Understanding the Latin American Regulatory Landscape:

The Impact of Recent Regulatory Developments on the Mexican Therapeutic Landscape

A Regional Virtual Forum
Conducted by CIRS
July 28, 2020

Clarivate Analytics

	Topic	Speaker
	Introduction to CIRS	Dr Jamie Munro Executive Director, CIRS
	RDB 76: Objectives and methodology,	Dr Lawrence Liberti Head, Regulatory Collaborations, CIRS
	RDB 76: Analysis and main results,	Dr Lawrence Liberti Dr Mario Alanis Senior Consultant, CIRS
	Participant Reflections	Participants
	Question and Answer Chat	Participants
	Summary and closing comments	Dr Jamie Munro

Your CIRS Hosts

Neil McAuslane, PhD
Prisha Patel, MSc
Celine Rodier, PharmD
Jenny Sharpe, PhD

Mission

To advance patient access to quality, safe and effective medicines

through

maintaining a thought leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and access policies and processes

*For over 25 years CIRS has provided a **neutral, independent, international** forum*

for industry, agencies and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policies

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Dr John Patrick Stewart, Director General, Therapeutic Products Directorate, Health Canada
Dr Roopal Thakkar, Vice President, Global Regulatory Affairs, Abbvie
Dr Max Wegner, Head Regulatory Affairs PH & CH, Bayer AG

15 & 16 September

Effectiveness of the Regulatory Approval Process – Moving from Measuring Performance to Operational Excellence

Pre-Workshop Agency Survey

8 & 9 December(Alasdair Breckenridge Memorial Workshop)

Reimagining medicines regulatory models: Implementing fit for purpose activities for sustainable patient access

Regulatory Agencies with whom we Interact

Americas- Country	Authority
Argentina	ANMAT
Brazil	ANVISA
Canada	Health Canada
Chile	ANAMED
Colombia	INVIMA
Cuba	CECMED
Ecuador	ARCSA
El Salvador	DNM
Haiti	DPM/MT-MSPP
Mexico	COFEPRIS
Peru	DIGEMID
USA	FDA
Regional Initiatives	CARICOM-CRS/PAHO

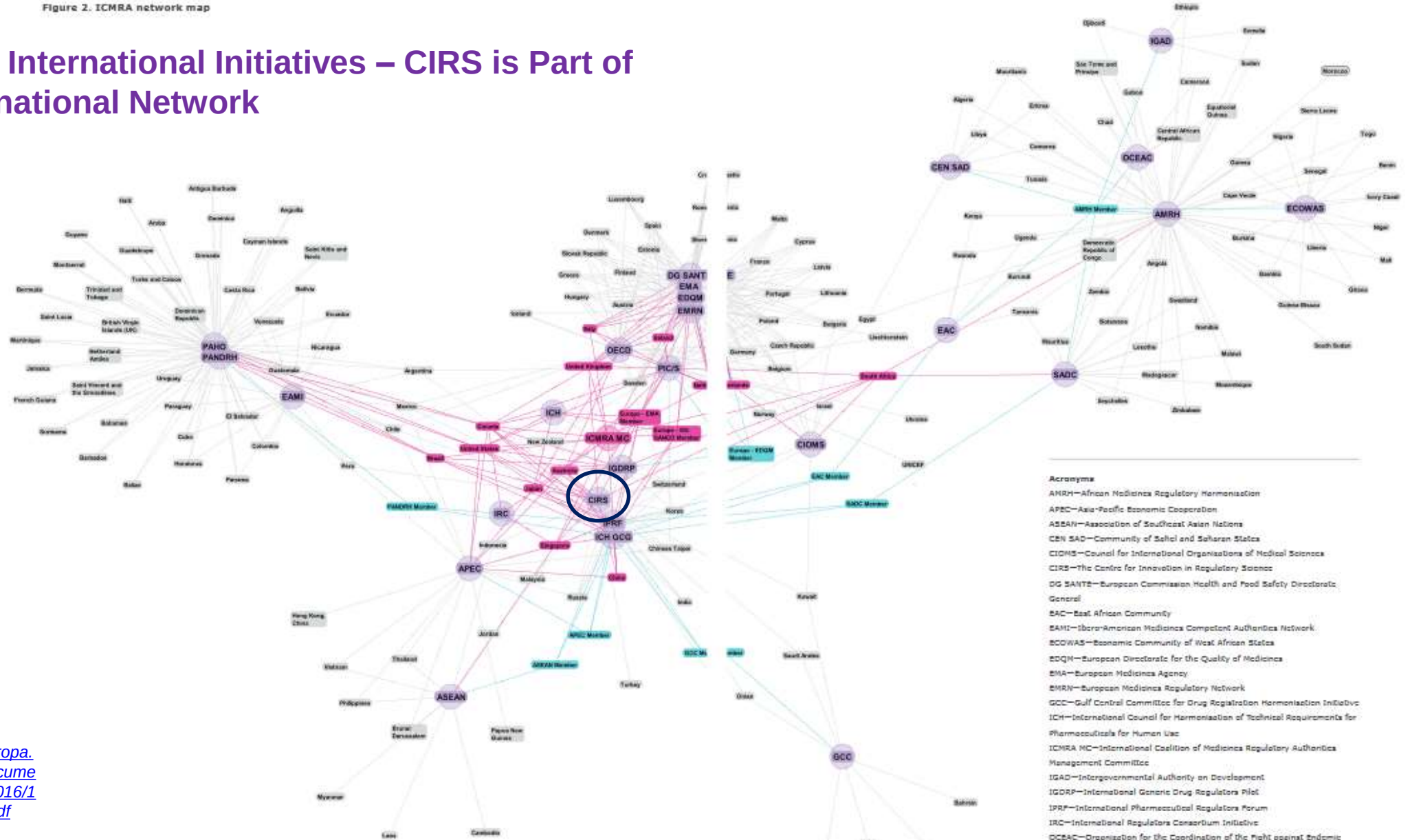
EME- Country	Authority
Denmark	DKMA
EU	EMA
Israel	MoH
Jordan	JFDA
Kuwait	KDFC
Oman	MoH
Qatar	SCH
Saudi Arabia	SFDA
Sweden	MPA
Switzerland	Swissmedic
Turkey	TITCK
United Arab Emirates	MoH
United Kingdom	MHRA
Regional Initiatives	GHC

