Starting in 2000, guidelines developed under SEAMRAC were reviewed and updated under the SADC structure. The development of guidelines has been a fairly lengthy process which was finalized with the approval by the Health Ministers in 2007. To date 14 documents have been published and ratified by member states for either adoption or adaptation while others are still outstanding as shown in Table 24 below:

Table 24 - Harmonized guideline development in SADC

Approved Guidelines	Outstanding Guidelines
Application Form and its Guidelines	Complementary Medicines
Stability	African Traditional Medicines
Bio-availability/Bio-equivalence studies	Clinical Trials for HIV Vaccines
GMP Guideline	Registration of Vaccines
Clinical Trials for Human Participants	Destruction of Unwanted Medicines
Licensing for Export/Import of Medicines	Terminology/Glossary
Validation (Analytical and Process)	
Clinical Trials for HIV Vaccines	
Advertising Code	
Donation of Medicines	
Licensing of Pharmacies and Wholesalers	
Marketing Surveillance	
Nutritional Supplements	
Recalls	

Challenges

SADC Member States are at various levels of pharmaceutical sector development and pharmaceutical services delivery. There are those with relatively good access to medicines, fairly advanced medicines quality assurance systems, relatively less challenging human resources constraints in the areas of pharmaceutical and medical personnel, and up-to-date legislation. On the other end of the scale there are countries struggling to deliver good quality medicines to patients through their public health facilities and without a well developed private sector serving the entire country. Still other member states experience a situation in between these two extremes.

The varying level of economic development has had an impact on the progression of medicines regulation harmonization initiatives in the region.

Differences in medicines regulatory capacity led to limited participation of less developed member states in the development of harmonized guidelines. In addition, some well resourced countries see no value in participating in the process of developing harmonized guidelines as they are more advanced than others in the region.

Other limiting factors include language differences (English and French), and a rather weak Secretariat to coordinate harmonization initiatives at the SADC offices in Gaborone (the Secretariat is expected to facilitate the guideline development and approval process and monitoring, and provide guidance to member states for implementation). This has contributed to delayed

development and approval processes and limited implementation of harmonized guidelines by member states.

Strengths
Some countries with regulatory capacity have been willing to share their resources including training of regulatory staff from member states with less developed regulatory systems[21]. A number of medicines regulatory authorities in the region have benefited from the training program with subsequent improved regulatory capacities.

6.1.5 The Pan-American Network for Drug Regulatory Harmonization (PANDRH)

PANDRH is a Pan-American initiative that started with the first Pan-American Conference on Drug Regulatory Harmonization convened by PAHO in 1997. The network was formally established during the second conference in 1999. The fifth conference was held in November 2008 in Buenos Aires. During the 42nd meeting of the PAHO Directing Council (PAHO 2002), health ministers of the region of the Americas formally stated their support to PANDRH.

PANDRH members are the national medicines regulatory authorities of the 35 PAHO member states and representatives of pharmaceutical industry associations represented by the Latin American Federation of the Pharmaceutical Industry (FIFARMA), and the Latin American Association of Pharmaceutical Industries (ALIFAR).

The mission of PANDRH is to promote the harmonization of all aspects of drug regulation – quality, safety, and efficacy – as a contribution to the quality of life and health care of the national populations in the Americas. The network is governed by a statute and regulations that are currently being revised.

Existing structures are Working Groups, the Executive or Steering Committee that meets at least annually, and a Secretariat provided through PAHO head quarters. The Secretariat supports both, Steering Committee and Working Groups. Steering Committee and Working Group country representation is organized along the lines of the existing sub-regional economic groupings (NAFTA, MERCOSUR, SICA, Andean Community, and CARICOM). The conference, held every 2-3 years, is the highest organ and takes decisions on adoption of technical documents.

At international level PANDRH is represented at the meetings of the Global Cooperation Group, a sub-committee of the ICH steering committee.

The 12 working groups are charged with - amongst others - developing proposals/ guidelines that facilitate regional harmonization of medicines regulation within their thematic area, and developing implementation strategies (including training courses) for those proposals that have been approved by the conference. Work group membership consists of regulatory authorities of each of the 5 sub-regional integration groups and the two industry organisations. Additional technical resource persons may be invited.

The work of PANDRH is being financed mainly through contributions of governments, pharmaceutical industry associations, and PAHO.

CARICOM member states' involvement
CARICOM is currently represented in the PANDRH Steering Committee by Trinidad & Tobago, with Barbados as alternate member.

[21] At one point the NRA of Zimbabwe was the WHO appointed regional training centre for NRAs.

Only a few CARICOM member states' regulatory authorities have been actively involved in PANDRH working groups as main members. This appears to be changing. Table 25 provides an overview of countries' participation as per November 2008[22] and as per May 2009[23].

Table 25 - CARICOM membership in PANDRH working groups

Working Group	CARICOM representation per November 2008	CARICOM representation per May 2009
Prevention and Combat of Counterfeiting of Medicines	SLU (by OECS/PPS)	BAR, GUY, HAI
Registration of Medicines	not involved	BAH, BAR, HAI
Good Laboratory Practices	JAM (CRDTL)	BAR, GUY, JAM, TRI
Medicines Promotion	BAR	BAR, GUY, HAI
Good Manufacturing Practices	not involved	BAR, GUY, TRI
Good Clinical Practices	not involved	BAR, TRI
Bioequivalence / Bioavailability	JAM (university resource person)	BAR, TRI
Vaccines	not involved	BAR
Pharmacovigilance	not active?	BAR, GUY, TRI
Medicines Classification	not active?	BAH, BAR, HAI
Pharmacopoeia	not active?	HAI
Medicinal Plants	not active?	JAM, BAR, TRI

In response to our questionnaires involvement in PANDRH working groups was reported as follows:

- Barbados: Pharmacovigilance, Counterfeit Medicines, GMP, Promotion, Classification
- Guyana: Registration, Pharmacovigilance, GMP, Counterfeit Medicines

OECS member states' respondents felt that they are being represented in PANDRH by OECS/PPS. In practice, none of the OECS member states being part of the study had knowledge about any of the guidelines produced by PANDRH working groups.

According to our survey findings, PADNRH issues are not discussed widely between regulators in countries. Only Belize mentioned that officials participated in workshops organized within the framework of PANDRH, and that there are plans to adopt some of the working group guidelines (registration requirements, licensing of vaccines, and counterfeit medicines).

These findings coincide with some of the challenges identified by the network itself:

- effective participation of countries (regulatory authorities and other sectors of drug regulation)
- acceptance of PANDRH products at national and sub-regional level
- communication among stakeholders mainly at country level and between regulators and regulated sectors (Di Fabio 2007)

We noted the words of caution expressed by Health Action International / Latin America at the last PANDRH conference in Buenos Aires. Concerns were expressed regarding the prominent participation of pharmaceutical industry in the network's decision making structures, and that the guidelines and standards proposed to be adopted by the network might not adequately consider the experiences and capacities of drug regulatory authorities in all its member states (AIS/LAC 2008, PAHO 2008).

[22] as per working group presentations at the 5th conference/November 2008

[23] RED PANAMERICANA PARA LA ARMONIZACIÓN DE LA REGLAMENTACIÓN FARMACÉUTICA Miembros y PUNTOS Focales nacionales por área temática. MAYO 2009 (updated membership list received from PAHO/CPC)

6.2 Other Initiatives for global collaboration and support

In addition to the harmonization initiatives discussed above, there are global schemes aimed at increased collaboration between countries, and projects where regulatory support is provided by WHO and well established NRAs. These include

- the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S), whose members must comply with established standards for GMP inspection for mutual acceptance of inspection results
- the WHO pre-qualification scheme, which supports the UN procurement agencies and NRAs, through the pre-qualification of products based on certain standardized regulatory requirements, and
- the US-FDA Tentative Approval and the EMEA Scientific Opinion, aimed at expanding access to medicines and supporting developing country regulators as they build capacity.

6.2.1 PIC/S

The PIC/S is an international instrument between national pharmaceutical inspection authorities, aimed at providing active and constructive co-operation in the field of GMP.

PIC/S' mission is "to lead the international development, implementation and maintenance of harmonized GMP standards and quality systems of inspectorates in the field of medicinal products."

This is to be achieved by developing and promoting harmonized GMP standards and guidance documents; training competent authorities, in particular inspectors; assessing (and reassessing) inspectorates; and facilitating the co-operation and networking for competent authorities and international organizations. There are currently 36 participating authorities in the PIC/S.

Accession to the Scheme requires meeting and consistently applying PIC/S standards in GMP inspection. As a result members and non-members have increased confidence in GMP inspection decisions performed by PIC/S member countries. For example, in the context of procurement funded by the Global Fund to combat AIDS, TB, and Malaria, PIC/S member countries were until recently recognized as having stringent NRAs, and medicinal products manufactured in these countries were considered to be of adequate efficacy, safety, and quality for being procured with Global Fund money[24].

In addition, the scheme provides an avenue for the voluntary exchange of GMP inspection reports between member states, and thus facilitates more formalized mutual recognition agreements.

