
Lilit Ghazaryan
Scientific Center of Drug and Medical Technology Expertise

[Logos of USAID, SIAPS, World Health Organization, Stop TB Partnership]
MEDICINES REGULATION IN ARMENIA

Regulatory and quality challenges for TB drugs in small markets
Republic of Armenia

Territory:
29,74 thousand square kilometers

Population:
3,100,236 (as of 2011)
REGULATION GOAL

to implement national drug policy and ensure the

- EFFICACY
- SAFETY
- QUALITY
- ACCESS

of medicinal products
ORGANIZATIONAL STRUCTURE OF Drug Regulatory Authority DRA

Established in 1992

Ministry of Health

Advisory committee

DIRECTOR

Deputy director

Inspection department

Import -Export control department

Narcotics and psychotropic substances control department

Deputy director

Registration department

Pharmacovigilance department

Information department

Deputy director

Finance and Economy department

General affairs department

Administration and human resource department

QC Laboratory

Information department

QC Laboratory
WHO: Membership in International Drug Monitoring Program (2001),


Medicine Regulatory Authorities: Intergovernmental committee on Standardization and control of medicinal products in CIS Countries (2002)

PIC/S: Application for pre accession (2011)
LEGAL BASIS OF REGULATION

- Law on Drugs (1998)
- Law on Licensing (2001)
- Law on Advertisement (1996)
COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

7 APRIL 2011 WORLD HEALTH DAY
Quality requirement

COMPLIANCE TO PHARMACOPOEIA MONOGRAPHS

The product should comply with quality standards described by the officially used current pharmacopoeias in Armenia.

- European Pharmacopoeia
- British Pharmacopoeia
- International Pharmacopoeia
- United States Pharmacopoeia
- Russian Pharmacopoeia
- German Homeopathic Pharmacopoeia
A medicinal product may only be placed on the market when registration certificate has been issued.

**LEGISLATION**

- LAW ON DRUGS/1998
- GOVERNMENT DECREE 347/2001
- MoH order 123/2006

**REGISTRATION LEGISLATION REQUIREMENTS RESPONSIBLE BODIES**

- Type of procedures for different products
- Format and content of dossiers
- Packaging and labeling
- Approval and rejection criteria
- Variations and postapproval changes submission

- Drug Agency
- Ministry of Health
Risk assessment

Application

USAID
SIAPS

The procedure for evaluating dossiers must be completed within maximum 180 days.
Number of registered medicines, 2002-2012
Total number 4450 (as of December 2012)

Armenia-288 (6%)
EU-2346 (53%)
CIS-752 (17%)

Number of registration refusals from 2002-2012
Lack of registered medicinal products

CHALLENGES

Might pose a problem in case the government switches to the state-funded procurement

REGISTRATION IS NOT MANDATORY FOR MEDICINAL PRODUCTS IMPORTED/ARRIVING AS HUMANITARIAN AID
Registered medicinal products Containing Isoniazid, 2002-2010

ISONIAZID, 300mg, tablets

Sanavita
Germany

Sanitas
Lithuania

Darou Pakhch
Iran

Darnitsia JSC
Ukraine

Fatol Arzneimittel
Germany

Verofarm
(Belgorod)
Russia

Not registered since 2010
Registered anti-TB medicinal products

Total number - 60

Ethambutol /2/
Pyrazinamide /2/
Rifampicin /4/
Streptomycin /2/
Isoniazid, pyridoxine hydrochloride/1/

Amikacin /4/
Capreomycin /1/
Cycloserine /1/
Ciprofloxacin oral /20/
Kanamycin /2/
Levofloxacin /7/
Moxifloxacin /1/
Ofloxacin /12/
Prothionamide /1/

Non-registered anti TB medicinal products

Ethionamide
P-aminosalicylic acid
Isoniazid
Lack of registered medicinal products

Absence of Dossier and Insufficient Quality Control

Registration is not mandatory for medicinal products imported/arriving as humanitarian aid.

