REAL WORLD EVIDENCE

RWE4Decisions

PUBLIC WEBINAR SERIES

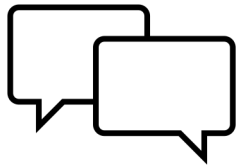
Supporting HTA/Payer decision-making: Spotlight on national health data initiatives from Finland, Spain and France

Tuesday, 3 May | 15.00-16.30 CEST

@RWE4Decisions

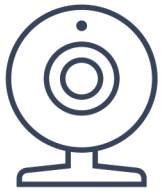
RWE4Decisions Public Webinar Series

Housekeeping rules



Use the **Q&A function** for questions and the chat for other comments – you can **comment and upvote** other participants' questions

Don't forget to mention your **affiliation** when asking a question



The meeting is being **recorded** and will be shared publicly

Today's webinar is scheduled for **1.5 hours**

RWE4Decisions: A payer-led initiative, a multi-stakeholder learning network about use of RWE for highly innovative technologies

What?

Pragmatic and agile Learning Network about use of Real-World Evidence (RWE) to inform HTA/Payer Decisions

Why?

Highly innovative technologies often have accelerated development pathways and immature clinical evidence - could robust RWE fill the gaps to help demonstrate value?

How?

Payer-led, multi-stakeholder
Built on principles of Collaboration and Transparency

Added Value?

'Learning by doing' approach

- share experience, pool resources
- sandbox approach - real problems, light-touch solutions
- build trust

Public outputs and events
Policy engagement – CAPR, Nordic Alliance, BENELUXAI, EU and beyond

Spotlight on Finland

Secondary use of health and social care data in Finland

RWE4Decision webinar

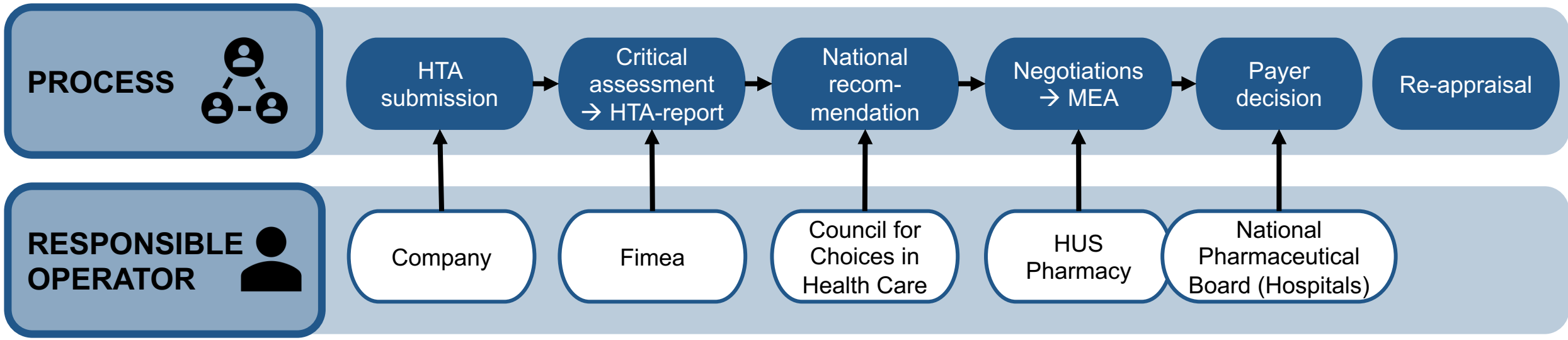
3.5.2022

Lääkealan turvallisuus- ja kehittämiskeskus
Piia Rannanheimo
03/05/2022

RWE APPLICATIONS – EVIDENCE GENERATION THROUGHOUT A PRODUCT'S LIFECYCLE

Image courtesy of Business Finland

Managed entry process for new hospital medicnes – How does the Finnish data ecosystem support HTA/payer decion making?