See: http://www.picscheme.org/

6.2.2 WHO pre-qualification

The pre-qualification project, established in 2001, is a service provided by the World Health Organization (WHO) to facilitate access to medicines that meet unified standards of quality, safety and efficacy for HIV/AIDs, malaria, tuberculosis and reproductive health. Prequalification was originally intended to give United Nations procurement agencies, such as UNICEF and UNAIDs, the choice of a range of quality medicines. But, the list has become a vital tool for any agency or organization involved in bulk purchasing of essential medicines from the international market.

Any manufacturer wishing their medicines to be included in the pre-qualified products list is invited to apply, provided the medicines are included in the invitation for Expression of Interest. Each

[24] From July 2009 the new Global Fund quality assurance policy is to be applied. PIC/S member countries are no longer automatically considered as having stringent NRAs (Global Fund 2008).

manufacturer must present extensive information on the product (or products) submitted to allow qualified assessment teams to evaluate its quality, safety and efficacy. If the product is found to meet the specified requirements, and the manufacturing site complies with GMP, both the product linked to this manufacturing site and the company are added to the list of pre-qualified products published on the WHO web site.

Assessment of product dossiers is based on guidelines established in "Marketing authorization of pharmaceutical products with special reference to multisource (generic) products (WHO 1999-3) and on specific sections of the ICH "Common Technical Document for the Registration of Pharmaceuticals for Human Use".

The pre-qualification process usually involves local NRA staff through 6-week attachments in order to build capacity in dossier assessment and GMP inspections.

See: http://healthtech.who.int/pq/default.htm

6.2.3 US-FDA tentative approval

Since May 2004, in support of the President's Emergency Plan for AIDS Relief (PEPFAR), the FDA has actively encouraged any sponsors worldwide to submit U.S. marketing applications for single entity, fixed dose combination, and co-packaged versions of previously approved antiretroviral therapies. FDA reviews the marketing applications using its normal standards for authorization. If the product still is under patent protection in the US, FDA issues a "tentative approval" rather than a "full" approval. The "tentative" approval signifies that the product meets all safety, efficacy, and manufacturing quality standards for marketing in the U.S. but for the legal market protection, it would not be allowed on the US market. The United States Agency for International Development (USAID) allows, under PEPFAR, purchase of any product that has either a "full" or "tentative" FDA approval. In addition both full and tentative approvals are included in the WHO pre-qualification list for UN agency procurement. Due to the significant public health impact of these products, FDA prioritizes the review of these submissions and has met its announced commitment to complete the reviews in as little as two to six weeks after submission of a high-quality application.

See: http://www.fda.gov/oia/pepfar.htm

6.2.4 EMEA scientific opinion

The EU has created a mechanism to issue a scientific evaluation of medicinal products intended exclusively for markets outside the EU. Article 58 of Regulation No. 726/2004 established a mechanism whereby the EMEA - on application by WHO - may give a scientific opinion for the evaluation of certain medicinal products for human use intended for markets outside the Community. It serves as a response to the need for protection of public health and provision of scientific assistance to non-member countries within the context of cooperation with WHO, while at the same time allowing rapid access by those countries to important new medicinal products intended to prevent or treat diseases of major public health interest. Its use can be further explored in the context of neglected diseases, which have no market in the EU.

See: http://www.emea.europa.eu/htms/human/non_eu_epar/background.htm

6.3 Harmonization in the context of CARICOM

In 2001, CARICOM member states signed the *Revised Treaty of Chaguaramas Establishing the Caribbean Community including the CARICOM Single Market and Economy (CSME)* (CARICOM 2001) - the successor of the original treaty establishing CARICOM in 1973. The objectives of the revised

treaty include improving standards of living and work, accelerated economic integration of member states, improved trade relations with outside nations, and enhanced international competitiveness.

The CSME was formally launched in 2006, and aims to create one large market among the participating member states, key elements of which are the free movement of goods, common external tariffs, free circulation, free movement of capital, a common trade policy, free movement of labor, and - in Article 74 - harmonization of laws, including "standards and technical regulations, labeling of foods and drugs, and sanitary and phytosanitary measures".

Part 2 of the Treaty addresses consumer protection and, amongst others, provides for member states to enact harmonised legislation, including legislation ensuring that goods supplied to consumers are labelled in accordance with standards and specifications prescribed by the competent authorities, and that hazardous or other goods whose distribution and consumption are regulated by law are sold or supplied in accordance with applicable regulations. All this provides a good window for harmonization of medicines regulation.

A recent regional development is the Caribbean Public Health Agency (CARPHA), planned to be formally established in early 2010. It is foreseen that CARPHA becomes the legal entity under which the existing 5 regional health institutions will be functioning under one management structure, with one strategic and one resource mobilisation plan. The 5 existing institutions are

- the Caribbean Epidemiology Center (CAREC), based in Trinidad
- the Caribbean Food and Nutrition Institute (CFNI), based in Jamaica
- the Caribbean Environment Health Institute (CEHI), based in St Lucia
- the Caribbean Health Research Council (CHRC), based in Trinidad
- the Caribbean Regional Drug Testing Laboratory (CRDTCL), based in Jamaica

The physical location of CARPHA has not yet been decided, but a proposal by the government of Trinidad & Tobago to host CARPHA head quarters is being discussed (CARICOM/PAHO 2009).[25] Following the rationale for creating the CARPHA, any regional medicines regulatory entity should probably be integrated in the CARPHA structure.

6.3.1 Legal systems

Twelve of the 15 CARICOM member states operate under a common law system, 3 under a civil law system (Dominican Republic, Haiti and Suriname), and 1 (Guyana) has a mixed system.

Discussing the approaches on which the different legal systems are based is beyond the scope of this study. In any case, it is not anticipated that the existence of the different legal systems will present a barrier per se for medicines regulatory harmonization.

For example, in the European Union, where common, civil and mixed legal systems are prevalent, the EU treaties empower specific EU institutions to legislate on matters with EU competence. This secondary legislation is done in the form of regulations, directives, decisions, recommendations, and opinions. Harmonized medicines registration in the EU is based on the respective directives. Similarly, the differences in the legal systems did not prevent that legally binding treaties could be drafted and were ratified by CARICOM member states.

[25] In the meantime CARICOM Ministers of Health have agreed to Trinidad & Tobago as the seat of CARPHA (www.caricom.org/jsp/pressreleases/pres226_09.jsp)

6.3.2 Countries' perceptions towards harmonization

In general, respondents feel that harmonization of drug regulation within the CARICOM region will be beneficial. Especially those countries that do not have a registration system in place would welcome a central body for assessment of applications for marketing authorization. The main reason given is lack of expertise and human and financial capacity.

Most of these countries procure pharmaceuticals for the public sector from OECS/PPS and have trust in the quality assurance systems of OECS/PPS. However, many respondents were worried about the lack of control related to medicines circulating in the private market.

> ***Response:***
> "As a small country with limited resources it is not feasible for us to establish a full drug registration system and the idea of harmonization is one that we will benefit from."

Respondents from countries that are registering medicines tend to be more skeptical towards a centralized regional registration body. While enhanced exchange of information between medicines regulatory authorities is generally supported, there are also fears that centralized harmonized systems would mainly benefit smaller member states, and that current standards would decrease (1 respondent). Views were expressed that countries would benefit more from strengthened collaboration with the more advanced regulatory authorities of e.g. Argentina, Brazil and Cuba (1 respondent). Table 26 provides an overview of the replies differentiated by countries that do have an operational registration system, and those that do not currently register medicines.

Table 26 - Countries' perceptions regarding harmonization of medicines regulation

Type (and number) of respondent	Priority areas for harmonization	Caveats	Comments
With registration system (5)	Regional body to assess dossiers (3)	Country's sovereignty to be respected (1); Body only to provide recommendations -country decides (2)	What will be the common standard / should requirements be harmonized? What fees to charge?
	Technical support & information sharing (3)		
	Standardization of protocols and processes (1)		
Without registration system (8)	Regional registration body (7)	Country's sovereignty to be respected (1)	CARICOM to support existing agencies (1)
	Quality control supported at regional level (4)		
	Norms for GMP and distribution channel inspections (1)		
	Scheduling of non-controlled medicines (1)		
	Mutual recognition of registration within CARICOM (1)		

In one country respondents categorically stated that they are not interested in harmonization, because of the particularities of their country's geography, health system, and medicines market.

Most officials stressed that any agency that might be established at regional level should be built using one of the already existing structures. Some additional comments to be considered when designing strategies for medicines regulatory harmonization within CARICOM included the following

- How to ensure assessment by the regional body of products only needed in one or two countries?
- Representation of countries in technical committees of the regional body should be provided for.
- Implementation of any strategy eventually chosen should use a phased approach.

During a meeting in Barbados in 2006, 9 CARICOM member states[26] and the Dominican Republic were discussing possibilities for harmonizing medicines regulation. During that meeting the regulatory function of evaluation and assessment of dossiers submitted for registration was identified by all participants to be done at regional level. There could be regional registration, but licensing for use in countries should be under the jurisdiction of individual member states. With regard to other regulatory functions there was general agreement on having regional (and international) guidelines for licensing and inspection of pharmaceutical businesses. A regional body could play a role in inspection and licensing of manufacturers, while regulation of the distribution chain was felt to be a national competency using harmonized guidelines (PAHO/WHO 2006).