CHALLENGES
REGULATION OF MEDICINAL PRODUCTS

IMPORT CONTROL

LEGISLATION

- LAW ON DRUGS/1998
- GOVERNMENT DECREE 581/2000

REQUIREMENTS

- Contract, invoice and batch certificate
- Compliance with the registration samples
- Minimum one year (or 2/3 if the shelf life is less than one year) of remaining expiry date at the time of importation

RESPONSIBLE BODY

- Ministry of Health
- Drug Agency
The procedure for import authorization must be completed within a maximum of 10 days.
Import rejection from 2002-2012

Rifampicin -2009
A computerized information system is established, which includes all product and shipment details:

- Date of importation
- Name and address of the importer
- Name and address of the supplier
- Medicines name, dosage form and strength, manufacturer
- Unit price
- Quantity
- Batch number
- Expiry date
<table>
<thead>
<tr>
<th>Name of the Drug</th>
<th>Dosage Form</th>
<th>Dosage and Form of Production</th>
<th>Manufacterer</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>300mg (672)</td>
<td>Swiciera</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>100mg (1000)</td>
<td>Swiciera</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>100mg (672)</td>
<td>Swiciera</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>300mg (672)</td>
<td>Cadila</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>300mg (100)</td>
<td>Lupin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>100mg (100)</td>
<td>Lupin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>300mg (672)</td>
<td>Macleod</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td>tablets</td>
<td>100mg (100)</td>
<td>Macleod</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not all Imported anti-TB medicinal products are prequalified*
<table>
<thead>
<tr>
<th>Medicinal Product</th>
<th>Dosage</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Packaging Details</th>
<th>Prequalification Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Isoniazid + Pyrazinamide</strong> + Rifampicin</td>
<td>50mg + 150mg + 60mg</td>
<td>Macleods Pharmaceuticals Limited</td>
<td>Kochigam, Daman, India</td>
<td>Triple laminated LDPE/PET/AL bag further packed in HDPE container 1000, PVC/PVDC/Alu blister 10, 25, Alu/Alu strip 5 x 10, 10 x 10, 20 x 3, 14 x 6, 5 x 20, 6 x 14</td>
<td>Feb 2014</td>
</tr>
<tr>
<td><strong>Isoniazid + Pyrazinamide</strong> + Rifampicin</td>
<td>50mg + 150mg + 60mg</td>
<td>Lupin Ltd</td>
<td>Chiklathana, Aurangabad, India, Bari Brahmana, Jamnagar (Guj), India</td>
<td>Alu/PVC/PVDC blister 15 x 6, 14 x 6</td>
<td>Jul 2012</td>
</tr>
<tr>
<td><strong>Isoniazid + Rifampicin</strong></td>
<td>75mg + 150mg</td>
<td>Lupin Ltd</td>
<td>Aurangabad, India, Bari Brahmana, Chiklathana</td>
<td>Blister 15, HDPE bottle 100, 500, 1000</td>
<td>Feb 2015</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 300mg</td>
<td>Mieco Labs Limited</td>
<td>Hosur, Tamilnadu, India</td>
<td>PE bag further packed in HDPE container 1000</td>
<td>Nov 2010</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 100mg</td>
<td>Mieco Labs Limited</td>
<td>Hosur, Tamilnadu, India</td>
<td>PE bag further packed in HDPE container 1000</td>
<td>Nov 2010</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 100mg</td>
<td>Macleods Pharmaceuticals Limited</td>
<td>Kachelgam, Daman, India</td>
<td>LDPE bag further packed in HDPE container 1000, PVC/PVDC/Alu blister 10, 28</td>
<td>Apr 2008</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 100mg</td>
<td>S.C. Antibiotics S.A</td>
<td>Iasi, Romania</td>
<td>PVC/Alu blisters 3x10, 150x10</td>
<td>Feb 2010</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 300mg</td>
<td>Macleods Pharmaceuticals Limited</td>
<td>Kachelgam, Daman, India</td>
<td>LDPE bag further packed in HDPE container 1000, PVC/PVDC/Alu blister 10, 28</td>
<td>Apr 2008</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 100mg</td>
<td>Lupin Ltd</td>
<td>Chiklathana, Aurangabad, India</td>
<td>AIPVC/PVDC blister 100, HDPE bottle 100, 1000</td>
<td>Oct 2012</td>
</tr>
<tr>
<td><strong>Isoniazid</strong></td>
<td>Tablets 100mg</td>
<td>S.C. Antibiotics S.A</td>
<td>Iasi, Romania</td>
<td>PVC/Alu blisters 2x10, 150x10</td>
<td>Feb 2013</td>
</tr>
</tbody>
</table>
REGULATION OF MEDICINAL PRODUCTS