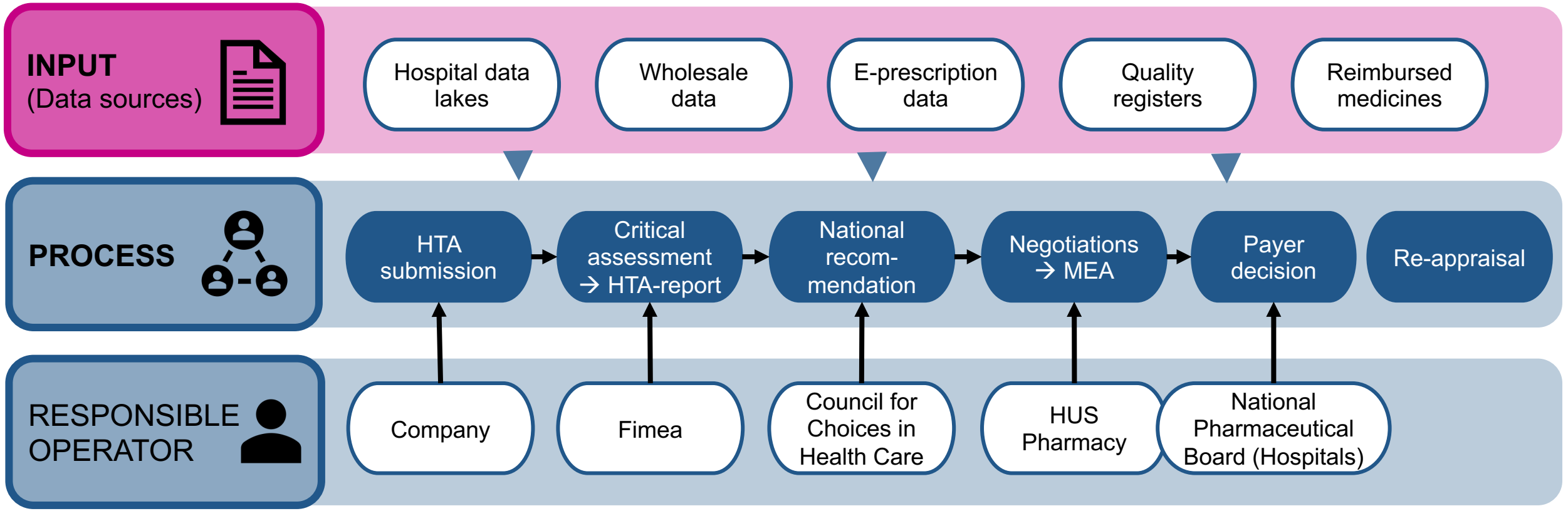
Finnish data sources

National Registers	Biobanks	Hospital data lakes	Laboratory data	Examples of quality registers
• Drug Reimbursement Register (Kela) • Drug Prescription Center (Kela) • Care Register for Health Care (THL) • Benefits Register (Kela) • Cause of Death Register (Statistics Finland)	• Auria biobank • Arctic Biobank – University of Oulu • Helsinki Biobank • Hematological Bioband (FHRB Biobank) • Biobank of Eastern Finland • Northern Finland Biobank • Finnish Clinical Biobank Tampere • Etc.	• Auria (TYKS) • HUS • TAYS • KYS • OYS	• HUSLAB • TYKSLAB • ISLAB • NORDLAB • FIMLAB	• Diabetes register • HIV register • Registry for kidney diseases • Psychosis care register • Back register • Coronary artery disease register • Oral and dental care register • Intensive care register • Rheumatology register

Examples Finnish data sources

Register / data source	Description
E-Prescription Center	• **Register holder:** The Social Insurance Institution of Finland (Kela) • **Key data content:** all electronic prescriptions: e.g. ATC codes, product names, prescription dates, dose, quantity • **Data availability:** since 2010, became mandatory for public and private healthcare in 2017
Hospital Data Lakes	• **Register holder:** Hospital Districts of Helsinki and Uusimaa, Northern Savo, Nothern Osterbothnia, Pirkanmaa, and Southwest Finland. • **Key data content:** All demographic and clinical data in patients health records that can be combined with data from different operational sources of the secondary care. Data consists of enormous amounts of structured and unstructured data, including patient chart texts, laboratory records, imaging data, prescribed medications (including hospital-administered), data on HCRU and related costs, diagnoses (ICD-10) and procedures • **Data availability:** Availability of variables varies between the hospitals

Managed entry process for new hospital medicnes – How does the Finnish data ecosystem support HTA/payer decion making



