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Cofepris
Comisión Federal para la Protección contra Riesgos Sanitarios

COFEPRIS:

Regulatory actions to improve access to medicines and health

Mario Alanís Garza

IX Annual meeting
2014 ICORD Conference
Ede, Netherlands

October, 2014

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- The Federal Commission for the Protection Against Sanitary Risks (COFEPRIS) is the Mexican institution responsible to guard and preserve the citizen´s constitutional right to Health through sanitary vigilance, regulation, and outreach.
- COFEPRIS was conceived by law as a macro sanitary regulator compared to other international sanitary agencies which regulate specific industries individually.

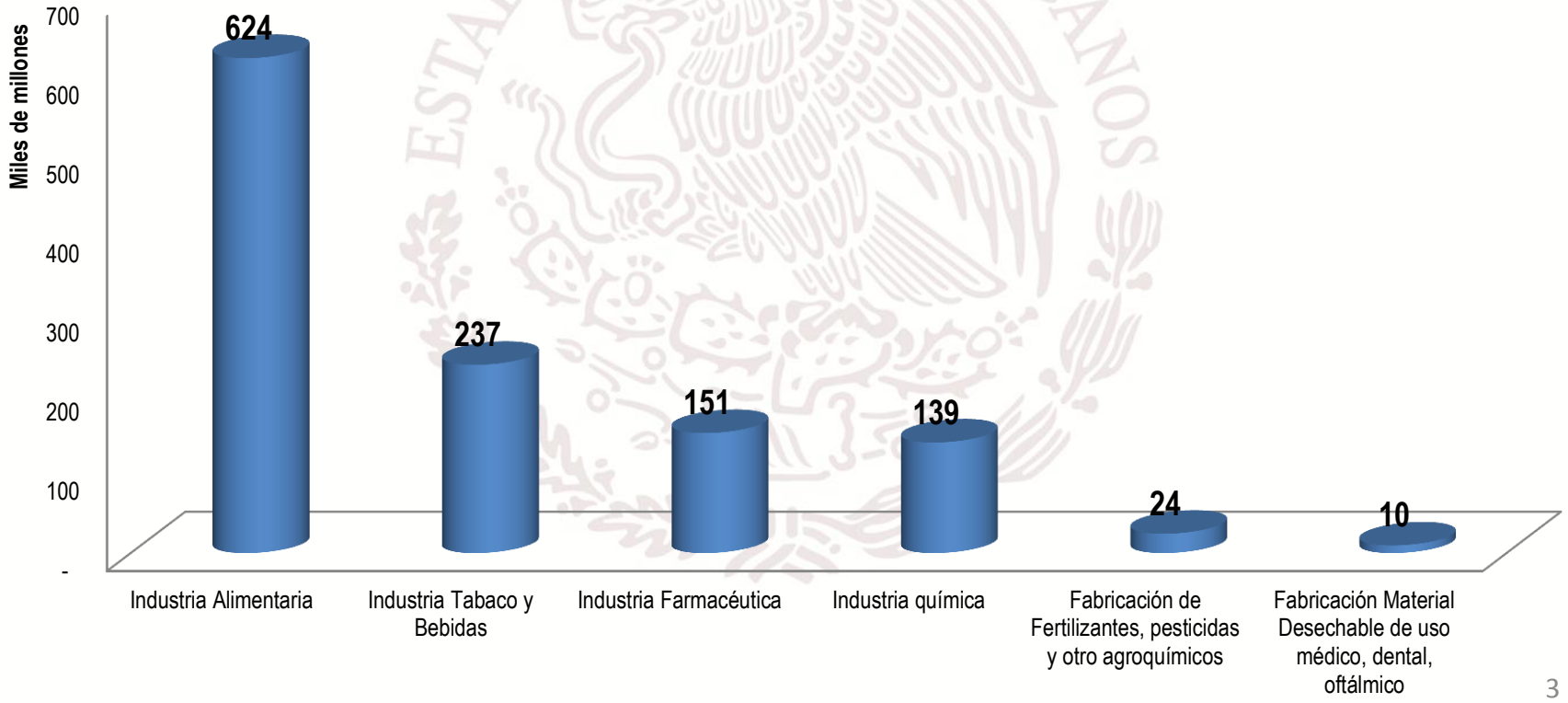
Regulated Sectors

1. Food and Beverages
2. Health Supplies
3. Health Services
4. Cosmetics and beauty products
5. Pesticides, Vegetable nutrients and Toxic substances
6. Emergencies
7. Labor Safety and Health
8. Environmental Risks

The value of the products regulated by COFEPRIS represents **9.8% of Mexican GDP.**

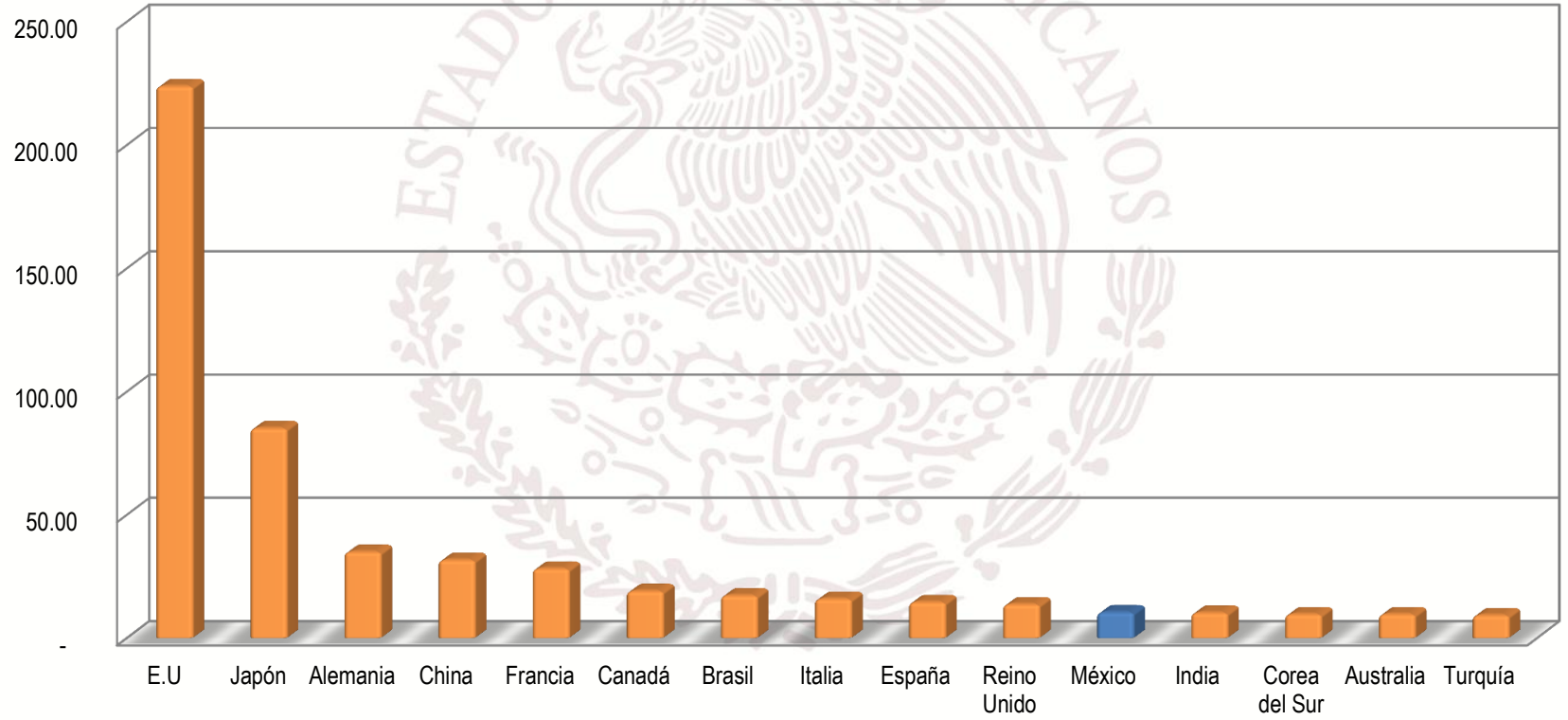
Industries Regulated by COFEPRIS

(2009 last available year)



- México tiene el lugar **11** dentro de los **quince principales mercados internacionales**.