AFRICA- Country	Authority
Botswana	BoMRA
Burkina Faso	MoH
Ethiopia	EFDA
Gambia	MCA
Ghana	FDAG
Kenya	PPB
Namibia	NMRC
Nigeria	NAFDAC
Mozambique	MoH
Senegal	MoHP
South Africa	SAHPRA
Tanzania	TMMDA
Zambia	ZAMRA
Zimbabwe	MCAZ
Regional Initiatives	AMRH-EAC Zazibona/SADC WAHO

ASIA- Country	Authority
Australia	TGA
China	NMPA
Chinese Taipei	TFDA; CDE
Indonesia	NAFDC
Japan	MHLW, PMDA
Malaysia	NPRA
Philippines	PFDA
Singapore	HSA
South Korea	MFDS
Thailand	TFDA
Vietnam	DAV
Regional Initiatives	APEC

Mapping International Initiatives – CIRS is Part of the International Network

Figure 2. ICMRA network map



Key

Initiatives*—indicated by purple nodes and matching halos

Organisational members*—indicated by blue nodes

Country members*—indicated by light grey nodes

*ICMRA members are indicated by pink nodes and halos

Acronyms

AMRH—African Medicines Regulatory Harmonisation

APEC—Asia-Pacific Economic Cooperation

ASEAN—Association of Southeast Asian Nations

CEN SAD—Community of Sahel and Saharan States

CIOMS—Council for International Organizations of Medical Sciences

CIRS—The Centre for Innovation in Regulatory Science

DG SANTE—European Commission Health and Food Safety Directorate General

EAC—East African Community

EAMI—Ibero-American Medicines Competent Authorities Network

ECOWAS—Economic Community of West African States

EDQM—European Directorate for the Quality of Medicines

EMA—European Medicines Agency

EMRN—European Medicines Regulatory Network

GCC—Gulf Central Committee for Drug Registration Harmonization Initiative

ICH—International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

ICMRA MC—International Coalition of Medicines Regulatory Authorities Management Committee

IGAD—Intergovernmental Authority on Development

IGDRP—International Generic Drug Regulators Pilot

IPRF—International Pharmaceutical Regulators Forum

IRC—International Regulators Consortium Initiative

OCEAC—Organization for the Coordination of the Fight against Endemic Diseases in Central Africa