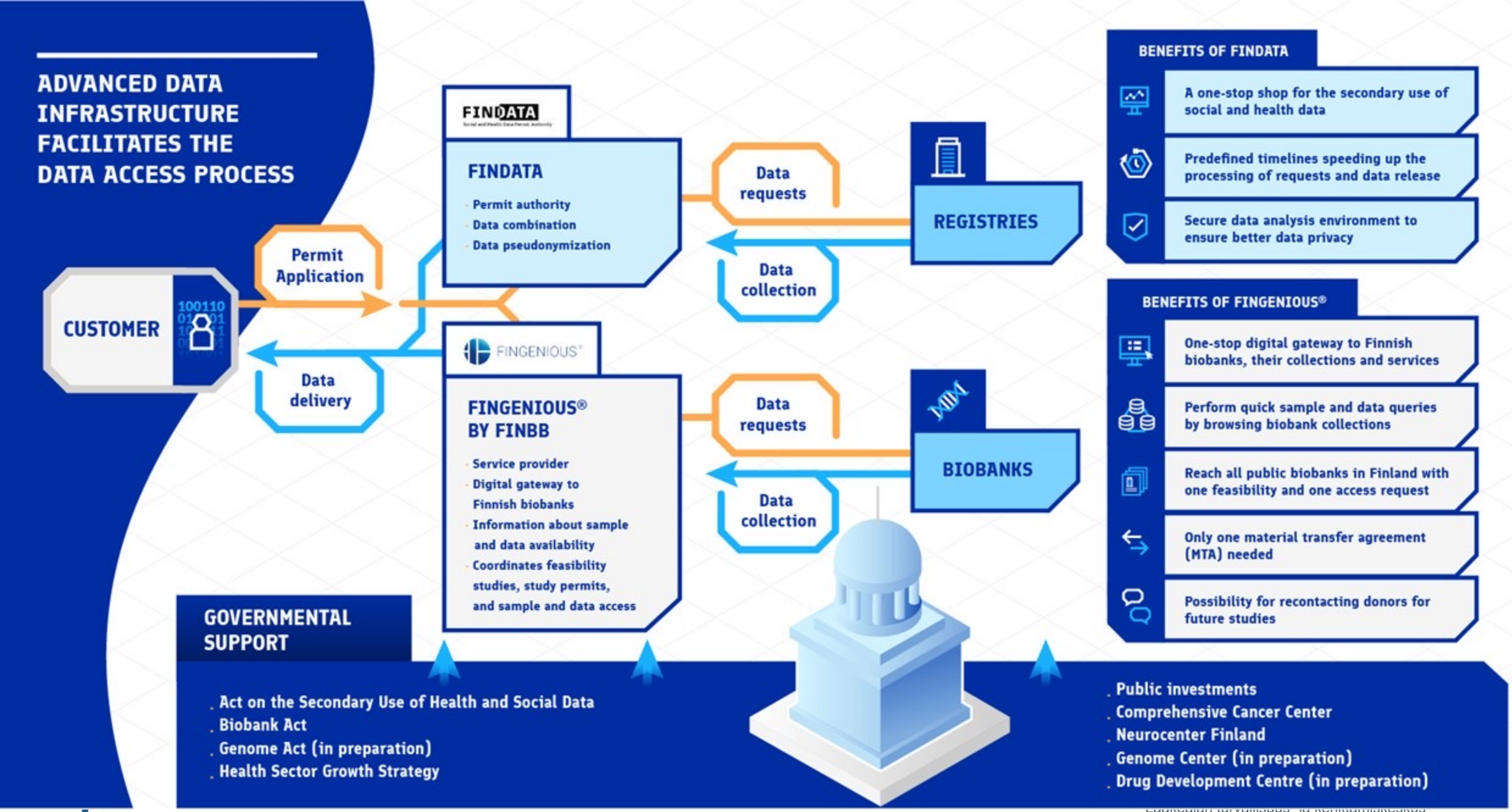


Image courtesy of Business Finland

fimea

Image courtesy of Business Finland

Lääkealan turvallisuus- ja kehittämiskeskus
Piia Rannanheimo
03/05/2022

Reference:

https://www.businessfinland.fi/en/whats-new/news/2022/finland--a-treasure-trove-for-real-world-evidence-rwe-research-and-innovation