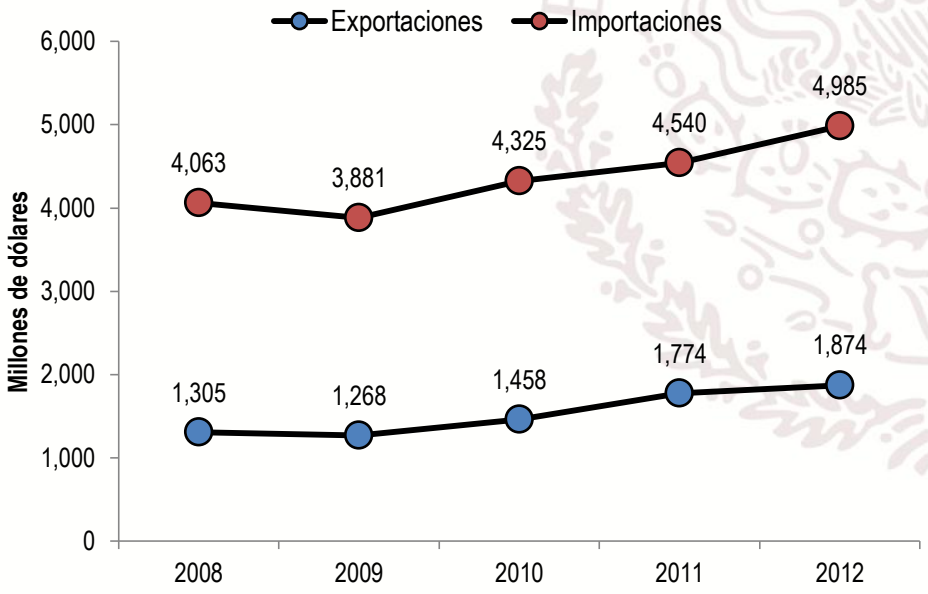
Valor 15 mercados nacionales principales
(2009)
(Miles de millones de dólares)



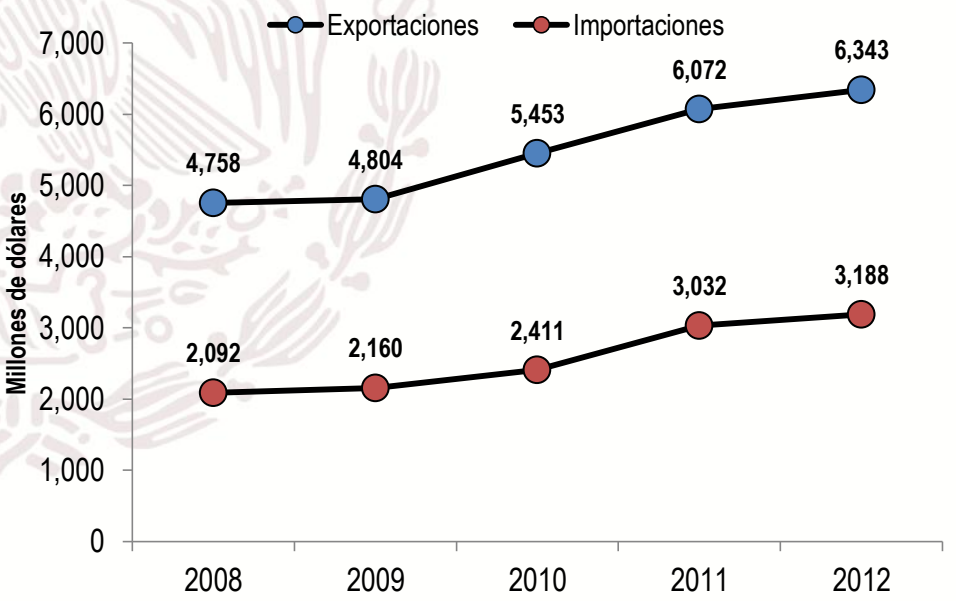
Fuente: IMS Health (2010).

- The trade balance of pharmaceutical products in Mexico shows a deficit. During 2012, imports of pharmaceutical products totaled 4 billion 985 million USD. Exports on the other hand reached **1,874 million USD**. The deficit was close to **3 billion 111 million USD**.
- In reference to the medical devices, the trade balance showed a surplus. During 2012, exports of medical devices reached 6 billion 343 million USD while imports totalled 3 billion USD. The trade balance surplus excedeed 3 billion USD.

Exports and Imports of Pharmaceutical Products, México (2008-2012)



Exports and Imports of Medical Devices, México (2008-2012)



Fuente: Estadísticas del Comercio Exterior, INEGI (2013).

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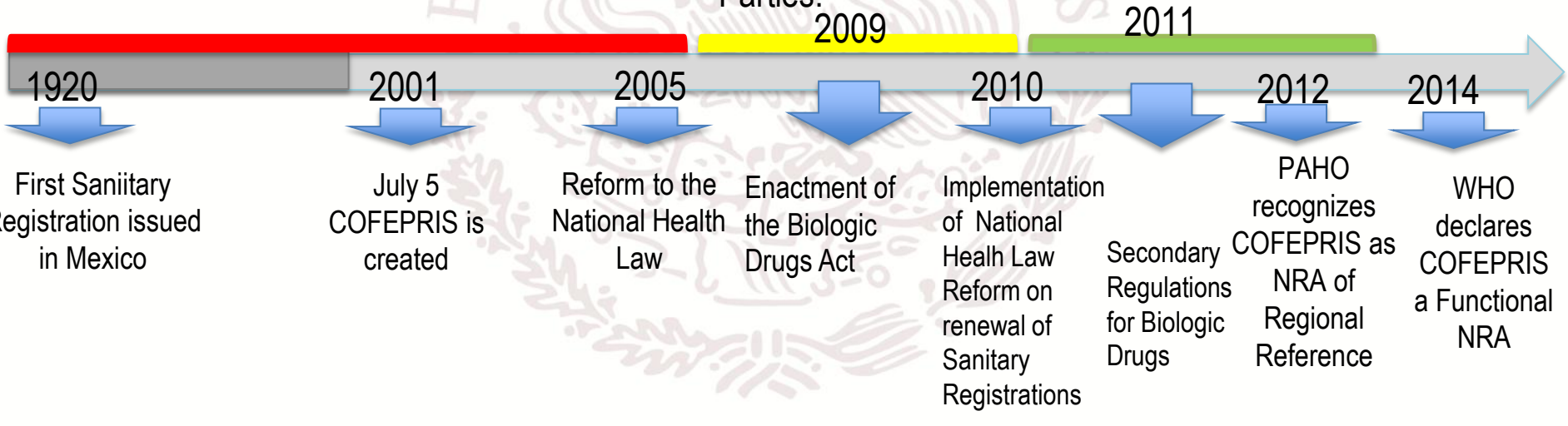
Evolution of the Mexican Pharmaceutical Regulation

During this period the sanitary registrations for medicines had indefinite duration and without the legal obligation to be bioequivalent.

1. The legal requirement of bioequivalence is implemented.
2. A network of laboratories is created to perform bioequivalence tests through Authorized Third Parties.

Domestic market with only two types of medicines:
1. Innovative Drugs
2. Generics



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PAHO Recognition

- On June 2012, COFEPRIS achieved international recognition as a Regulatory National Agency of regional reference in matter of drugs and vaccines by PAHO.
- **COFEPRIS is the first regulatory agency of Level IV for drugs and vaccines.**
  - The first sanitary agency to score 100% in its evaluation.
  - The first sanitary agency to be recognized by PAHO for drugs and vaccines.
- In **Latin America only 5 out of 45 (10%)** national sanitary regulatory agencies have been recognized by PAHO with level 4 which is the highest level possible.
- This measure is triggering significant benefits to the health systems, and is increasing investment opportunities and the foreign trade for the pharmaceutical sector.