The benefit of a regional quality control laboratory was confirmed. However, participants felt that the existing one was currently not performing adequately.

Response:
"I think that attendance at this biannual conference is a must if the region is to begin to understand the importance of drug regulation."

Country involvement in collaborative structures at international level, e.g. the International Conference of Drug Regulatory Authorities (ICDRA) is limited. At the 12th conference (2006) representatives from Barbados, the Dominican Republic, Guyana, Haiti and Trinidad & Tobago participated, at the 13th conference (2008) only Barbados and Saint Lucia were represented.

Some respondents stated that participation in these conferences is expensive and funding cannot easily be obtained. In this context it is noted that participation at the ICDRA conferences is free, and sponsorship can be sought to cover travel and subsistence costs.

A challenge that was not mentioned by participants is the possibility of divergence of existing pharmaceutical markets in terms of products: local production capacity is relatively low, as is the level of export of locally manufactured products within the region. A substantial share of the pharmaceutical products available in public and private sectors are sourced from outside CARICOM. Except for OECS countries' public sector supplies that are sourced through the OECS/PPS it is not known to what degree importers are using the same sources and procure products from the same manufacturers. Consequently there might be a wide variety of multi-source products for the same medicines, increasing the burden of NRAs and a hypothetical regional assessment body. A more detailed pharmaceutical market analysis that could also be performed within the framework of Coordinated Buying (see Annex 3) is recommended.

[26] Bahamas, Barbados, Belize, Guyana, Jamaica, St Lucia, St Vincent, Suriname, and Trinidad & Tobago

7. Strategic options for medicines regulatory harmonization in CARICOM

Regarding the current situation of medicines registration systems CARICOM countries can be divided into three groups:

Group 1: registration is required by law (exception: Guyana) and pharmaceutical products are being assessed by a dedicated authority before marketing approval is granted (Guyana, Haiti, Jamaica, Suriname, Trinidad & Tobago); all countries have at least one local pharmaceutical manufacturing company (18 in total); all countries inspect manufacturing companies for licensing purposes, but only Guyana issues official GMP certificates for export.

Group 2: registration is planned to be instituted in the near future (Bahamas, Barbados); Barbados has 1 pharmaceutical manufacturer and issues GMP certificates for export.

Group 3: there are currently no concrete plans for establishing medicines registration systems (Antigua & Barbuda, Belize, Dominica, Grenada, Montserrat, St Kitts & Nevis, St Lucia, St Vincent & the Grenadines); legislation does provide for the registration of medicines in Grenada and St Vincent; pharmaceutical industry is not present in any of the countries; except for Belize all countries are members of the OECS.

Group 1 countries comprise approximately 91% of the total CARICOM population. For Group 2 and Group 3 countries it is unlikely that registration systems requiring submission of full, country specific product dossiers will attract sufficient industry interest to ensure access to medicines due to the small market sizes[27]. In addition, human capacity constraints to implement these systems are expected to be a major limiting factor.

On the other hand, public health needs to be protected by ensuring that only safe, effective and quality medicines are circulating and made available to patients in **all** countries. This - together with availability of the different therapeutic choices on local markets - could be the overall mission of a CARICOM medicines quality assurance policy and harmonized structure:

> **Mission:** To ensure that in all CARICOM member states adequate pharmaceutical products to address prevalent health conditions are marketed timely, and that these products are of proven safety, efficacy and quality.

The approach taken to achieve this mission would need to address the existing disparities focusing on the one hand on improving efficiency and effectiveness of the more developed medicines regulatory systems in Group 1 countries, and on the other hand instituting new mechanisms for Group 2 and 3 countries.

[27] Reference is made to Suriname with its relatively small market, where for a considerable number of essential medicines no product is registered.

7.1 Harmonization of medicines regulation - strategies[28]

Objective: To ensure safety, efficacy and quality of medicines marketed in the region making best use of limited human and financial resources.

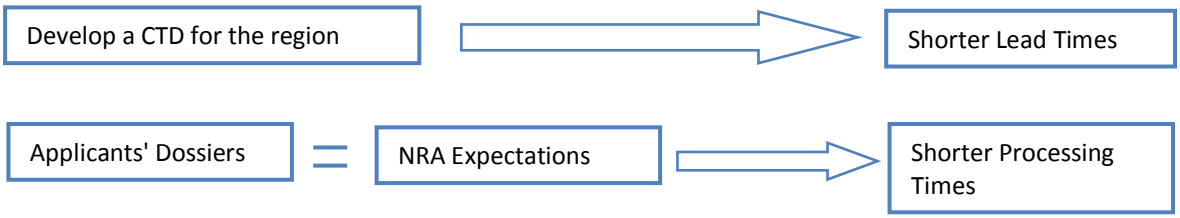
Policy Principles:

- Member states governments commit to support all areas of medicines regulation considering this a critical step for protecting public health.
- Only medicines that have been assessed for safety, efficacy, and quality will be allowed to be marketed.
- The assessment process will as far as possible be based on harmonized requirements and guidelines appropriate for the region.
- Existing guidelines developed by PANDRH will be considered.
- There will be distinct requirements for the assessment of products containing new chemical entities and well known multi-source (generic) products.
- There will be procedures to ensure priority assessment of dossiers dealing with priority medicines for the region (e.g. those for treatment of certain non communicable chronic diseases, or multi-source essential medicines without an adequate number of registered alternatives)
- Joint support will be provided for member states without a registration system to implement licensing requirements using a phased approach
- Existing resources will be shared between member states.

Strategy 1: Harmonized guidelines/requirements for application for registration and assessment of dossiers

CARICOM member states adopt harmonized guidelines in the form of a common technical document (CTD). This will translate into shorter lead times to dossier submission, as manufacturers will no longer have to invest time and resources in preparing dossiers tailored to each country's requirements. It will also reduce processing times through a reduction in subsequent queries, provided that the technical guidelines and requirements are clear and unambiguous (Figure 3).

Figure 3 - Benefits of a Common Technical Document (CTD)

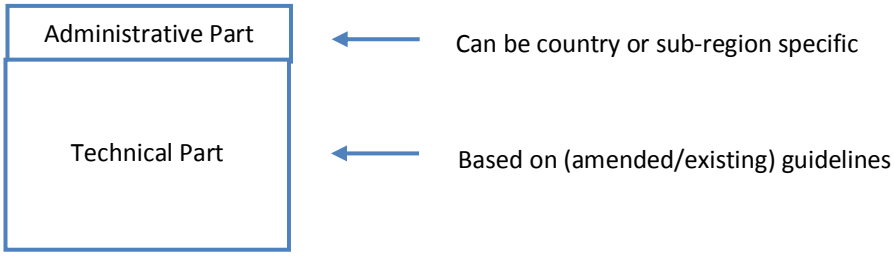


A significant opportunity is the availability of internationally accepted standards and guidelines. It is therefore recommended that member states consider existing guidelines under PANDRH to fast track harmonization and move swiftly to the implementation phase. The draft document prepared by the PANDRH working group on registration could be a starting point (PAHO 2008-3). Also, the current basic requirements for application of registration are already quite similar between Group 1 countries (see Section 4.4).

28 Note: options for strategy implementation will be presented in the section on institutional frameworks

A similar approach to the ICH is recommended, whereby the CTD comprises an administrative part, which can remain country or sub-region specific, and a technical part, which should be common to all countries (Figure 4).

Figure 4 - Recommended basic structure of the CTD



The CTD should clearly specify the different requirements for new products and well known multi-source (generic) products. The requirements for Bioavailability/Bioequivalence studies for the submission of well known multi-source products should be harmonized taking a risk based approach for in vivo studies as suggested in the framework document presented to and approved by the PANDRH conference in November 2008 (PAHO 2008-4).

Taking into account the still very low capacity in CARICOM in post-marketing pharmacovigilance/ surveillance and using as an example the Jamaica guidelines, applications for a new product should only be accepted if the product has been on the market in the manufacturer's or exporting country for a specified period. Exceptions for life-threatening diseases may apply.

Strategy 2: Capacity building NRAs

In view of the varying levels of capacity in dossier evaluation, GMP inspection and laboratory analysis across NRAs, there is a need for a continuous training program for medicines regulators in the region. This should involve participants from different member states with a view to building regional as well as national capacity in various areas of expertise.

Joint training programs coupled with work sharing (joint evaluations, joint inspections etc.) based on agreed guidelines in the region provide a more practical acquisition of knowledge and skills (competency) and will facilitate trust building among participating experts. It especially builds confidence of small NRAs who might otherwise feel marginalized by stronger NRAs in the region.

In this regard, there is need to identify existing capacities within the region including experts in different areas on medicines regulation particularly in evaluation of dossiers, GMP inspection and laboratory analysis. The identified pool of expertise can serve as a resource for training others in the region. In addition, NRAs with capacities in specific areas of expertise can be identified so as to serve as training centers for the region.