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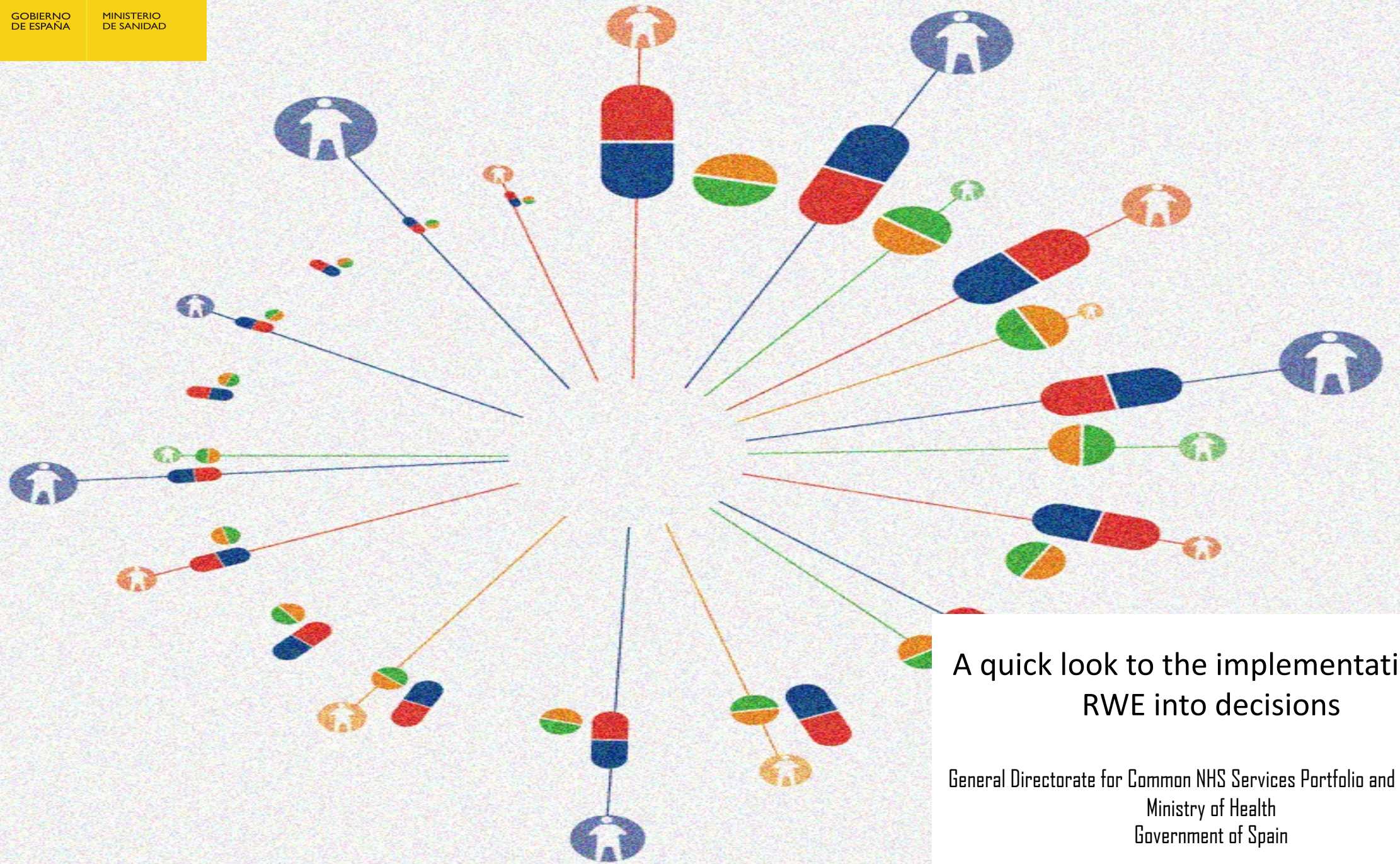
MINISTERIO DE SANIDAD



A quick look to the implementation of RWE into decisions

General Directorate for Common NHS Services Portfolio and Pharmacy
Ministry of Health
Government of Spain

Welcome to VALTERMED

An information system to determine the therapeutic value in real clinical practice of medicines with a high health and economic impact on the NHS

A quick look

- The context
- Current use of RWE collected in Valtermed
- Building the administrative resolution
- Successes
- Hurdles

The Context

- High uncertainty about the clinical outcomes:
  - Reduced clinical benefit
  - Underrepresentation of population
  - Surrogates
  - High risk of bias
- Valtermed currently includes 20 drugs (14 protocols)
- Every drug is linked to a PHARMACOCLINICAL PROTOCOL designed by consensus between experts from the Autonomous Communities of Spain, professional societies and the manufacturer
- Protocols and reports can be found here:

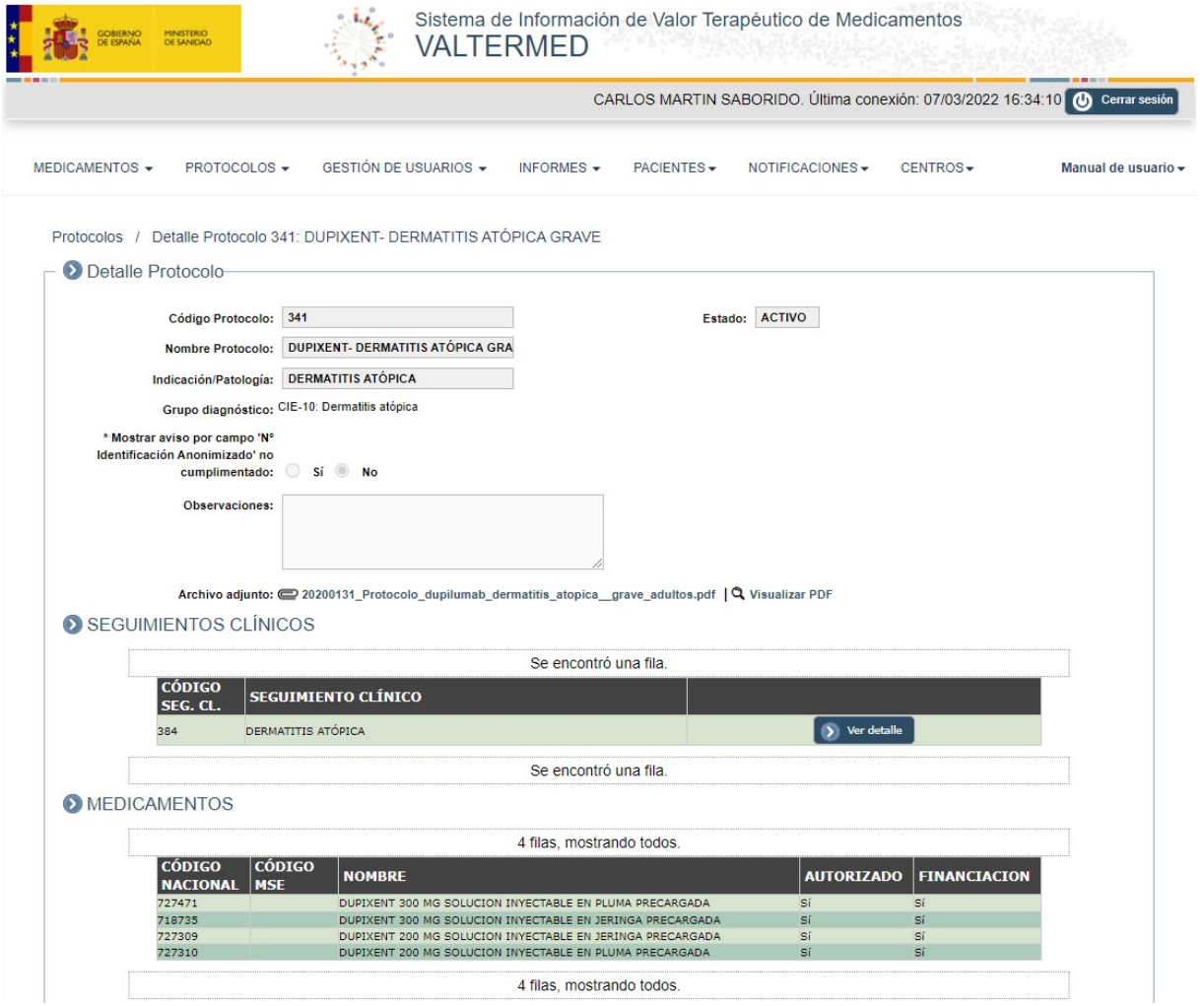
https://www.sanidad.gob.es/profesionales/farmacia/valtermed/home.htm