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Recognition by the WHO of COFEPRIS for vaccines

- COFEPRIS completed the process of recognition to the World Health Organization on vacciones.
- As a result of the evaluation process done by WHO, COFEPRIS was declared FUNCTIONAL on vaccines for the period from June 2014 to June 2017.
- Thus, Mexico joined the elite group of 28 countries in health regulation. This is, only 14% of health agencies in the world hold the classification of functionality.
- Due to the above, WHO will support Mexico at implementing a roadmap for the Prequalification of Biologic Products seeking to enter the Vaccine Revolving Fund, which value is $6 billion a year.
- Finally, Mexico will participate as a leader in the experts panel for consultation, in order to generate a evaluation tool globally harmonized in drugs and vaccines evaluation.
- The first meeting will be held in December 2014, in Geneva.

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Characteristics of pharmaceutical policy

- Rests on four fundamental pillars
- The pillars are aligned with the **3 priorities of health policy** established by the Federal Government.
- Its main objective is to improve access of the population to a well-supplied drug market that offers innovative and generic medicines at the best prices.

Pillars of Pharmaceutical Policy	Government's Health Policy Priorities
A **regulatory agency that guarantees the safety, quality and eficacy** of all drugs.	**1. Effective Access** **2. Service quality** **3. Prevention**
A reliable scheme to **authorize sanitary registrations**.	
Removal of barriers to market entry for products that are safe and of high quality.	
Harmonization of the sanitary agency with best international practices.	

Pharmaceutical Innovation

Innovation in Health provides better treatments for patients, reduces hospital days and recovery periods, avoids expensive surgeries, improves quality of life and life expectancy, and increases productivity.

With an enabling environment for pharmaceutical innovation, Mexico can:

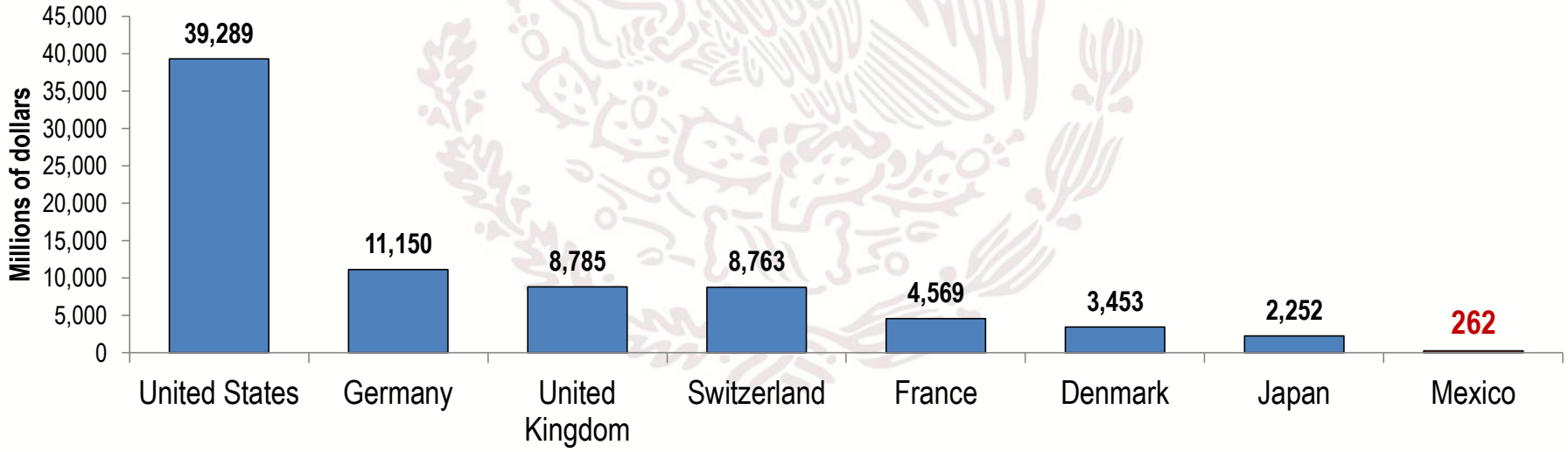
1. Be an example in offering innovative treatments and drugs for its population.
2. Increase the dynamism in the market for clinical research.
3. Be the first country to market innovative medicines.
4. Generate savings in public and private health expenditures.
5. Attract more domestic and foreign investment.
6. Encourage greater economic growth.

- Through the fostering of pharmaceutical innovation, there are more incentives for manufacturers to invest in Research and Development (R+D).

- Approximately, 50% of global spending in pharmaceutical R+D is done in the United States.
- The main countries that invest in pharmaceutical R+D are the **United States**, **United Kingdom**, **Switzerland**, **France**, **Germany**, **Japan** and **Denmark**.
- Investment in pharmaceutical R+D in Mexico is close to **262 million dollars**.

Spending in Pharmaceutical Research and Development in different Countries, 2010

(by main pharmaceutical companies of each country*)



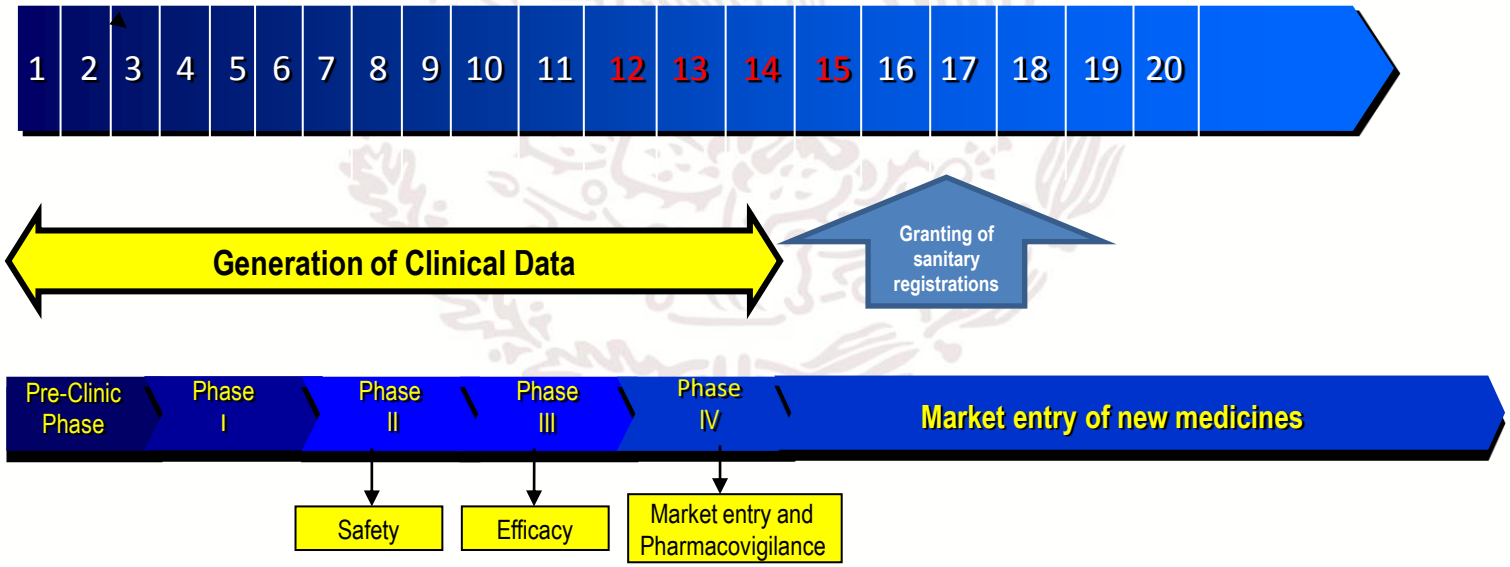
Source: COFEPRIS (2013) with information from IMS Health (2010) and *The Association of the British Pharmaceutical Industry*.

* Pharmaceutical countries considered represent 61% of the world pharmaceutical market.