OECD—Organisation for Economic Co-operation and Development

PAHO—Pan American Health Organization

PANDRH—Pan-American Network for Drug Regulatory Harmonization

PIC/S—Pharmaceutical Inspection Co-operation Scheme

SADC—Southern African Development Community

http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2016/10/WC500214180.pdf

Website

Member company only section – access to latest briefings, publications, workshop presentations and R&R Atlas
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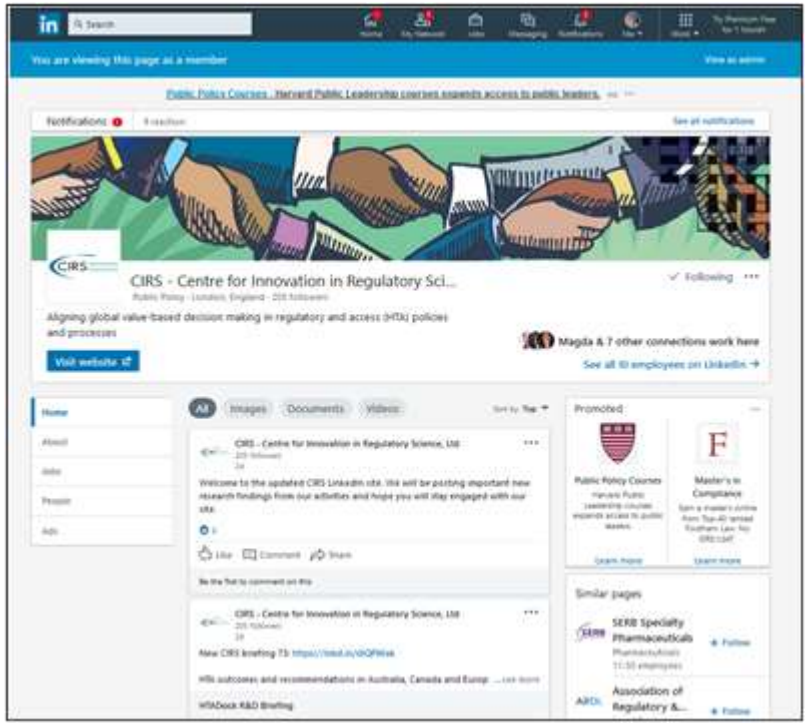

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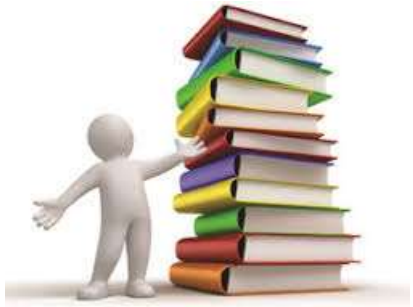
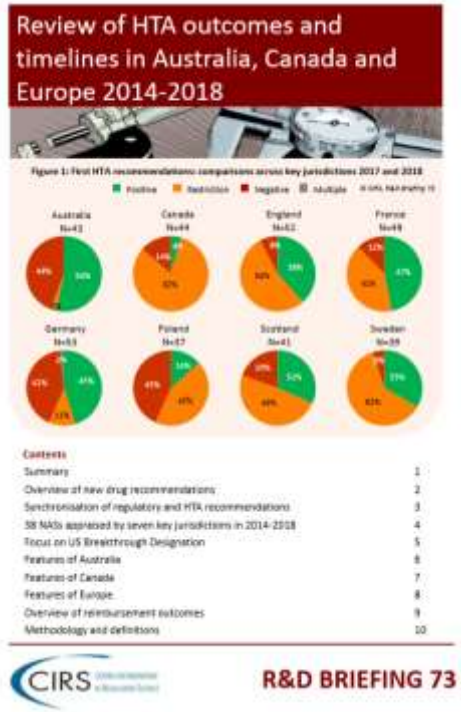
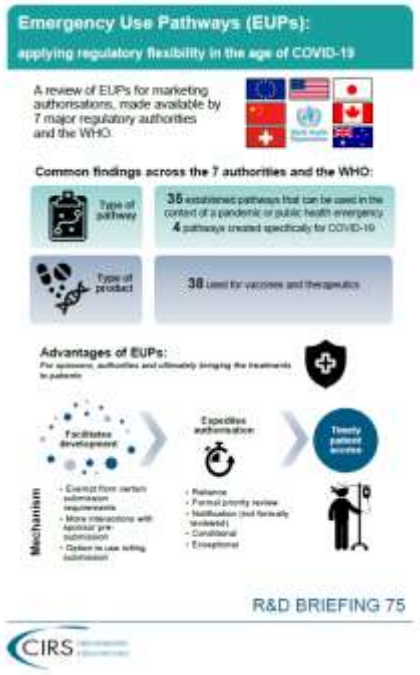
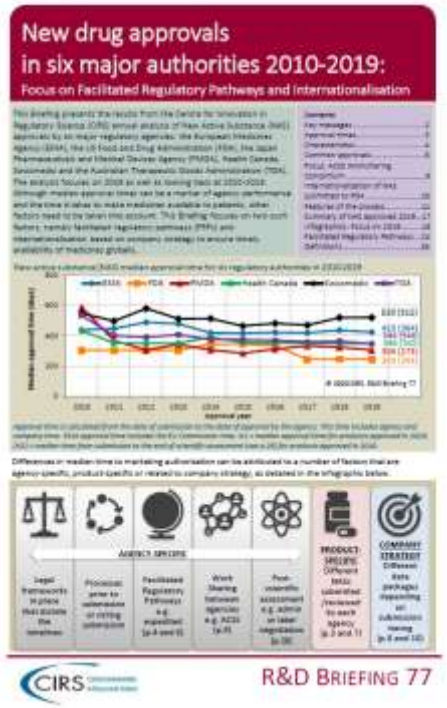
Recent Publications- R&D briefings