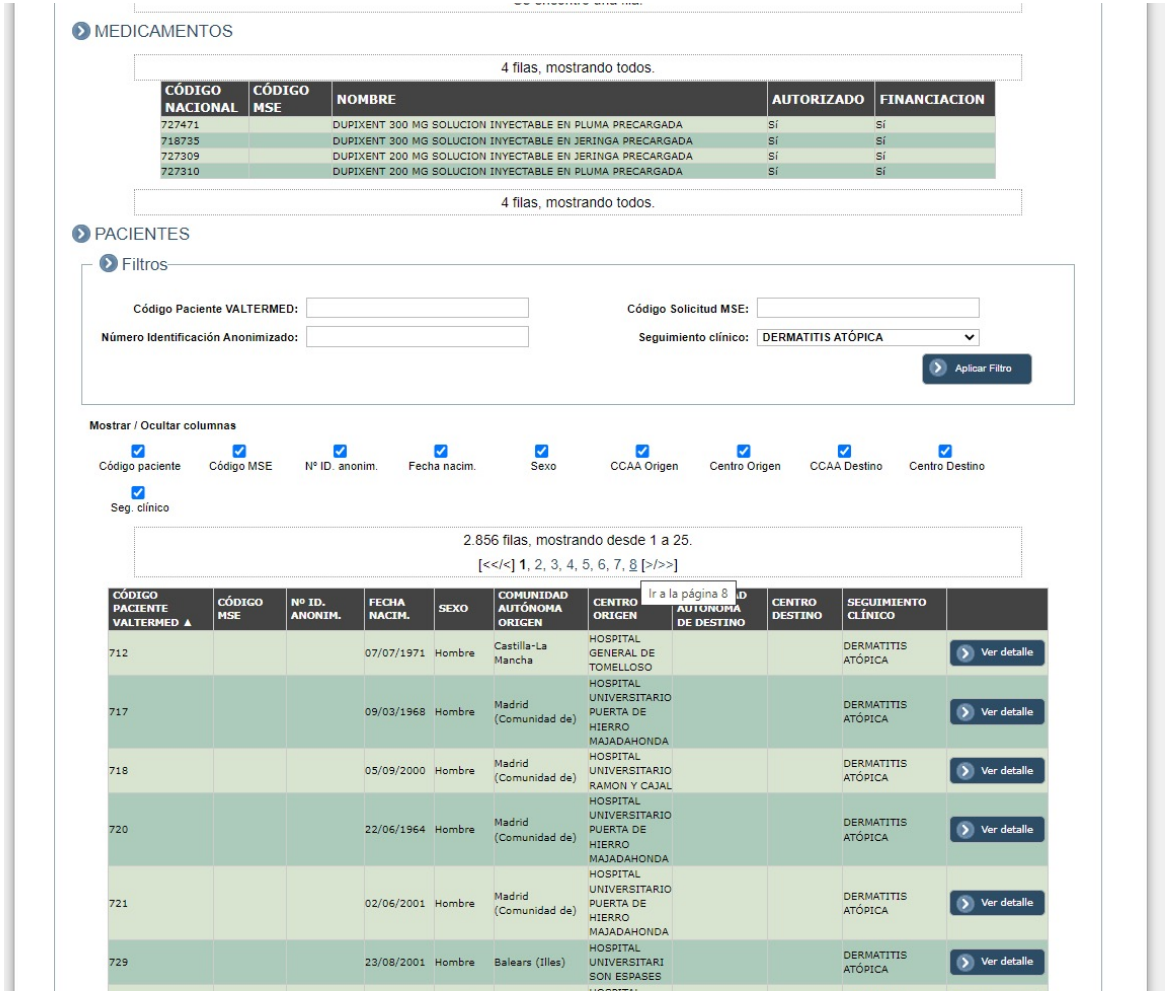
The Drugs in Valtermed

Drug	Indication(s)	Protocol
Crysvita (burosumab)	X-linked hypophosphatemic rickets in children	Yes
Veklury (remdesivir)	COVID-19	Yes
Besponsa (inotuzumab ozogamicin)	Acute lymphoblastic leukaemia	Yes
Dupixent (dupilumab)	Severe atopic dermatitis	Yes
Kymriah (Tisagenlecleucel)	Acute b-cell lymphoblastic leukaemia/ large b-cell lymphoma	Yes
Yescarta (axicabtagene ciloleucel)	Large b-cell lymphoma/ primary mediastinal b-cell lymphoma	Yes
Orkambi (LUMACAFTOR/IVACAFTOR)/Symkevi (tezacaftor + ivacaftor)/Kalydeco (Symkevi +ivacaftor)	Cystic fibrosis	Yes
Alofisel (darvadstrocel)	Complex perianal fistulas in Crohn's disease	Yes
ARI-0001 (CAR-T)	Acute b-cell lymphoblastic leukaemia	Yes

		Protocol
Oluminat (Baricitinib)	Severe atopic dermatitis	No
Rinvoq (Upadacitinib)	Severe atopic dermatitis	No
Adtralza (Tralokinumab)	Severe atopic dermatitis	No
Zolgensma (Onasemnogén abeparvovec)	Spinal Muscular Atrophy	Yes
Kaftrio (ivacaftor, tezacaftor y elexacaftor)	Cystic fibrosis	No
Venclyxto (venetoclax)	Chronic lymphocytic leukemia	No
Polivy (polatuzumab vedotin + bendamustine + rituximab)	Large b-cell lymphoma	Yes
Vestronidase alfa	Mucopolysaccharidosis VII	Yes
Tecentriq (atezolizumab)	Extensive-stage small cell lung cancer /Triple-negative breast cancer	Yes
Luxturna (voretigene neparvovec)	Inherited retinal dystrophy	Yes