Pharmaceutical Products Discovery, Development and Approval Process

- Developing a new medicine takes an average of 10-15 years
- For every 5000-10,000 compounds, only about 1 is approved
- Research and development of new medicines entails a complex, risky, and costly process involving several actors along three phases: basic research, pre-clinical trials and clinical trials.

Development of pharmaceutical products

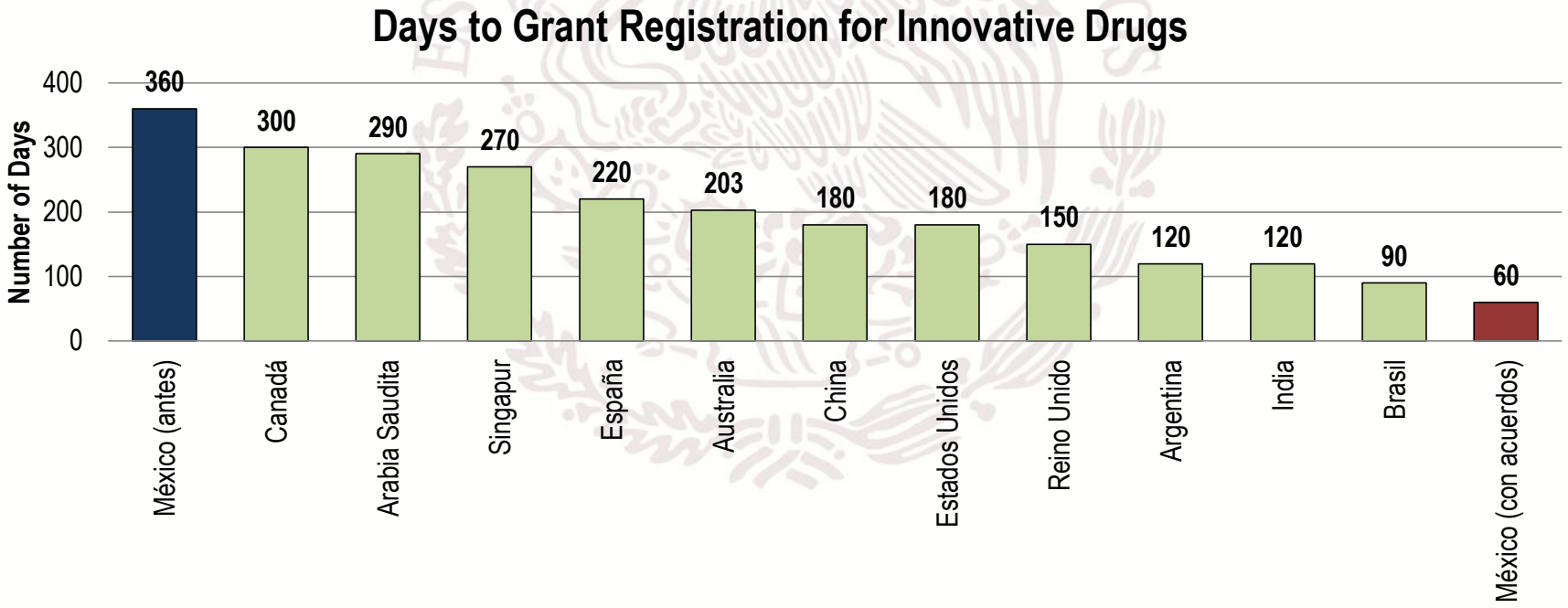


Agreement for the Promotion of Innovation

- In the past, new molecules in Mexico took an average of 360 days to enter the pharmaceutical market.
- The agreement on new molecules represented an effort to strengthen the access of Mexican families to medicines, reduce health care costs and encourage innovation in three key areas:
    1. Foster projects of innovation in Mexico.
    2. Strengthen the entry of molecules from other countries to the Mexican market.
    3. Mexico becoming a first country to market an innovative drug.

Innovation Policy

- Mexico implemented equivalence with the USA, Canada, Europe, and Australia and **became the fastest country to authorize the marketing for new molecules** while, at the same time, ensure **efficacy**, **safety,** and **quality** of medicines.
- Mexico also substituted the requirement of a foreign free sale certificate with a report of clinical studies in Mexican population.
- Two new molecules have entered the Mexican market as a global launch pad: **Lixisenatide** used to treat **Type 2 Diabetes** and **Fluticasone/Vilanterol** used to treat **Chronic Obstructive Pulmonary Disease (COPD)**.



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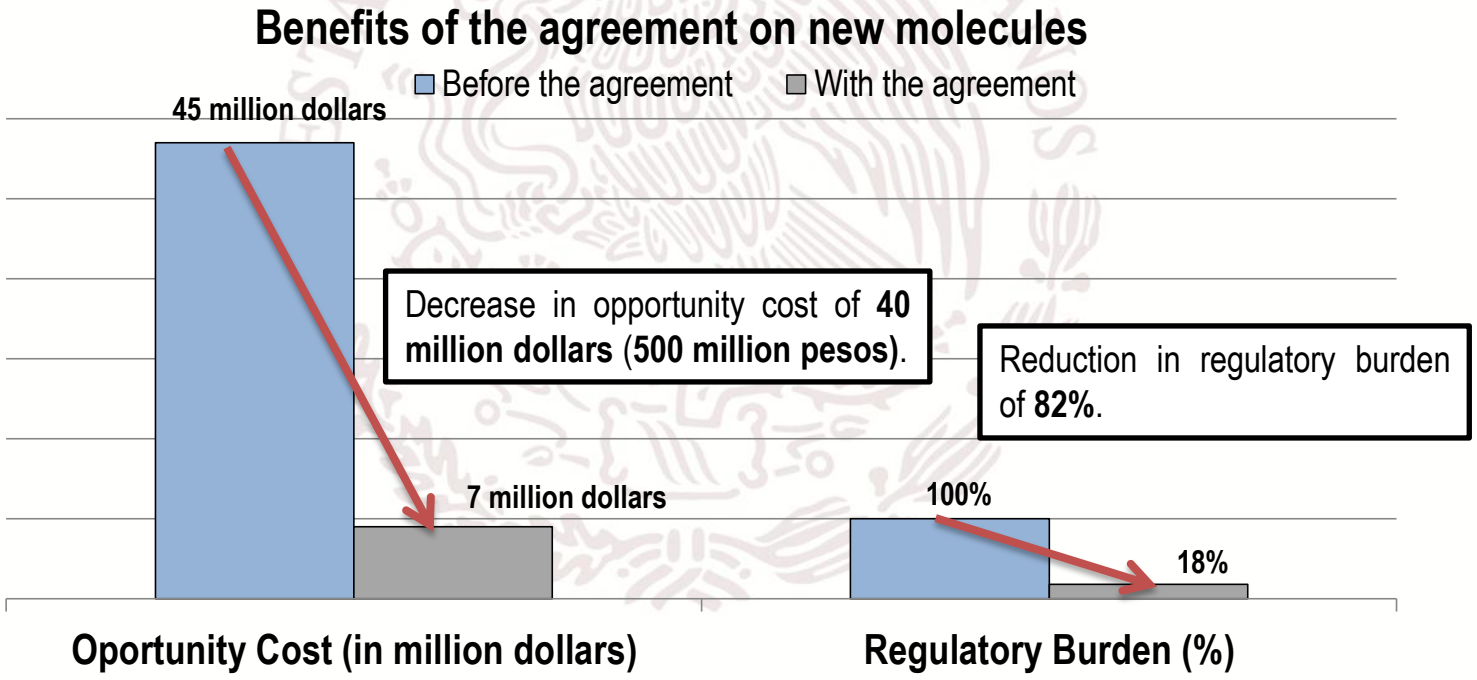
Agreement for the Promotion of Innovation

- **The opportunity cost** associated with the days a file is processed has decreased in approximately **40 million dollars** (500 million pesos). This cost was estimated in **45 million dollars** (570 million pesos).*
- Further, with the equivalence agreement on new molecules, the **regulatory burden** for each file decreases in **82%**.