INSPECTION

LEGISLATION

☐ LAW ON DRUGS/1998
☐ GOVERNMENT DECREE 867/2002

REQUIREMENTS

Compliance with
- Good Manufacturing Practice
- Good Distribution Practice
- Good Storage Practice

RESPONSIBLE BODY

- Drug Agency
- Ministry of Health
Deviations found during inspection

- Inappropriate storage conditions: temperature, humidity, transportation
- Dispensing prescription-only medicines without prescription
- Falsification

Counterfeit Rocephin

Registered

Counterfeit
Survey of the quality of anti-TB medicines circulating in selected NIS collected samples

Compliance with specifications
Number of non-compliant samples per product in each country

Storage conditions for Anti-TB medicines at the facility level
REGULATION OF MEDICINAL PRODUCTS

PHARMACOVIGILANCE

LEGISLATION

- LAW ON DRUGS/1998

REQUIREMENTS

- ADR Reporting is obligatory for industry and voluntary for health professionals
- PSUR

RESPONSIBLE BODY

- Drug Agency
- Ministry of Health
**PHARMACOVIGILANCE**

PSUR shall be submitted:
- every 6 months during the first two years
- once a year for the following two years
- Thereafter
  - at five –year intervals or
  - immediately upon request

Spontaneous reporting system:

- Reporting form
  - Easy to fill out
  - Available on-line

www.pharm.am
Average number of ADR reports received from health professionals from 2001-2012

22 Anti TB medicinal products
Assessments of Anti TB medicine regulatory system

THE GLOBAL DRUG FACILITY
MISSION REPORT
ARMENIA
Direct Procurement Monitoring Mission
Andre Zagorski
Archil Salakaia
11-15 May 2009

MOH ARMENIA
Report on Assessment of existing legislation regulating antibiotic prescription and dispensing practices and their implementation, rational use of anti-TB medicines and adverse reaction monitoring system 2010-2011
National TB Program, Scientific Center of Drug and Medical Technology Expertise

THE GLOBAL DRUG FACILITY
MISSION REPORT
ARMENIA
DP monitoring mission
Andre Zagorski
June 14-19, 2010

WORLD HEALTH ORGANISATION
Mission Report
Extensive Review of TB Prevention, Care and Control Services in Armenia
21 April – 4 May 2011
Masoud Dara, Andrei Dadu, Smiljka de Lussigny, Brenda van den Bergh, Alejandra Gonzalez Rossetti, Bert Schreuder, Askar Yedilbayev, Doris Hillemann, Kristin Kremer, Nonna Turusbekova, Andre Zagorski,
What shall we do?

- Establish fast track procedure for registration of medicines already registered by the stringent drug regulatory authorities (ICH member countries: EU DRA, US FDA, Japan PMDA) or WHO-prequalified
- Include all anti TB medicine in the list of priority medicines liable for state registration
- Urge the GDF manufacturers to submit application for registration
- Establish the requirements and procedure on emergency import of non-registered essential medicines
- Require GMP compliance of all manufacturing sites
THANK YOU FOR YOUR ATTENTION

Lilit Ghazaryan
Scientific Center of Drug and Medical Technology Expertise
lili@pharm.am