Capacity building need also to include organizational management, such as planning & monitoring, standard operating procedures, transparency, and information management (computerization of registers and other regulatory information).

Strategy 3: Capacity building local industry

Currently the local pharmaceutical industry in CARICOM countries as well as in the Dominican Republic does not have the capacity to conduct bioequivalence studies. Requirements for bioequivalence to be established as per Strategy 1 would need to be implemented in a phased approach to assist local industry to adapt to these requirements.

Strategy 4: Reduce duplication of efforts and promote formal cooperation/exchange of information between NRAs

Information sharing and networking can help building capacity and trust, expedite decision making and pave the way for mutual recognition. Currently limited regulatory information is pro-actively shared among the CARICOM member states.

There is need to create a mechanism of making available medicines regulation information for member states' NRAs. This is an important aspect from a trust building perspective in case NRAs work towards mutual recognition of regulatory decisions.

This strategy could extend to formal cooperation agreements with other well established NRAs (e.g. Administración Nacional de Medicamentos, Alimentos y Tecnología Médica/Argentina, Centro estatal para el control de la calidad de los medicamentos/Cuba, US FDA, Health Canada, EMEA, Anvisa/Brasil).

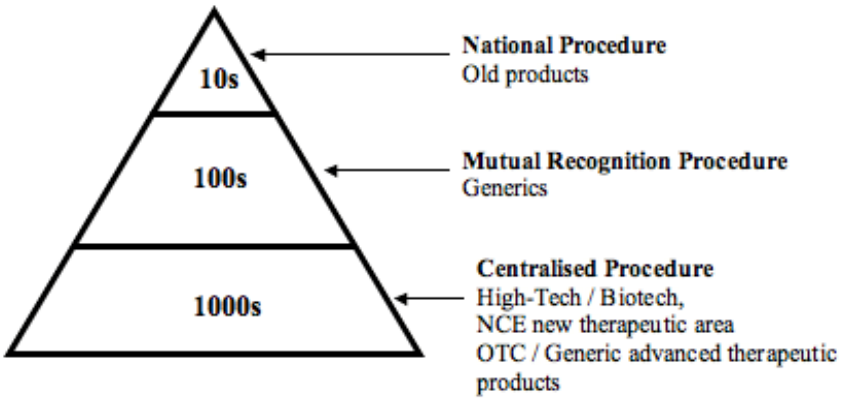
Strategy 5: Resource sharing

Resource sharing makes sense in any environment, but particularly in resource-constrained settings. The question is not so much whether this should be done, but rather how it should be done.

Under EU harmonization, mutual recognition by different regulatory agencies is a result of assessment and recommendations for registration by one of the existing agencies while under the centralized procedure assessment and recommendations for registration are done by EMEA.

The EU centralized procedure started in 1995 with new and complex products. The idea was to identify the best expertise within the region in order to produce the best health protection versus promotion outcomes. Note that other products continue to gain market access through the mutual recognition or national procedure. Overtime, the scope of products subject to the centralized procedure has widened and continues to widen. The EU long-term vision is that the majority of marketing authorizations will be granted through the centralized procedure, followed by the mutual recognition and national procedures (Figure 5).

Figure 5 - EMEA long-term vision



Source: EMEA

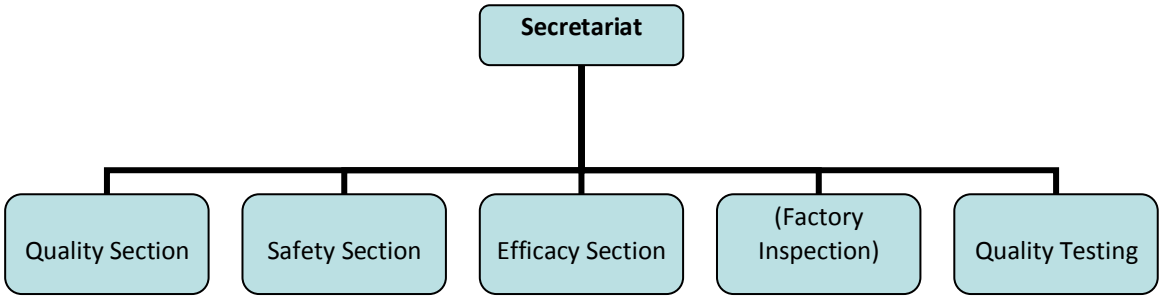
As explained earlier, the centralized procedure relies on member states to perform the product evaluation in order to reach a central decision that will apply across the EU. For this the EMEA Committee for Medicinal Products for Human Use (CMPH) designates two member states, known as the rapporteur and the co-rapporteur, to coordinate the evaluation and prepare the draft report and final reports. The decision to recommend marketing authorization is taken by the CMPH (all member

states have the opportunity to comment) - the Commissioner for Enterprise and Industry is empowered to officially grant the marketing authorization.

This approach works well in an environment characterized by multiple NRAs that have the capacity and expertise to act as rapporteurs and perform the entire evaluation single-handedly. However, a more viable approach in the CARICOM region would be to flip this around and perform joint evaluations with de-centralized decisions. This circumvents issues relating to national sovereignty and has the added advantage of building national capacities. It would also allow CARICOM member states to fast track harmonization in the absence of legal backing.

A WHO-Pre-qualification style approach, which splits the separate parts of the dossier into its constituent parts, namely quality, safety, efficacy, factory inspection and quality testing sections could be considered (Figure 6). It should be noted that at this time none of the existing NRAs do inspect factories outside their countries, and this area of expertise should include getting access to GMP inspection reports of the relevant country NRA for evaluation.

Figure 6 - WHO Pre-qualification model



In principle, this procedure should be aimed at evaluating new chemical entities or highly complex products, which individual NRAs may struggle to evaluate independently. It would make sense, however, to start with simpler multi-source products, whilst establishing the necessary mechanisms and building the necessary competence to evaluate more complex products on an ongoing basis. This approach would also increase the number of multi-source products that receive marketing authorization in **all** CARICOM member states - an important criterion for benefitting from any form of regional public sector procurement cooperation.

For maximum benefit and to move towards a system of mutual recognition, the evaluation should involve representatives of all member countries and efforts should be made to incorporate an element of training through linking joint evaluations with the regional training program outlined above.

Importantly, it should be noted that since this approach relies on the submission of one product registration application centrally, participating states must first agree on a CTD.

Strategy 6: Support licensing of medicines in countries without registration systems

Group 2 and Group 3 countries need yet to start licensing medicines that are circulating in their markets. While through the public procurement agencies and OECS/PPS the list of medicines available in the public sector can be established from contract documents, this is more difficult for those products that are being bought, distributed and sold in the private sector.

As recommended by WHO the first step would be to establish an inventory of products available on the market, which would then be subject to assessment in order of priority (potential risks, public health relevance). At the same time the requirements for licensing for all pharmaceutical products need to be established. It has been suggested that while capacity of the new NRA is being built minimum standards for licensing could be a WHO product certificate together with proof of registration with a minimum number of recognized NRAs (WHO 1999-1).

Cooperation with and support through the more developed NRAs in the region should be provided. In addition, it might not be viable for the small island states that are also OECS members to establish their own licensing authorities.

Strategy 7: Strengthening of quality control capacity

The assessment showed that the existing quality control capacity is not adequate to meet the need of countries' NRAs. This relates to quality control laboratory infrastructure, human and financial resources, management, and other required inputs.

As regulatory inspection activities will be strengthened the number of samples to be subjected to quality control will increase and simultaneously the capacity requirements. The principle of a regional quality control laboratory should be maintained but more support from member states will be needed. It could also be considered to upgrade one of the existing regulatory quality control laboratories in Guyana or Trinidad & Tobago to establish a second regional institution.

Table 27 provides an overview of the 7 strategies, their requirements for implementation, risks and opportunities.