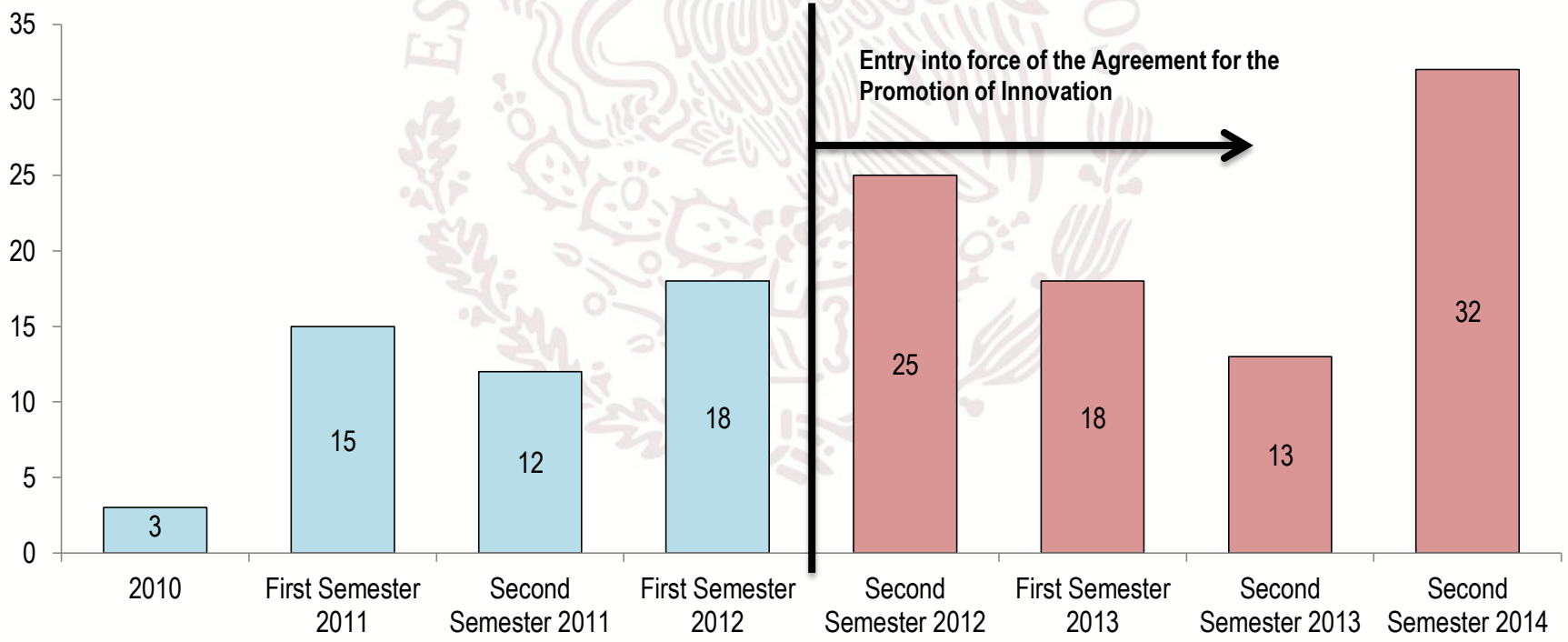
* Calculation of the opportunity cost consists of the daily administrative cost to process registrations for new molecules multiplied by the number of days requeried to grant authorization.

Incentives for New Molecules

- Pharmaceutical innovation directly benefits consumers through: 1) lower drug prices; 2) reductions in hospital stay days; and 3) increases in the quality of life and life expectancy.

- During 2011 and 2014, COFEPRIS issued **133 sanitary registrations** for innovative drugs for the treatment of cardiovascular diseases, oncological diseases, and other medical conditions. This represents an increase of **4,333%** relative to 2010.

Sanitary Registrations issued to innovative medicines



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Removal of the requirement to have a manufacturing plant on national soil

- In 2011 the Mexican Government removed the requisite to have a manufacturing plant in Mexico to market a medicine.

- Approval of the first **303** registrations in this category which had been requested more than 10 months before.

BENEFITS:

- Increase the **supply of pharmaceuticals**.
- Availability of **new molecules** for research and development.

Impact:

Investment above 100 million dollars in the next five years.

100% increase in the workforce of the firms involved.

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Actions to facilitate access of Orphan Medicines

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ORPHAN Medicines

Background

- Before 2010 Mexico did not officially recognized the existence of orphan medicines and consequently and no sanitary authorization was identified.
- During 2010, COFEPRIS reached an Agreement Pharmaceutical Industry by which the holder of the authorization could request the import permit .
- The authorization of an Orphan drug would result of the authority evaluation and classification.
- The authority issues an authorization not an official registration.
- The official authorization of orphan drug entered as an emergency measure to facilitate entry while the RIS modification is published and is a free process.
- The Mexican Health Law recognized orphan medicines in March 2012 defining as that which affects no more than 5% of the population.
- The new regulation are currently under discussion.

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- The Certification is an official document, allowing to import .
- Allows population to utilize the medicine .

Comparison of drug evaluation requirements

Requirement	Generics	New molecule	Orphan drugs
Legal Framework	Yes	Yes	No
Sanitary Authorization	Yes	Yes	No
Certification	No	No	Yes
Guidelines for obtaining recognition	No	No	Yes
Administrative - Legal	Yes	Yes	No
New Molecules Committee	No	Yes	No
Chemical Evaluation	Yes	Yes	Yes
Medical Evaluation	Yes	Yes	Yes (original country)
Interchangeability Test	Yes	No	No
Labels and Prescribing information	Yes	Yes	Yes (origin labels)

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Sanitary Authorizations for Orphan Drugs

Year	Applications	Number of Recognitions Granted
2010	21	14
2011	11	07
2012	12	13
2013	11	07
2014	07	07
Total	62	48

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Other regulatory reforms that increase access

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Health Supplies

Simplified Vaccine Liberation

- The guidelines for the scheme were published in the Official Gazette of the Federation (DOF) on June 1st, 2011.
- The new scheme implies a **2-month waiting time reduction**.
- The maximum allowed response time was reduced from **three** to only **one month**.
- During 2013, a total of **40.5 million doses of vaccine** were released.
- Since the new guidelines were published, a total of **111.8 million doses** have been released.

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Regulation on Biologic Medicines

Comprehensive Legal Framework for Biologic Medicines

- This new biotechnology regulation places Mexico's legal framework among the most modern and forward looking legislation currently operating in the European Union and the United States.
- In Mexico, **35%** of the new applications for innovative pharmaceutical sanitary registrations are related to molecules derived from biotechonology processes, especially in fields related to cancer and neurological diseases.

1. **2009.** Enactment of the Biologic Medicines Act.
2. **October 18, 2011.** Issuance of the Administrative Regulations regarding Biologic Medicines by the President. **Enactment on April 16, 2012.**
3. **September 20, 2012**. Issuance of specific requisites to produce and commercialize biologic medicines by COFEPRIS.

Benefits of changes to legislation

COFEPRIS has issued registrations to 14 biologic medicines: Axuares, Illaris, Infinitam, Advate, Ryzodeg, Benlystia, Xgeva, Perjeta, Etart, Tresiba, Arzerra IV, Wetlia, Kadcyla and Simponi.

These reforms place Mexico among the nations with leading legislation in biologic medicines.

Comparative Law of Biological Medicines		
Country	**Type of Law**	**Valid since**
United States	•Classification of biologic medicines into: "Biologics" and "Follow-On Biologics (FOB)". 1. The applicant must comply with requirements and test which prove eficacy, safey and quality based on a case by case basis. 2. Generic biological medicines must duplicate the innovative process of the innovator. It is intended to have an fast aproval process	**Abril, 1996**
European Union	•Classification of medicines: biologicals and biosimilars 1. The applicant receives a user guide showing the relevant guidelines 2. The biosimilar medicines are approved based on the comparability principles. Studies must show comparability with innovative biologicals 3. It si not necessary to duplicate the whole process like in the FDA.	**Octubre, 2005**
Mexico	•Classification of biological medicines: innovatives and biocomparables 1. The applicant must comply with requirrements and test proving quality, safety and efficacy (case by case) 2. Once inthe market, there must be farmacovigilance 3. In-vitro" and clinical studies are utilized for biocomparables.	**Agosto, 2009**

The introduction of biologic medicines, innovative drugs and follow-on biologics increases benefits for the agents participating in the pharmaceutical market.