Disseminate high level findings from original research to address important policy and practical development issues









Focus on Mexico and LatAm

The Impact of Recent Regulatory Developments on the Mexican Therapeutic Landscape

Access to innovative medicines is key to improving overall population health, reducing hospitalisation time and decreasing morbidity and mortality. An efficient regulatory process can be reflected in measurable positive health impacts; conversely, activities that slow or impede regulatory efficiency and predictability can be detrimental. Recent developments in the Mexican regulatory system for the assessments of innovative new products have had a negative impact on Mexican public health.

This Briefing addresses the impact of suspending the activities of the New Molecules Committee (NMC) on the Mexican therapeutic landscape. First, we compared the way that "new medicines" are defined within the context of the Mexican regulatory system, with definitions used by comparable regulators and health organisations. We have also investigated the extent to which new drugs approved by the US FDA have also been approved by other important jurisdictions, specifically Mexico, Brazil, Europe, and Canada. In this manner, we expect to gain a better understanding of the impact the absence of NMC evaluation sessions is having on the availability of new medicines for Mexican patients.

NMC's regulations require that all new innovative products (including innovative biologics and biosimilars) considered for the Mexican market be assessed by this committee prior to formal submission for market authorisation. The last time this committee held a session was in May 2019. Since that time COFEPRIS has not received any new submissions for the registration of innovative products.

Our findings indicate the regulatory approval system that had been in place prior to the NMC ceasing its activities provided an opportunity for innovative products to obtain regulatory approval, despite recognised long timelines and process inefficiencies. The current situation has severely curtailed the availability of innovative products; this landscape could be improved by the reinstitution of the NMC, the more effective use of accelerated pathways and by prioritising the assessment of critically important new medicines.

El acceso a medicamentos innovadores es clave para mejorar la salud de toda la población, para reducir los tiempos de hospitalización, la morbilidad y la mortalidad de un país. Un proceso regulatorio eficiente tiene un impacto positivo medible en la salud, y por el contrario, acciones que retrasan o impiden la eficiencia regulatoria y su predictibilidad pueden ser perjudiciales. La parálisis reciente del Sistema regulatorio mexicano respecto a la evaluación de nuevos medicamentos innovadores conlleva un impacto negativo en la salud de la población mexicana.

Este informe analiza el impacto de la suspensión de las actividades del Comité de Moléculas Nuevas (NMC, por sus siglas en inglés) sobre el horizonte terapéutico de México. En primer lugar, comparamos la definición de nuevos medicamentos según el contexto regulatorio mexicano con las definiciones adoptadas por otras agencias reguladoras u organizaciones de salud del mundo. Asimismo, investigamos en qué medida los nuevos medicamentos que han sido autorizados por la agencia de los Estados Unidos (FDA) han obtenido también registro sanitario en otras jurisdicciones importantes; en particular, comparamos el caso de México con los de Brasil, Europa y Canadá. De esta forma esperamos lograr una mejor comprensión del impacto que ha tenido la falta de reuniones de evaluación del NMC en la disponibilidad de nuevos medicamentos para los pacientes de México.