Table 27 - Summary of strategies, requirements, risks and opportunities

Strategy	Rationale	Requirements	Challenges/risks	Opportunities
1. Harmonized guidelines & requirements	step towards mutual recognition; increased efficiency; incentive for applicants; condition for common evaluations	Government& NRA commitment; coordinating body; expert advise; might require amendment of existing regulations where they are very specific	three different languages; little extra capacity at NRAs to fully engage in process of guideline and CTD development	existing guidelines from WHO, PANDRH;
2. Capacity building NRAs	developing regulatory competency in all member states; trust building; upgrading of organizational procedures & information management	needs assessment & training plan; leadership; experts / centers of excellence (can also be outside CARICOM); funding	human resource shortages; reluctance to change	training conducted by different PANDRH working groups; possible interest of WHO/PAHO to provide technical & financial support; WHO self assessment tool for NRAs
3. Capacity building industry	upgrading manufacturing standards to agreed GMP levels; implementing BE requirements	GMP standards adequate for regional realities; GMP inspection capacity of NRA; agreed upon risk based BE requirements	reluctance of industry to invest in required improvements;	existing pharmaceutical umbrella organization; incentives: increased possibilities for export
4. Formal cooperation & information exchange	capacity & trust building; promotes preparation of standard assessment reports	Measures to ensure confidentiality	three different languages; exchange of assessment reports might need legal empowerment	experiences with PANDRH networking; Guyana already accepts registration with Jamaica and Trinidad as a pre-condition for accepting application dossiers
5. Resource sharing / common assessments	capacity & trust building; efficiency; step towards mutual recognition or centralized decision making; use of scarce resources	CTD approved; adequate competency in assessment areas; coordinating body; funding; agreement on applicants' fees; applicants' interest to market in whole of CARICOM	three different languages mean different labeling requirements; lack of confidence in other NRA's assessors; requires legal provision for central application for registration	
6. Product licensing in countries without registration system (Group 2 and 3)	ensure protection of public health	Government commitments; legal provision; extra human and financial resources; support by other NRAs and sub-regional body	human and financial resource constraints	good experience with sub-regional body (OECS/PPS); legally provided for in 3 countries and plans to implement in 2 countries
7. Strengthening quality control capacity	decrease lead times; required to support enhanced inspection activities	human & financial resources; equipment; cooperation of member states		existing regional and national laboratories; activities under the PANDRH GLP working group

7.2 Institutional framework

The Revised Treaty of Chaguaramas (CARICOM 2001) forms a good foundation for harmonization. The objectives of the revised treaty are in line with medicines regulation harmonization objectives i.e. improving standards of living and work, accelerated economic integration of member states, improved trade relations with outside nations, and enhanced international competitiveness.

For a sustainable harmonization effort, it is imperative to have a formal structure that enables effective coordination of issues agreed by member states, where the guiding principle should be to create efficient and effective systems without expensive structures.

In line with international experiences and stakeholders' comments we did not propose as an immediate strategy to establish a centralised authority with the mandate to assess and register pharmaceutical products for the CARICOM region. This might be a long term vision member states could discuss and decide on, but it is not a viable option for the short to medium term.

We believe that the objective of harmonization expressed in the Terms of Reference, i.e. ensure timely availability of safe, effective, quality medicines for the diseases prevalent in the region in the context of human and financial resource constraints, will best be addressed by first concentrating on the development of harmonized guidelines and a CTD, general capacity building, strengthening of quality control laboratories, and implementation of licensing of medicines in those countries where this is currently not done. In a phased approach additional strategies can then be added.

In that line any structure to be established could start small and develop with increasing responsibilities. For the start a small but permanent **Secretariat** is suggested that will be charged with e.g. establishment of relevant databases of guidelines, legislations, experts etc.; communication with countries, relevant regional and international organizations, pharmaceutical industry, and the public; coordination, and organisation of meetings (physical or virtual) as per established business and work plan. The Secretariat should be lead by either an experienced public health/pharmaceutical manager, or respected expert in medicines regulation[29] and supported by administrative staff. The expert should preferably be sourced from a 'neutral' environment (e.g. university) to avoid sensitivities, and any conflict of interest would need to be excluded. NRA staff from countries could be seconded to the Secretariat (rotation principle), and experts from well established NRA's outside CARICOM could be requested to assist the Secretariat with defined assignments.

Due to its regional public health responsibility it is recommended to establish the Secretariat under CARPHA, and that any Caribbean Medicines Agency that might be established at a later state would also be integrated in the CARPHA framework. This arrangement would have the following benefits:

- infrastructure and administrative support services can be shared
- collaboration with other regional health institutions that can support the Secretariat within relevant inputs will be facilitated (e.g. CRDTL, CAREC, CHRC)
- none of the member states would feel disadvantaged (which might happen if the Secretariat would be established under one of the existing NRAs)

In case the establishment of CARPHA would be delayed possible options for provisional housing of the Secretariat include, PAHO/CPC in Barbados or the CRDTL in Jamaica.

[29] Both expertises will be required, but in the start-up phase managerial, organisational and negotiation capacity is priority.

In addition, there is need for an institution that handles medicines licensing for Group 3 countries and might provide support for this activity to Group 2 countries. Although OECS member states felt that OECS/PPS would be well placed to handle sub-regional registration of medicines this is not recommended because of the potential conflict of interest arising from shared responsibilities for procurement activities and medicines regulation. The licensing requirements will, however, have an impact on OECS/PPS activities as after implementation OECS/PPS will only be allowed to establish contracts for pharmaceutical products that have been registered.

Due to the amount of work that will arise from listing products, and the time needed for establishing the legal requirement for registration it is suggested to handle this as a special project. Within the framework of this project the options for establishing a sub-regional regulatory authority for the OECS should be explored. One option could include linking this authority to the Secretariat in charge of regional harmonization activities. In that case this sub-regional authority could serve as a 'pilot' for a CARICOM medicines regulatory agency that might be envisaged.

7.3 Critical steps towards harmonization

Medicines regulatory harmonization needs strong political back up by participating governments, and be convincing and non-threatening for technical agencies and officers in charge of national medicines regulation. Table 28 summarizes the steps that need to be completed, including expected results and responsible actors.

Table 28 - Critical steps for harmonization

	Result	Actor/s
1. Formulate regional quality assurance policy	Common framework for harmonization of medicines regulation	CARICOM Secretariat, in consultation with member states, TAG, PAHO CPC
2. Officially adopt policy	Policy supported by governments	COHSOD or Council of Ministers?
3. Establish Secretariat	Focal point for policy implementation	Member states in collaboration with PAHO/CPC?
4. Develop strategic and annual work plan for policy implementation	Roadmap for harmonization	Secretariat in consultation with country NRAs
5. Secure funding for work plan implementation	Implementation of work plan made possible	Member states and interested cooperating partners

The regional quality assurance policy should include the basic policy principles, main objectives, strategies, and responsible institutions. Policy principles suggested in Section 7.1 could serve as a starting point. The policy should also clearly express the commitment of member states to support implementation of the policy with financial and human resources, and through adaption of national legislation where required.

Possible policy components include:

- CARICOM context
- brief situational analysis of medicines regulation in CARICOM (information provided in this report) and rationale
- underlying principles (e.g. protection of public health; sustainable access; prioritizing for need; sharing of resources, decision making - national or centralized or mixed)
- Overall vision, objective and strategy (this could include whether in the long term a central medicines agency for CARICOM is envisaged)
- Specific objectives and strategies (e.g. registration of medicines; post-marketing surveillance, distribution channel licensing & inspection)
- Implementation, and monitoring and evaluation provisions and responsibilities

The regional quality assurance policy should be integrated into a comprehensive CARICOM regional medicines policy.

It is important that the Secretariat will be established as early as possible in order to have a focal point dedicated to pushing the process forward. For implementation of work plan elements, PAHO could be approached for providing technical assistance as did the WHO in other regions, e.g. in the context of the WHO-AFRO Pilot of the Drug Registration Package (WHO 2007-1, WHO 2008-2)). The overall objective of the project was to increase the capacity of the NRAs through provision of administrative and technical instruments that permit countries to establish their decision-making processes regarding the marketing authorization of pharmaceutical products. Seven African countries participated in finalizing and field testing the WHO Drug Registration Package, which included a common medicines dossier and a standard format for assessment reports. At the conclusion of the pilot, countries met to discuss their experience and concluded that the technical package was satisfactory and that WHO should actively participate in regulatory capacity building in member states with an emphasis on practical training. In addition, it was agreed that WHO should encourage harmonization through regional blocks and sensitize other member states in addition to the seven pilot countries to join the process.

8. Concluding remarks

We would like to end this report by re-stating the key issues related to harmonization of medicines regulation:

Medicines regulation serves the protection and promotion of public health: Regulation is required to ensure that medicines reaching the consumer are safe, effective and of quality. All functions of the regulatory system need to be implemented to achieve this objective (registration of products, licensing of premises, inspection and surveillance, quality control). The right balance between protecting (regulating effectively) and promoting (making necessary medicines available without undue delay) public health needs to be maintained.

Harmonization takes time: For example, the current system in the European Union is the result of more than 40 years of cross-country work. The vision of the current system was already there at the beginning of the process, but could only be realized in very small steps.

Commitment is essential: For a harmonization effort to work it needs commitment at every level i.e. political commitment, economic commitment and a fully functioning Secretariat. One of the reasons that the ICH initiative has been so successful is its powerful Secretariat, combined with research-based industries and strong motivation for driving forward simplification and harmonization. Similarly in the EU the strength of new members' desire to accede to the Union has provided a very powerful political impetus for harmonization.

Legal backing is not absolutely necessary: Legal backing is not necessarily required when the parties involved are committed. The EU effort has legal backing whereas the ICH effort does not, demonstrating that both can work.

Trust building is key: Trust building is the cornerstone of any harmonization effort. Accession of the new EU member states is a good example. New member states were initially reluctant to accept central EMEA decisions, but process transparency helped them overcome this reluctance. Mutual recognition proved more difficult because the decision-making process in individual member states is less transparent, but was addressed through enhanced access to information including opportunities to observe decision-making processes.