Dupilumab in severe atopic dermatitis in adult patients in the NHS





Dupilumab in severe atopic dermatitis in adult patients in the NHS

	A	B	C	D	E	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA
1	CÓDIGO PACIENTE VALTERMED	Edad checked	EDAD	FECHA NACIMIENTO	SEXO	COMUNIDAD AUTÓNOMA DESTINO	CENTRO DESTINO			SEGUIMIENTO CLÍNICO		Edad igual a 18 años o más	EASI mayor o igual a 21	PGA mayor o igual a 3	BSA mayor o igual al 10%	Candidatos a tratamiento sistémico	Refractarios a medicación tópica	Respuesta insatisfactoria o contraindicación al tratamiento con ciclosporina	Historial de inmunosupresión	Tratamiento sistémico con antimicrobianos en las 2 semanas previas a iniciar tratamiento	VIH+	Infección activa por virus Hepatitis B	Infección activa por virus Hepatitis C
2	9006	23,00	23,00	17/07/1999	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
3	9005	27,00	27,00	19/04/1995	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
4	9004	34,00	34,00	01/05/1988	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	S	N	N	N	N
5	9003	21,00	21,00	14/03/2002	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
6	8987	58,00	58,00	20/02/1965	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
7	8969	25,00	25,00	09/03/1998	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
8	8943	42,00	42,00	12/11/1980	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
9	8927	30,00	30,00	30/03/1992	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
10	8901	51,00	51,00	15/07/1971	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
11	8900	51,00	51,00	06/12/1971	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	S	N	N	N
12	8899	21,00	21,00	26/05/2001	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
13	8895	39,00	39,00	16/02/1984	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
14	8886	41,00	41,00	02/06/1981	Mujer					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N
15	8880	53,00	53,00	09/12/1969	Hombre					DERMATITIS ATÓPICA		S	S	S	S	S	S	S	N	N	N	N	N

Current use of RWE collected in Valtermed

- The data collected in Valtermed are linked to the evaluation of the financial conditions agreed in the administrative resolution
- The administrative resolution establishes the criteria of reimbursement using the RWE collected in Valtermed
- The administrative resolution may include a review clause at any time point
- We currently have reviewed 2 protocols after 12 months of data collection and the PPP is over

Administrative Resolution Dupilumab

MINISTERIO
DE SANIDAD, CONSUMO
Y BIENESTAR SOCIAL

SECRETARÍA GENERAL DE SANIDAD Y CONSUMO

DIRECCIÓN GENERAL DE CARTERA BÁSICA DE SERVICIOS DEL SISTEMA NACIONAL DE SALUD Y FARMACIA

R/ 18159/2019

- Pacientes que alcancen el EASI-50 respecto a su valoración inicial y
- Reducción en el PGA ≥ 2 puntos vs. puntuación inicial basal.

En los pacientes que no se cumplan las variables anteriores se les considerará no respondedores y será interrumpido su tratamiento.

Las mediciones se realizarán a la semana 16, 24 y 52, con una desviación justificada de ±2 semanas, y las condiciones de pago son las siguientes:

3. Condiciones de pago.

[redacted]