- Direct Benefits for the public sector:
  - Savings in government expenditures.
  - Increases in the capacity to receive more patients and treat complex diseases.
- Direct Benefits to the consumer:
  - Increases in the supply of drugs for complex pathologies.
  - Decreases in the price of drugs and increase in accessibility.

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Drugs and Medical Devices Specialized Lanes

- In the past and before this strategy was implemented, every document filed before COFEPRIS was processed through a single authorization lane.
- To expedite the sanitary authorization process, specialized lanes considering a risk-based approach were implemented:

	Lane	Characteristics and Operation
LANE 1	Administrative Paperwork	
LANE 2	Pharmaceuticals, Classes I, II, III	Subdivided in 3 production lines: i) Extensions ii) Modifications iii) New sanitary registrations
LANE 3	Pharmaceuticals, Class IV	Subdivided in 3 production lines based on a risk point system
	Pharmaceuticals, Classes V, VI	Subdivided in 3 production lines: i) Extensions ii) Modifications iii) New sanitary registrations

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Pre-verification of administrative paperwork

Waiting time was reduced from 1 year to 3 working days for administrative procedures

COFEPRIS has issued **10,507 sanitary registrations** under the simplified procedure within 3 to 15 working days.

	STATUS	NUMBER
Allopathic Drugs • **Lane started on June 16th, 2011** • On average processes 112 files per month, or 4 per day	AUTHORIZED	4,081
	WARNINGS	484
	IN PROCESS	298
	WITHDRAWALS	31
	SUB TOTAL	**4,894**
Medical Devices • **Lane started on August 5th, 2011** • On average processes 107 files per month, or 4 files per day	AUTHORIZED	4,391
	WARNINGS	10
	IN PROCESS	70
	SUB TOTAL	**4,471**
Instructions for Prescriptions • **Started on May 1, 2012** • **On average processes 37 files per month or 1 per day**	AUTHORIZED	864
	WARNINGS	154
	IN PROCESS	124
	SUB TOTAL	**1,142**
	TOTAL	**10,507**

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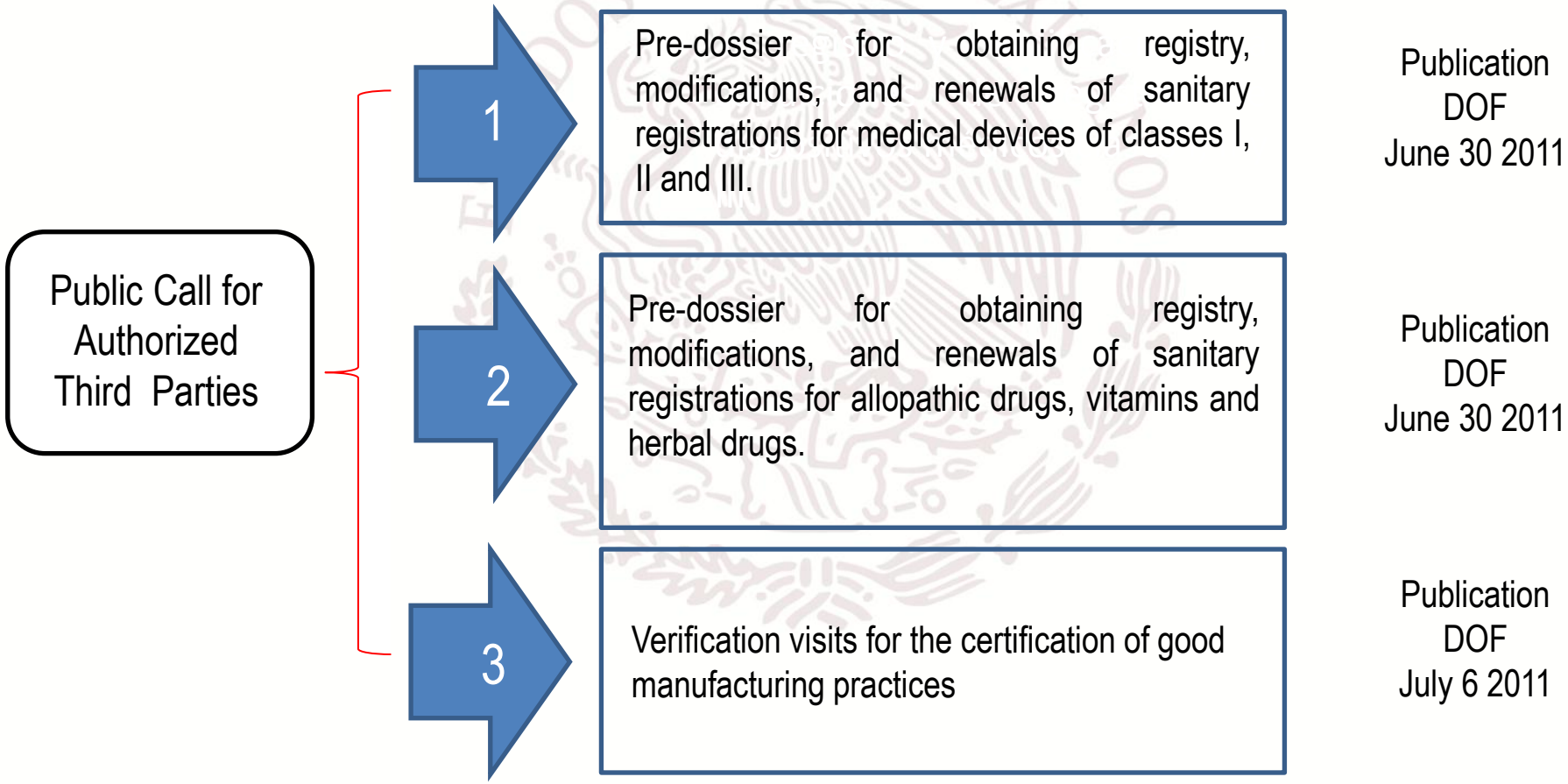
Calls for Authorized Third Parties
Allopathic drugs, medical devices and plants

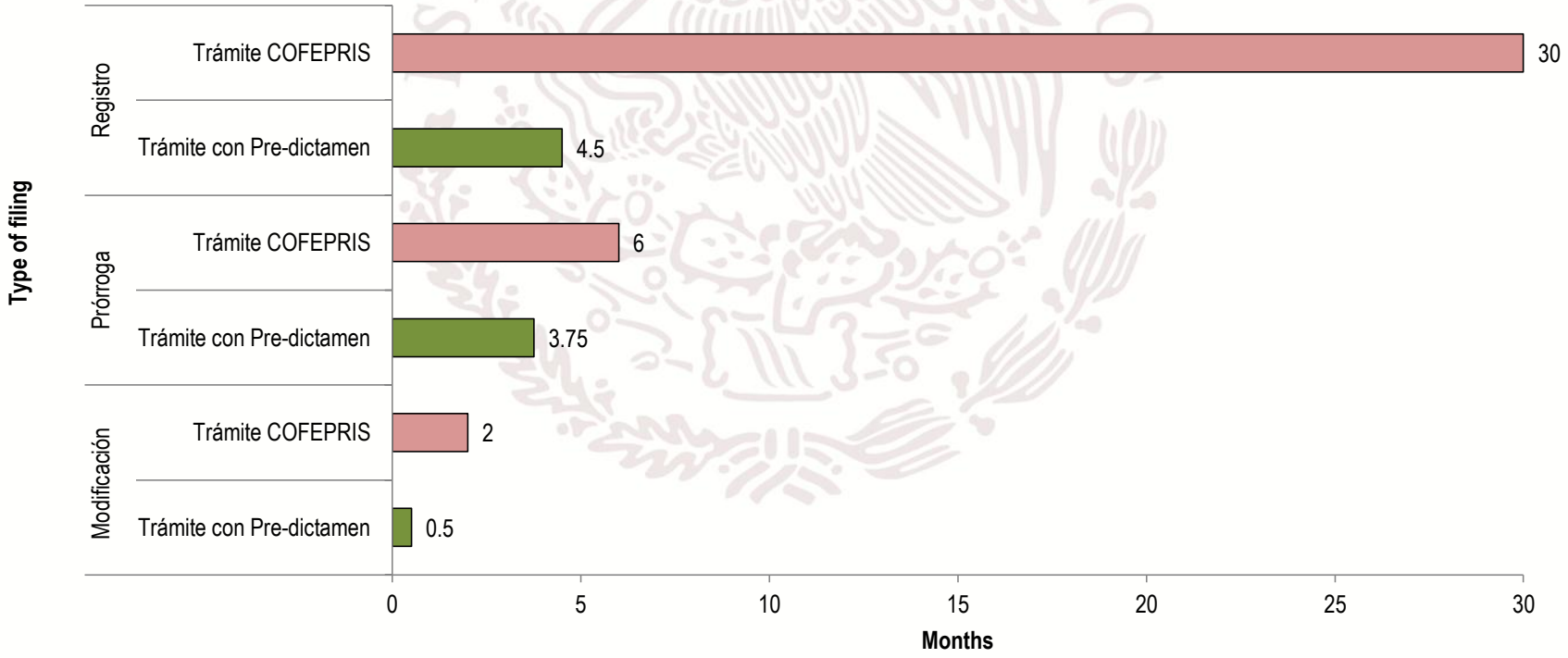
- Public calls were published with the objective of reducing the sanitary authorization waiting times by two thirds, (i.e. going from 2 years to 4 months).