ANNEXES

Annex 1. Terms of Reference

REGIONAL ASSESSMENT OF THE REGULATION OF PHARMACEUTICAL PRODUCTS

TERMS OF REFERENCE FOR THE CONSULTANT

A. Background

1. Continuous availability of favorably priced pharmaceuticals is an important aspect of any national health system. Providing quality and low priced pharmaceuticals to the population is a complicated undertaking, ranging from the identification and selection of drugs to the procurement and quality control processes.

2. National registration of pharmaceuticals is a way to manage and monitor the quality of drugs being provided to the population. However, registration of drugs can be cumbersome and requires much information from manufacturers or from countries where the drug is manufactured. It may be difficult to get companies to cooperate fully in the registration process as the cost may outweigh the benefits.

3. The care and treatment of non-communicable chronic diseases ("NCCD"), which are steadily rising in the region, need to be facilitated and ensured. As more and more HIV/AIDS and NCCD patients will require treatment, escalating demand for medicines and related supplies will increasingly strain the capacity of national drug regulatory systems to ensure the timely availability and safety, quality and efficacy of medicines on the Countries' markets. It would, therefore, be beneficial for Caribbean countries to develop consensus on the regional (Caribbean) registration of pharmaceuticals as this will open up a larger market and will be more efficient and effective for the Region.

4. Ministers of Health, at the 10th Council of Human and Social Development (COHSOD), mandated the establishment of a technical advisory group (TAG) to work in collaboration with the Caribbean Regional Negotiating Machinery (CRNM) to access to HIV/AIDS ARVs and other pharmaceuticals to address the region's public health needs. The TAG, at its 1st meeting in Port of Spain, Trinidad, recommended, in addition to the assessment of regional patent systems and legislation, a regional assessment of the regulation of pharmaceutical products. Such an assessment would provide useful information for developing consensus on, and establishing a regional registration system for pharmaceuticals. A regional registration system, within the context of the CARICOM Single Market and Economy (CSME), was seen as one possible approach to make full use of the flexibilities in the Trade Related Intellectual Property Rights (TRIPS).

5. CARICOM, with a grant from the International Development Association, wishes to conduct an Assessment of the Regulation of Pharmaceutical Products in Member States and the Dominican Republic and as such, will engage the services of a consultant (s) to undertake this exercise.

B. OBJECTIVES

The general objectives of the Assessment are:

(a) To make recommendations on the adequacy of the systems in Member States for regulation of the pharmaceutical market to ensure the timely supply of safe, effective and quality medicines

(b) To explore the possibilities and identify the requirements and process for establishing a harmonized, pro-public health regional (Caribbean) drug regulation policy (to include generic drugs) and registration system

(c) To identify mechanisms for the development of regional country coalition for joint procurement strategies

C. SPECIFIC OUTPUTS

The specific outputs of the Assessment are:

(i) An evaluation and analysis of the current status of registration of pharmaceuticals in CARICOM Member States and the Dominican Republic[30]

(ii) Recommendations, with Plan of Action, for establishing a regional (Caribbean) drug regulatory system

D. SCOPE OF WORK

The Consultant will perform all the investigative work and analyses to realize the objectives stated above and in consultation with the Technical Advisory Group (TAG), and PANCAP agree on the work plan for undertaking the assignment. The consultant shall:- conduct a thorough review of all laws, regulations, forms and instructions pertaining to drug regulatory systems in all Member States and the DR, collect new data; inspect and analyze processes and systems; evaluate institutional capacity and provide a qualitative assessment of the data collected. The consultant shall make recommendations and propose strategies for addressing needs and gaps identified at national levels and the technical requirements for the establishment of a regional platform for future decision-making in drug regulation.

The Consultant shall perform the following specific tasks:

(a) Using the WHO Data Collection Tool for Review of National Regulatory Functions, draft a detailed checklist of questions and submit it for approval to the TAG (the approved checklist is hereafter referred to as "the Assessment Instrument").
(b) The Assessment Instrument should seek to capture a sense of drug counterfeiting in the region and the extent to which regulatory systems may facilitate this.
(c) Test and modify the Assessment Instrument in two agreed on countries
(d) Conduct interviews with the relevant persons and agencies at the country and regional levels. The CARICOM Secretariat will provide a list of the persons/agencies to be interviewed
(e) Document the guidelines and regulations governing OTCs
(f) Determine the categories and definitions used in-country, the prescriptions required, OTCs, cosmetics, the essential medicine lists, generics, disposables, otodontologica, diagnostic reagents, labeling and dispensing requirements
(g) Identify the necessity for training programs and the need for continuing education
(h) Make a presentation of the draft report to the TAG and PANCAP, and in light of ensuing discussions, make revisions to the draft report.
(i) Prepare and submit a Power Point presentation on the final report to the Council for Human and Social Development at the request of the TAG

[30] The Dominican Republic has been specifically identified as a beneficiary of this element of the PANCAP/World Bank Grant Agreement

E. DELIVERABLES AND TIME FRAME

(a) REPORTS

(i) Work Plan and a revised assessment tool
(ii) An Interim report
(iii) A draft final report which will take on board recommendations from the TAG
(iv) A Final Report with a Power Point presentation of the findings and recommendations

All reports and presentation shall be submitted in hard and electronic copies and disseminated as follows:

i. The TAG for TRIPS – Access to Pharmaceuticals
ii. PANCAP/ CARICOM Secretariat
iii. The Caribbean Regional Negotiating Machinery
iv. The Ministry of Health, the Dominican Republic

(b) TIME SCHEDULES

The Consultant shall submit to the Project Authority:

(i) A Work Plan and Assessment Instrument within **one month** of signing of this Agreement. Any changes in the Assessment Instrument shall be made within **one week** of receipt of comments and recommendations from the TAG.

(ii) The consultant shall ensure that data collection for the assessment shall start not later than **one month** after any such changes have been made. In the event there are no changes, the consultant shall be so notified by the TAG and work on the data collection for the full assessment shall start not later than **one month** from the date of notification.

(iii) The consultant shall submit the draft report within **three weeks** of completion of the data collection. The TAG will be required to submit to the consultant, written comments within **two weeks** of the receipt of the draft report.

(iv) The consultant shall submit, within **3 weeks** after receipt of written comments from the TAG, the final report which incorporates the adjustments recommended by the TAG and PANCAP

F. PROFILE OF THE CONSULTANT

The consultant/consulting firm should have expertise and experience in the area of health, specifically in the area of pharmaceuticals and drug registration procedures. The consultant should also be familiar with the Caribbean Region.

Annex 2. Main pharmaceutical legislation

Country	Legislation
Antigua and Barbuda	Antibiotics & Therapeutics Substances Act of 1951
	The Pharmacy Act of 1995
	The Caribbean Regional Drug Testing Laboratory Act of 1979
	The Misuse of Drugs Act 1974
Bahamas *	The Pharmacy Act of 1962 (rev 1998)
	The Penicillin Act of 1948 (rev 5 of 1987)
	The Health Professions Act of 1998 (rev 79/2001
	The Dangerous Drugs Act of 2000
Barbados	The Drug Service Act of 1991
	The Food and Drug Adulteration Act of 1933 (rev 168/1967
	The Pharmacy Act of 1986 (rev 1992-31)
	The Therapeutics Substances Act of 1950 (rev 168/1967)
Belize	The Antibiotics Act of 1948 (with amendments in force as 31/12/2000)
	The Chemists and Druggists Act of 1940 (with amendments in force as 31/12/2000)
	The Food and Drugs Act of 1953 (with amendments in force as 31/12/2000)
	The Misuse of Drugs Act (revised edition 2000)
Dominica	The Pharmacist Professions **Bill** of 2007
	The Medical Act of 1938
	The Dangerous Drugs Act of 1938
Dominican Republic	Medicines Regulations (Dec No 246-06) of 2006 (rev2006)
	Ley General De Salud de 2002 (Ley No 42-01)
	Ley No 22-06 (Amendment to Ley 42-01 making falsifications a criminal offence)
	Ley No 87-01 (El Sistema Dominicano de Seguridad Social)
Grenada	The Pharmacy Act of 1987 (plus amendments of 1992 and 1995)
	The Medicinal Products (Regulations) Act (1995)
	The Drug Abuse (Prevention and Control) Act (1992)
	The Food and Drugs Law (1986)
Guyana	The Antibiotics Act of 1952 (rev 3/1998)
	The Food and Drugs Act of 1971 (rev 1998)
	The Narcotic Drugs and Psychotropic Substances (Control) Act of 1988
	The Pharmacy and Poisons Ordinance Act of 1956
	The Pharmacy Practitioners Act of 2003
Haiti	The Medicines and Pharmaceutical Products Act of 1948
	Law of 1955
Jamaica	The Dangerous Drugs Act of 1948 (rev 21/1987)
	The Dangerous Drugs Act Regulations of 1948 (rev 21/58)
	Food and Drugs Act of 1975 (rev 7/1996)
	Food and Drugs Act Regulations of 1975 (rev 55/2003)
	The Pharmacy Act of 1975 (rev 6/1996)
Montserrat	none according to respondents (dangerous drugs Act is available)
St Kitts and Nevis	The Medical Act of 1938
	The Drug (Prevention and Misuse) Act of 1986
	The Pharmacy **Bill** of 2000
St Lucia	The Pharmacy Act of 2003
	Pharmacy Forms and Fees Regulations of 2006
	Pharmacy Regulations of 2007
	The Drug (Prevention of Misuse) Act of 1988
St Vincent & the Grenadines	The Pharmacy Act of 2002
	The Chemical Act (precursor chemicals) of 2003
	The Penicillin (control) Regulation of 1947
	The Sulphonamide Regulation of 1949 (rev 1991)
	The Drug (Prevention of Misuse) Act and Dangerous Drug Regulations of 1988 (rev 2008)