La regulación del NMC exige que todos los medicamentos innovadores (incluyendo biotecnológicos y biosimilares) que pretendan entrar al mercado mexicano deben obtener una autorización del NMC antes de someter una solicitud de registro sanitario. La última vez que este Comité sesionó fue en mayo de 2019. A partir de entonces, COFEPRIS no ha recibido ninguna solicitud de registro sanitario de productos innovadores.

Nuestros hallazgos reflejan que la operación del sistema de autorización regulatoria previo a la suspensión de actividades del NMC, aun considerando los largos tiempos de evaluación e ineficiencias en el proceso, sí ofrecía una oportunidad para que productos innovadores obtuvieran un registro sanitario. La situación actual ha reducido drásticamente la disponibilidad de medicamentos innovadores. Esta tendencia puede mejorar si se restablecen las reuniones del NMC, y se adoptan procesos acelerados de autorización sanitaria y/o se le asigna alta prioridad a la evaluación de medicamentos innovadores que sean de importancia crítica.

R&D BRIEFING 76

CIRS Centre for Innovation in Regulatory Science

May 2020

June 2020

The Impact of Recent Regulatory Developments on the Mexican Therapeutic Landscape: Addendum

Access to innovative medicines is key to improving overall population health, reducing hospitalisation time and decreasing morbidity and mortality. As we have shown in the original version of this Briefing (CIRS R&D Briefing 76, May 2020), recent developments in the Mexican regulatory system for the assessments of innovative new products have had a negative impact on the availability of innovative medicines for the Mexican public.

The original Briefing addressed the impact of suspending in May 2019 the activities of the New Molecules Committee (NMC) on the Mexican therapeutic landscape. We investigated the extent to which new drugs approved by the US FDA have also been approved by other important jurisdictions, specifically Mexico, Brazil, Europe, and Canada. In this manner, we gained a better understanding of the impact the absence of NMC evaluation sessions is having on the availability of innovative new medicines for Mexican patients.

In this Addendum to R&D Briefing 76, we further compare the regulatory activities in Mexico in the context of the Level IV PAHO National Regulatory Agencies of Regional Reference (NRAr), excluding Cuba and Colombia. We have compared the regulatory approval activity of a cohort of products approved in the US FDA by Argentina, Brazil, Canada, Chile and Mexico. These countries account for over 75% of the population in the Americas and 93% of the region's GDP. Regulatory authorisation information for Mexico has been updated with the latest data available as of 31 May 2020.

Our updated observations reinforce those observed in our initial investigation, that despite some indication of a start of activity with the NMC, products are not progressing through the Mexican regulatory process efficiently. Further, when a similar cohort of products is compared across countries, we have observed a more limited availability of products in Mexico compared with some of the countries included in this analysis. The regulatory approval system that had been in place prior to the NMC ceasing its activities in 2019 provided an opportunity for innovative products to obtain regulatory approval, despite recognised long timelines and process inefficiencies. These current findings extend our previous observations that the current situation has severely curtailed the availability of innovative products; this situation could be improved by the full-scale reinstitution of the NMC, the more effective use of accelerated pathways and by prioritising the assessment of critically important new medicines.

El acceso a medicamentos innovadores es clave para mejorar la salud de toda la población, para reducir los tiempos de hospitalización, la morbilidad y la mortalidad de un país. Como se mostrado en la versión original de este Informe (CIRS R&D Briefing 76, May 2020), la evaluación reciente del sistema regulatorio mexicano respecto a la evaluación de nuevos medicamentos innovadores conlleva un impacto negativo en la salud de la población mexicana.

El Informe original analizó el impacto de la suspensión de las actividades del Comité de Moléculas Nuevas (NMC, por sus siglas en inglés) sobre el horizonte terapéutico de México. Se investigó en qué medida los nuevos medicamentos que han sido autorizados por la agencia de los Estados Unidos (FDA) han obtenido también registro sanitario en otras jurisdicciones importantes; en particular, comparamos el caso de México con los de Brasil, Europa y Canadá. De esta forma se logra comprender mejor el impacto que ha tenido la falta de reuniones de evaluación del NMC en la disponibilidad de nuevos medicamentos para los pacientes de México.