Benefits of Authorized Third Parties

- The **"Pre-dictamination"** of Third Parties allows the authoirity to reduce signifcantly the processing time of each individual filing. For example, in the case of new registrations the processing time reduction is approximately reduced by **2 years on average.**

Average processing time for filings of drug products (months)



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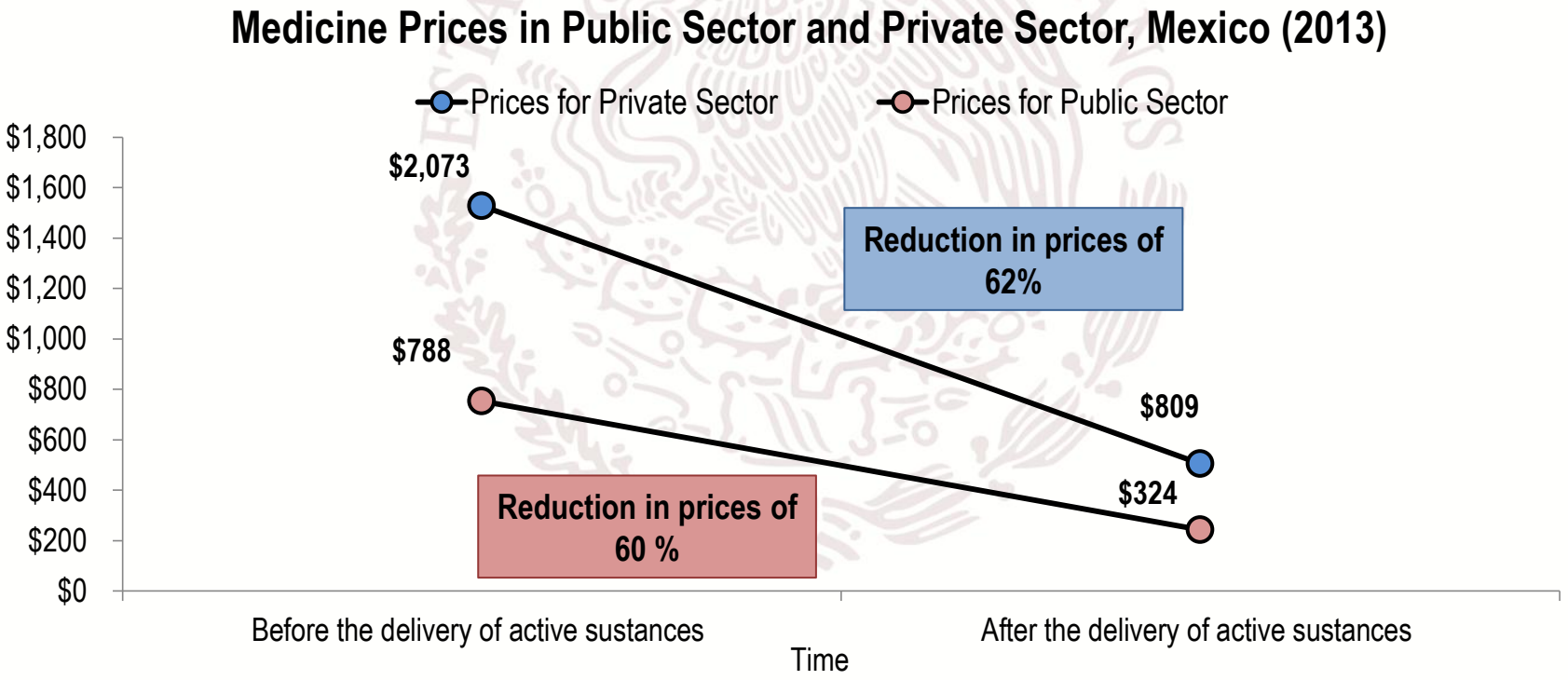
Increasing Access: Savings in medications in both private and public sectors (2011-2014)

- The average price of medications in drug stores has decreased **62%**.
- The average price for public purchases of medications has decreased **60%**.



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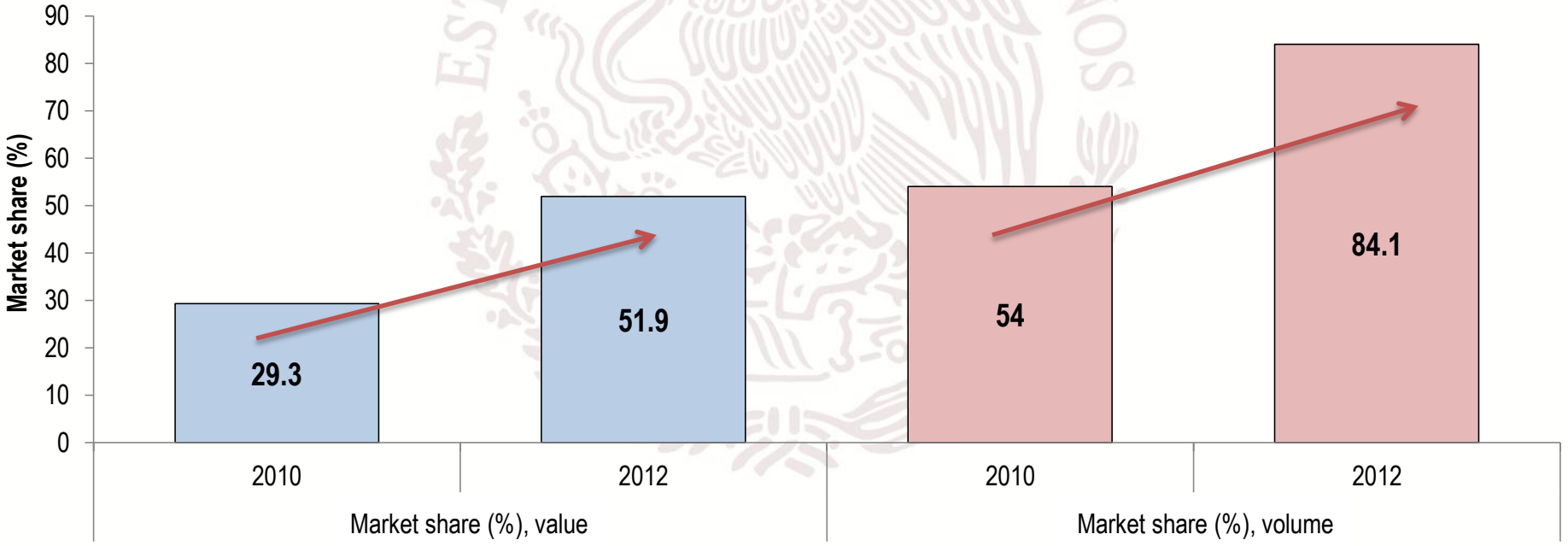
- In 2010, about 30% of the **market value** corresponded to generic drugs, while in 2012 this figure rose to nearly 52%. This represents an increase of 77% in just two years.