Country	Legislation
Suriname	**Verordening van 8 mei 1896** regelende de uitoefening der artsenijbereidkunst in Suriname (GB no. 26) zoals zij luidt na de daarin aangebrachte wijzigingen en aanvulling bij de landsverordening van GB no. 78, GB no. 26, GB 1929 no. 33 en GB no. 37.GB 1960 no. 77
	Landsverordening van 17 maart 1939, regelende de voorwaarden ter verkrijging van de bevoegdheid tot uitoefening der geneeskundige beroepen en de uitoefening van die beroepen (GB no. 12) zoals zij luidt na de daarin aangebrachte wijzigingen bij Landsverordeningen van GB no. 103, GB no. 139 en GB no. 98
	Landsverordening van 4 januari 1973 tot nadere wijziging van de Verordening van 8 mei 1896, regelende de uitoefening van de artsenijbereidkunst in Suriname (GB 1896 no. 26, GB 1960 no. 77) GB 1973 no. 1
	Regulation related to registration commission Landsbesluit van 16 oktober 1973 ter uitvoering van de artikelen 3c, 3d en 3^{e} van de Verordening van 8 mei 1896, regelende uitoefening der artsenijbereidkunst in Suriname (GB 1896 no. 26, GB 1960 no. 77, GB 1973 no. 1) Besluit Verpakte Geneesmiddelen GB 1973 no. 155. In werking treden bij GB 1975 no. 3 en 85 en 134 (opgeschort).
	Decreet van 4 februari 1983, houdende instelling van het Bedrijf Geneesmiddelen Voorziening Suriname SB 1983 no. 20. (ACT)
	Staatsbesluit van 4 september 1986, tot wijziging van het Besluit Verpakte Geneesmiddelen (GB 1973 no. 155) SB 1986 no. 56
Trinidad & Tobago	The Food and Drugs Act 1965 including regulations
	The Food and Drugs (Amendment) Act 2005 The Antibiotics Act of 1988 (including related orders and schedules)
	The Pharmacy Board Act of 1961 (including regulations and schedules)
	The Pharmacy Board (Amendment) Act of 2006
	The Dangerous Drugs Act of 1991

*: The Bahamas have a new Pharmacy Act 2009

Annex 3. Joint regional procurement strategies

Joint regional procurement strategies aim at reducing product cost and increasing procurement efficiency. Four basic models can be distinguished that are documented in Table 1:

Table 1 - Models for joint regional procurement strategies[31]

	1 - Informed Buying	2 - Coordinated Informed Buying	3 - Group Contracting	4 - Central Contracting & Purchasing (e.g. OECS/PPS)
Description	Price & supplier information are shared	Same as 1 plus joint market research	Joint tendering; individual contracting & procurement	Joint tendering & single contracting by agency; central management of purchases
Roles & Responsibilities Regional Level	Establish clearinghouse for price & supplier information	Provide forum for harmonization of information requirements; market research mechanism	Provide structure for countries for implementing joint negotiations & supplier selection	Establish agency to manage tenders & contracts
Roles & Responsibilities Country Level	Share procurement price & supplier information	Share agreed information; resources for market research	Provide reliable quantification; timely supplier payment; feedback on supplier performance & product quality	Provide reliable quantification; participation in tender committee; timely payment; feedback product quality

In the CARICOM region two mechanisms for collaboration in procurement exist, the pooled procurement for OECS countries by OECS/PPS (central contracting & purchasing), and the Caribbean Regional Network of Procurement and Supply Management Agencies (CARIPROSUM).

OECS/PPS was established in 1986 as Eastern Caribbean Drug Service by an agreement signed by all 9 OECS member states. The agreement clearly defines the governing arrangements, legal status, functions, and the role of the Eastern Caribbean Central Bank. OECS/PPS serves a population of approximately 607,000 (2007 figures).

Currently OECS/PPS is procuring around 700 different items (medicines, medical supplies and consumables) from a sub-regional essential medicines list through restricted international tender. Fifty-one suppliers are registered as pre-qualified for the period 2008-2010. Out of those 32 submitted bids, and 19 were contracted. Currently the 2 most important suppliers are distributors located in Barbados and Trinidad & Tobago.

OECS/PPS operations are financed through a mark-up on contract prices (11% in 2007-2008). During the same financial year purchase orders in the value of EC$ 15.8 million (app. USD 6 million) were processed.

OECS member states do not currently register medicines. The management of the pooled procurement is therefore not as challenging as it might be if it had to consider registration status of products in participating countries. Harmonized medicines registration plays an important role in pooled procurement as the full benefits can only be realized when an adequate number of products of the same medicine are registered across multiple countries. Without harmonization, highly

[31] Adapted from "Regional pooled procurement of drugs - Evaluation of Programs" (Center for Pharmaceutical Management 2002)

variable lead times and processing times would create barriers to procurement planning and implementation, and prices might remain high.

CARIPROSUM is a regional network of procurement agencies coordinated by PAHO/CPC in Barbados. The network was established in 2004 with the objective to "promote the continuous availability of affordable pharmaceutical products meeting standards in safety, quality and efficacy, for Caribbean public health program and services, through inter-country and regional cooperation". Meetings are held 1 to 2 times per year. So far the focus has been on development of standard documents and common indicators for monitoring performance of public sector procurement agencies in the wider context of Good Procurement Practices (PAHO 2008-5).

Some CARICOM countries participate in the **PAHO Regional Revolving Fund for Strategic Public Health Supplies (PAHO Strategic Fund)**. The PAHO Strategic Fund was established in 2000. The fund includes in its mandate a type of pooled procurement mechanism for strategic public health supplies for PAHO member countries. Participating countries are also technically supported in procurement and supply management. By May 2009, 20 countries from the region of the Americas had joined the PAHO Strategic Fund, including Barbados, Belize, Dominican Republic, Haiti, Jamaica, Suriname, and Trinidad & Tobago from the study countries (http://new.paho.org). Membership is established by signature of an agreement between the member state and PAHO. The PAHO Strategic Fund can also be used for the procurement of health supplies using Global Fund grants. In that case a Memorandum of Understanding will be signed between PAHO, the respective government and the Principal Recipient of the Global Fund grant (PAHO 2006).

OECS/PPS, the non-OECS CARICOM countries and the Dominican Republic participate in CARIPROSUM. The network is appreciated as a platform for information sharing, development of uniform procurement indicators, and identification of best practice. However, respondents felt that CARIPROSUM lacks a clear mandate and driving force, and therefore work done during the meetings tends not to have much impact on procurement practices in countries.

Non- OECS procurement agencies that were interviewed were somehow skeptical about a CARICOM wide pooled procurement mechanism for essential medicines and related supplies. Reasons given include differences in essential medicines lists, regulatory requirements, patent status, generic medicine policies, currencies and language. On the other hand, a more organized/official way of cooperation and information sharing between procurement agencies was considered beneficial.

In 1999, OECS/PPS facilitated a 'trial' tender, pooling requirements for 25 items for OECS countries, Barbados, Guyana, Jamaica, and Trinidad & Tobago. Twelve potential regional and international suppliers were approached, and 9 submitted quotations (not always for all 25 products). Subsequent analysis did not provide evidence that this pooled procurement would result in significant cost savings for participating countries, even though administrative costs related to pooled procurement had not yet been considered (Burnett F 1999). In that context the findings of a recent study assessing strategies to reduce the costs of anti-retrovirals are of interest:

Global Strategies to reduce the price of anti-retroviral medicines (Waning B et al 2009):

Findings For 19 of 24 ARV dosage forms, we detected no association between price and volume purchased. For the other five ARVs, high-volume purchases were 4–21% less expensive than medium- or low-volume purchases. Nine of 13 generic ARVs were priced 6–36% lower when purchased under the Clinton Foundation HIV/AIDS Initiative (CHAI). Fifteen of 18 branded ARVs were priced 23–498% higher for differentially priced purchases compared with non-CHAI generic purchases. However, two branded, differentially priced ARVs were priced 63% and 73% lower, respectively, than generic non-CHAI equivalents.
Conclusion Large purchase volumes did not necessarily result in lower ARV prices. Although current plans for pooled procurement will further increase purchase volumes, savings are uncertain and should be balanced against programmatic costs. Third-party negotiation by CHAI resulted in lower generic ARV prices. Generics were less expensive than differentially priced branded ARVs, except where little generic competition exists. Alternative strategies for reducing ARV prices, such as streamlining financial systems, improving demand forecasting and removing barriers to generics, should be explored.