En este addendum al R&D Briefing 76, comparamos la actividad regulatoria de México dentro del contexto de las autoridades Nivel IV de la Organización Panamericana de la Salud que son Autoridades de Referencia Regional (NRAr), excluyendo a Cuba y Colombia. Los países considerados son Estados Unidos, Brasil, Canadá, Argentina, Chile y México. Estos países representan más del 75% de la población total del continente y 93% del PIB total de la región. La información referente a medicamentos de México se actualizó y ahora incluye datos el 31 de mayo de 2020.

La nueva información refuerza los hallazgos de hace un mes, esto es, que a pesar de que hay alguna indicación de que el NMC ha iniciado actividades, no se observa que los productos estén avanzando eficientemente a través del proceso regulatorio de México. Además, al comparar la disponibilidad de los mismos productos entre los países, se observa más limitada la disponibilidad de productos en México que en los nuevos países que se han incluido en este análisis. La operación del sistema de autorización regulatoria previo a la suspensión de actividades del NMC, aun considerando los largos tiempos de evaluación e ineficiencias en el proceso, sí ofrecía una oportunidad para que productos innovadores obtuvieran un registro sanitario. Los nuevos hallazgos refuerzan nuestras observaciones previas respecto a que la situación actual ha reducido drásticamente la disponibilidad de medicamentos innovadores. Esta situación puede mejorar si se restablecen las reuniones del NMC, y se adoptan procesos acelerados de autorización sanitaria y/o se le asigna alta prioridad a la evaluación de medicamentos innovadores que sean de importancia crítica.

ADDENDUM TO R&D BRIEFING 76

CIRS Centre for Innovation in Regulatory Science

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RDB 76: Objectives

To gain a better understanding of:

- the impact of changes in the Mexican regulatory environment on the availability of new medicines for Mexican patients
- the way ‘new medicines’ are defined
- the impact of suspending the activities of the New Molecules Committee (NMC)
- the extent to which new drugs approved by the US FDA have been approved by other important jurisdictions specifically Argentina, Brazil, Canada, Chile, EMA and Mexico

What is a “New Medicine”?

Agency	Alternate terms	Small molecule	Bio-logic	Combination product	New therapeutic indication	Radio-pharmaceutical	Not previously approved in the country
COFEPRIS (Mexico)	New Molecule	X		X	X		X
FDA (USA)	New Drug, New Active Ingredient, New Molecular Entity	X		X	X		
EMA (EU)	New Active Substance (NAS)	X	X	X	X	X	X
Health Canada/ TPD	New Drug, New Active Substance, New Chemical Entity	X	X	X	X		X
ANVISA (Brazil)	New Medicinal Product	X	X				X

CIRS *R&D Briefing 76 – The impact of recent regulatory developments on the Mexican therapeutic landscape*. Liberti L and Alanis M. 2020.

COFEPRIS: New Medicine

Agency: COFEPRIS
Alternate names: New molecule, New Molecular Entity
Characteristics:

- Active ingredient or medicinal product that has no registration (Registro Sanitario) worldwide and that is to be registered in Mexico
- Active ingredient or medicinal product that is registered in other countries with limited clinical experience or controversial information, is not registered in Mexico and is intended to obtain a registration in Mexico
- Medicinal product to be used in combination of two or more active ingredients and that does not exist in the national market
- Active ingredient or medicinal product that is already marketed and to be registered for any other therapeutic indication
- Herbal and homeopathic medicines with Cannabis and other Therapeutic schemes and pharmaceutical forms

Sources: Decree Amending the Regulation of Health Sector Products (Art. 2 - XV) Jan 2, 2008 On Feb 23, 2012. Internal rules of operation of the New Molecules Committee and creating the subcommittee on Biologicals, 20 July 2018. Special Technical Opinion is defined and incorporated. August 1, 2018. Guidelines for the operation of the New Molecules Committee

CIRS *R&D Briefing 76 – The impact of recent regulatory developments on the Mexican therapeutic landscape*. Liberti L and Alanis M. 2020.

We observed across agencies

- The definition of a new medicine varies across jurisdictions influenced by regulatory approaches and risk perceptions of the agencies.
- A trend towards simplifying the definition by focusing on ‘new molecules’ while limiting the inclusion of other types of products or compounds.
- This is key to providing transparency around assessment pathways and processes.
- Ensuring alignment with global approaches can provide predictability and facilitate the integration of an agency into global regulatory submissions.