- On the other hand, generic drugs in 2010 represented 54% of the **market volume**, while for 2012 accounted for 84% of the pharmaceutical market in Mexico. This represents a growth of 56% in the period 2010-2012.

Penetration of Generics in the Mexican Pharmaceutical Market, 2010-2012



Source: Funsalud. Analysis with information from IMS Health (2012).

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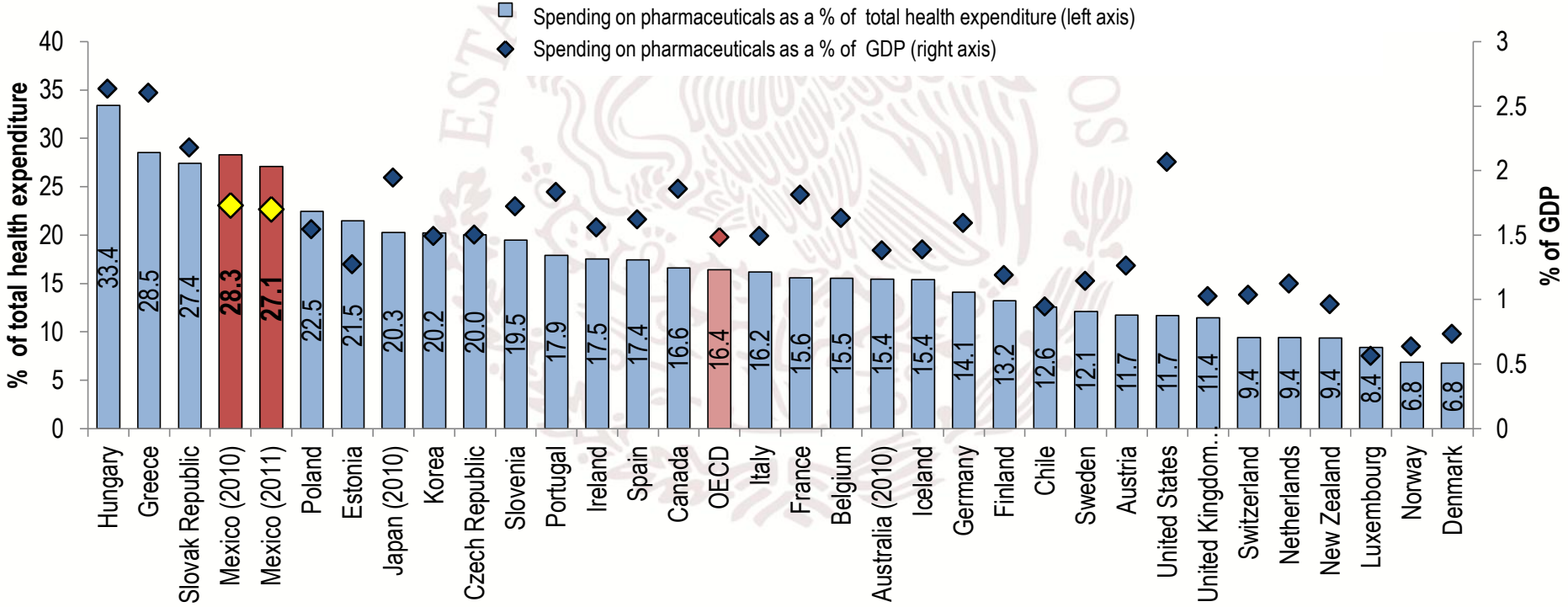
- Mexico gained two positions in pharmaceutical spending as a percentage of total health expenditure, from 28.3% in 2010 to 27.1% in 2011.
- This development is associated with the access strategy for pharmaceuticals from the Ministry of Health, which have generated savings of 20 billion pesos in 2 years. This rate will continue decreasing, according to the 2011 figure.

Spending on Pharmaceuticals in different countries



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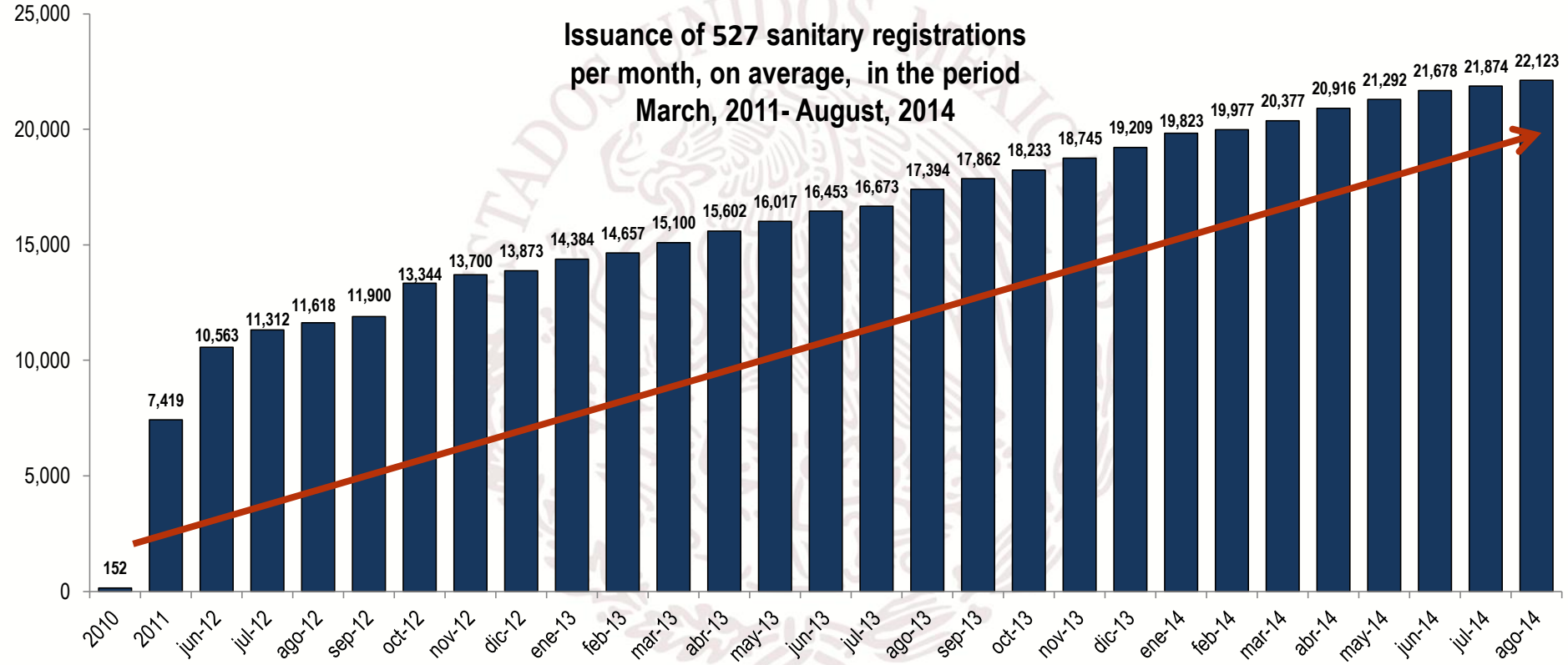
The issuance of **21,874** sanitary registrations from March 2011 to August 2014, represents a market value greater than **2.4 billion dollars**, and has a growth rate of **14,454%** relative to 2010. Progress has been as follows:



- A total of **11,877 sanitary registrations** have been issued from June 2012 to August 2014. This improvement implies an average of **439 monthly registrations**. The issuance of sanitary registrations will continue growing given that **COFEPRIS regulates 10% of GDP**.

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