Against this background it is recommended that CARICOM countries first work towards formal cooperation along the lines of **Informed Coordinated Buying**. This would require the following:

- formal agreement among member states on the objectives, the type of information to be shared, confidentiality arrangements required, commitment to make information available
- setting up a coordinating body (could be in the framework of CARIPROSUM with the same members, but would need a formal mandate and adequate resources, i.e. a permanent secretariat)

While detailed information requirements would need to be agreed upon by member states, some options are being suggested Table 2.

Table 2 - Informed Coordinated Buying

Type of Information	Rationale
Essential medicines lists (EML)	Establish database of common essential medicines
List of products registered amongst those on the EML	Basis for increasing number of registered alternatives for essential medicines where required;
Information about regular suppliers (company, prequalification status, experiences)	Broadening supplier base of individual countries
Products where sourcing is difficult (limited supplier base; limited quantities)	Market research on alternative suppliers; could be test case for group contracting
Procurement information including quotations, contracted price & quantities, supplier /manufacturer, lead times, quantities contracted etc.	Price benchmarking against international prices, PAHO Strategic Fund etc. Basis for negotiation

Annex 4. List of respondents and other stakeholders consulted

Country	Name	Position	Comments
Antigua & Barbuda	Mr. Casford F.F. King	Chief Pharmacist / Ministry of Health	
Bahamas	Ms Vivian Lockhart	Director National Drug Agency	by phone and e-mail
	Dr Marvin Smith	Deputy Director National Drug Agency	by e-mail
Barbados	Mrs. Maryam Hinds	Director, Barbados Drug Service	
	Mr. David Crawford	Assistant Director, Barbados Drug Service	
	Mrs. Pamela Payne-Wilson	Assistant Director, Barbados Drug Service	
	Dr. Adriana Ivama	Medicines, Vaccines and Health Technologies Sub Regional Advisor / PAHO/CPC	
	Mr. Leroy Williams	Senior Accountant, Barbados Drug Service	
	Ms. Delores Mascoll	Supplies & Inventory Officer, Barbados Drug Service	
	Ms. Audrey Francis	Supplies & Inventory Officer, Barbados Drug Service	
	Mr. Peter Bourne	CEO, Carlisle Laboratories Limited	
	Mr. Bassil Scantlebury	President, Caribbean Association of Pharmacists	
	Dr. Joy St. John	Chief Medical Officer, Ministry of Health	
	Mrs. Ersie Chase	Chief Dispenser/Senior Pharmacist, Barbados Drug Service	
Belize	Ms Sharon Anderson	Chief Pharmacist / Ministry of Health	
Dominica	Mr. Errol Thomas	Chief Pharmacist / Ministry of Health	
	Mr. Orin Jolly	Director Jolly's Pharmacy	
Dominican Republic	Lic. María Villa de Pina	Sub Secretaria de Salud / Director General Drogas y Farmacia	
	Lic. Pía Veras	Dir. Departamento de registro de medicamentos y productos farmacéuticos	
	Lic. Rosangel González	Dir. Departamento de establecimiento de farmacéuticos	
	Lic. Rayza Almanzar	Dir. Departamento de vigilancia sanitaria	
	Escarlen Heredia	Comité técnica de medicamentos	

Country	Name	Position	Comments
	Lic. Dalia Castillo	NPO PAHO Office	
	Lic. Karen Tamariz	Asociación Dominicana Farmacéutica	
Grenada	Mr. Anthony Kester Cyrus	Pharmacy Inspector / Ministry of Health	
	Ms Benedict Newton	Chief Pharmacist / Ministry of Health	
Guyana	Dr Leslie Ramsammy	Minister of Health	
	Dr. Shameo Persaud	Chief Medical Officer / Ministry of Health & Chairman, Pharmacy & Poisons Control Board	
	Ms Yvette Irving	Director Standards and Technical Services / Ministry of Health	
	Ms Marilyn Collins	Director Food and Drugs Department / Ministry of Health	
	Mr Kameene Sepaul	Warehouse manager, Materials Management Unit / Ministry of Health	
	Ms Colette Gouveia	Chief Pharmacist / Ministry of Health	
	Mr Malcom Watkins	Procurement Manager, Materials Management Unit / Ministry of Health	
	Dr. Ranjisinghi Ramroop	Chairman/Managing Director / New Guyana Pharmaceutical Company	
	Mr Carl Bacchus	Director, Pharmagen Enterprises & Chairman, Pharmacy Council	
	Mr Geer	Inspector Pharmacy and Poisons Board / Ministry of Health	
	Mr Lee van de Santos	Senior Technical Support Advisor	
	Ms Beverly Reynolds	Program Manager / CARICOM Secretariat	
	Ms Rhonda Wilson	CARICOM Secretariat	
	Mr Edward Emmanuel	PANCAP Coordinating Unit	
	Mr Willys Ramirez Diaz	Ass Secretary General CARIFORUM	
Haiti	Ms Magalie Rosemond	Directeur Direction de control pharmaceutique / Ministry of Health	has resigned
	Ms Gloria Garrido	Act. PAHO/WHO representative	
	Dr Michel Klopfenstein	Pharmacist PAHO country office	by e-mail
	Ms Flaurine Joseph	Directeur Direction de control pharmaceutique / Ministry of Health	new Director; interviewed by A Ivama & S Laroche (PAHO/CPC & PAHO/Haiti)

Country	Name	Position	Comments
	Ms Martine Menard	DPM/MT Ministry of Health Haiti	interviewed by A Ivama & S Laroche (PAHO/CPC & PAHO/Haiti)
	Ms Jisette Letelier	DPM/MT Ministry of Health Haiti	interviewed by A Ivama & S Laroche (PAHO/CPC & PAHO/Haiti)
	Ms Judith R Roche	DPM/MT Ministry of Health Haiti	interviewed by A Ivama & S Laroche (PAHO/CPC & PAHO/Haiti)
	Mr Stanlety Merard	DPM/MT Ministry of Health Haiti	interviewed by A Ivama & S Laroche (PAHO/CPC & PAHO/Haiti)
Jamaica	Mrs. Princess Osbourne	Director, Standards and Regulations, Ministry of Health	
	Mrs. Valerie Germain	Act Director, Pharmaceutical & Regulatory Affairs, Ministry of Health	
	Dr. Lucette Cargill	Government Chemist & Director, Caribbean Regional Drug Testing Laboratory	
	Mrs. Marcia Chin See	Director Purchasing, Health Corporation Limited	
	Mrs. Verna Edwards	Chief Dangerous Drug Inspector & President, Pharmaceutical Society of Jamaica	
	Mr. Radcliffe Goulbourne	Deputy Registrar, Pharmacy Council of Jamaica	
Montserrat	Ms Ingrid Archer	Pharmacist Glendon Hospital	by telephone and e-mail
	Ms Rona Greenaway	Chief Pharmacist	by telephone and e-mail
Saint Lucia	Mr Francis Burnett	Managing Director OECS/PPS	
	Ms Dona Daniel	Chief Pharmacist / Ministry of Health	
	Ms Alison Jean	Medical Supplies Officer Central Procurement Unit / Ministry of Health	
St Kitts and Nevis	Ms Joann Ince-Jack	Chief Pharmacist / Ministry of Health	
St Vincent and the Grenadines	Mr Erickson France	Supplies Manager, Central Drug Procurement Unit / Ministry of Health	by telephone and e-mail
	Mr Robert Felix	Hospital Pharmacist	by telephone and e-mail
Suriname	Ms Miriam Naarendorp	Pharmacy Policy Coordinator / Ministry of Health	
	Ms Norma de Vries-Smith	Head Pharmaceutical Inspection / Ministry of Health	

Country	Name	Position	Comments
	Mr John Hasrath	Act. Chairperson, Drug Registration Committee	
	Ms Ingrid M May	Director Drug Supply Company Suriname	
	Ms Jolanda Pronck	Legal Consultant	
	Mr Rob Verhage	Pharmaceutical Consultant and Member Drug Registration Committee	
Trinidad & Tobago	Ms Cheryl Scott-Alvarez	Ag Chief Chemist and Director Food & Drugs Division / Ministry of Health	
	Ms Joan Bernadine	Drug Analyst Food & Drugs Laboratory / Ministry of Health	
	Mr Deoraj Ramcharan	Food and Drugs Inspector, Secretary Drug Advisory Committee / Ministry of Health	
	Ms Junia Walcott	Ag Chief Pharmacist / Ministry of Health	
	Ms Lynette John	Chief Pharmacist / Ministry of Health	by e-mail
	Mr Leo Alleyne	Director, International Cooperation / Ministry of Health	
	Dr Violet Forsylt Duke	HIV/AIDS Coordinator / Ministry of Health	
	Mr Nicholas George	Senior Pharmacist/Medical Supplies Coordinator / NIPDEC	
	Mr Roshan Harikaran	Country analyst / Clinton Foundation	
	Ms Bhabie Roopchand	Legal adviser / Ministry of Health	

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