N=33 FDA approved cohort

Mexico

Submitted:	26
Not submitted:	5
Indeterminate:	2

Approved:	14 (54%)
In Review:	12 (46%)

Brazil

Submitted:	19
Not submitted:	
Indeterminate:	14

Approved:	17 (89%)
In Review:	2 (11%)

Argentina

Submitted:	23
Not submitted:	8
Indeterminate:	2

Approved:	20 (87%)
In Review:	3 (13%)

Chile

Submitted:	22
Not submitted:	9
Indeterminate:	2

Approved:	16 (73%)
In Review	6 (27%)

Canada

Submitted:	29
Not submitted:	4
Indeterminate:	0

Approved:	29 (100%)
In Review	0

CIRS (2020) *Addendum to R&D Briefing 76 – The impact of recent regulatory developments on the Mexican therapeutic landscape*.

By 31 December 2019 for all countries except Mexico (May 30, 2020)

Target Regulatory Review Times

Country	Agency	Target agency times for standard review (calendar days)
USA	**FDA** (Food and Drug Administration)	**60 days filing** Determination plus 300 days for review
Argentina	**ANMAT** (Administración Nacional de Medicamentos, Alimentos y Tecnología Médica)	**168 days** (120 workdays)
Brazil	**ANVISA** (Agência Nacional de Vigilância Sanitária)	**365 days**
Canada	**TPD** (Therapeutic Products Directorate)	**300 days**
Chile	**ISP** (El Instituto de Salud Pública de Chile)	**180 days** (does not include 10 days filing)
Mexico	**COFEPRIS** (Comisión Federal para la Protección contra Riesgos Sanitarios)	**180 days** (does not include NMC time)

CIRS (2020) *Addendum to R&D Briefing 76 – The impact of recent regulatory developments on the Mexican therapeutic landscape*.

Comparisons of Approval Times

	Number of approved products	Median approval time	Fastest approval time	Slowest approval time
FDA	33	240	57	1088
ANVISA	17	305	213	665
TPD	29	343	201	871
ANMAT	20	241	97	812
ISP / ANAMED	16	356	189	789
COFEPRIS	14	267 (567*)	32 (332*)	717 (1017*)

* Estimated including 300 days of NMC time

CIRS (2020) *Addendum to R&D Briefing 76 – The impact of recent regulatory developments on the Mexican therapeutic landscape*.

Lag Time

Defined here as: The time **from the approval** of a product by the FDA to the date of **approval in a target country** (the time patients need to wait until products reach approval in their country compared to the availability in the United States)

Median Lag Times:

ANMAT 287 days	ANVISA 298 days
COFEPRIS 473 days	ISP 502 days

Lag Time is **affected by**:

- sponsor's ability to support the regulatory filing in the specific country
- the commercial opportunity and prioritisation for the country
- product availability
- local regulatory requirements that may impact submissions

CIRS: RDB 51: Characterising the influenceRs of submission Lag Time for medicines in the Emerging Markets: Analysis of short and long Lag Time factors

We observed for COFEPRIS

Mexico represents an important market for multinational pharmaceutical companies to submit innovative medicines within the countries of the Latin American region based on number of submitted products.

- Of the 33 products approved by FDA, 22 (67%) benefitted from the use of an expedited review pathway. Of the 13 products that were approved by COFEPRIS by the end of 2019, none used an expedited assessment pathway.
- Of the 33 products approved by FDA, 13 (39%) were Orphans; all had expedited (Priority) review. Acalabrutinib and midostaurin were submitted to COFEPRIS as Orphans. Median approval time was 227 days (company and agency time) for the Orphan products at FDA and 249 days at COFEPRIS.
- If the low approval rate prevails submission emphasis could change resulting in ore delay for Mexican patients to receive the benefits of innovative therapeutic alternatives.

	Topic*	Speaker
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	RDB 76: Objectives and methodology,	Dr Lawrence Liberti
	RDB 76: Analysis and main results,	Dr Lawrence Liberti and Dr Mario Alanis
	Participant Reflections	
	An Question and Answer Chat	
	Summary and closing comments	

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*Questions and comments will be taken at the end of each individual presentation

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