- Semanas 0-16

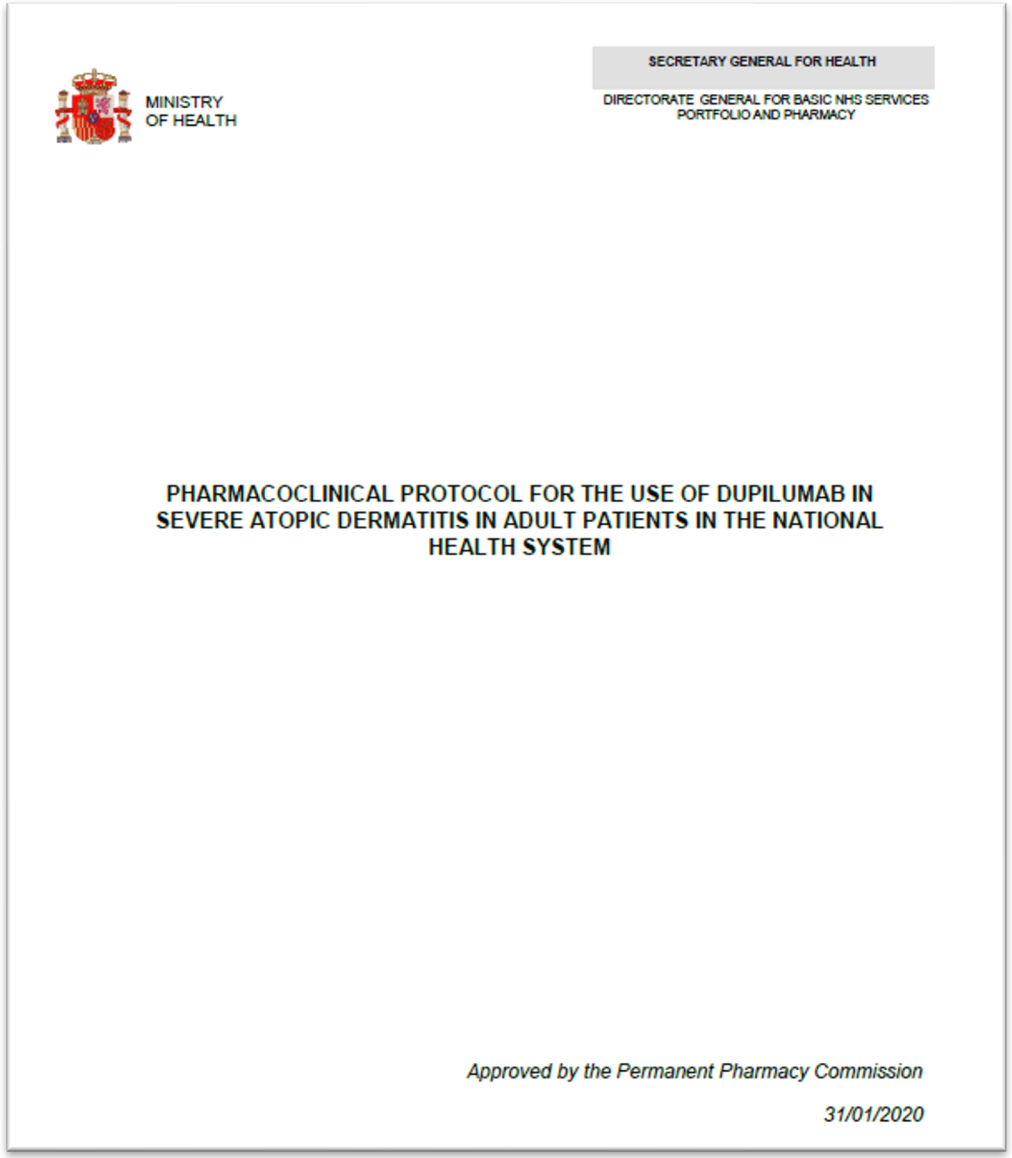
El SNS no realizará ningún pago al inicio del tratamiento hasta la semana 16.

En la semana 16 se procederá a la evaluación de la respuesta y si cumplen los criterios para considerarse respondedores, el SNS realizará el pago correspondiente al tratamiento para estas 16 semanas (a excepción de las 2 jeringas empleadas como dosis de carga, que serán asumidas por la compañía), lo que se corresponde a 7 jeringas.

Building the administrative resolution

- Administrative resolutions are built on a case-by-case basis, so there is not a general rule
- A minimum set of outcomes (effectiveness and safety) to assess the value of the drug is included in the administrative resolution
- Current RWE based designs:
  - A percentage of the manufacturer requested price per patient when data collection starts, then a pay-per-performance (PPP) for the remaining amount under the administrative resolution conditions.
  - 100% PPP :
    - All or Nothing attached to a unique response variable (pay back)
    - PPP by milestones: % of price per milestone achieved
  - Loading dose free of charge and maintenance using a PPP scheme

Dupilumab in severe atopic dermatitis in adult patients in the NHS



MINISTRY OF HEALTH

SECRETARY GENERAL FOR HEALTH

DIRECTORATE GENERAL FOR BASIC NHS SERVICES PORTFOLIO AND PHARMACY

PHARMACOCLINICAL PROTOCOL FOR THE USE OF DUPILUMAB IN SEVERE ATOPIC DERMATITIS IN ADULT PATIENTS IN THE NATIONAL HEALTH SYSTEM

Approved by the Permanent Pharmacy Commission

31/01/2020

5. OUTCOME VARIABLES (BASED ON OBJECTIVES INCLUDED IN THE PAYMENT-BY-RESULTS AGREEMENT)

Responders will be considered those patients who at 16 weeks meet the following results (both) and where these are maintained in the measurements at 24 and 52 weeks:

- ✓ Patients reaching EASI-50 from baseline and
- ✓ Reduction by ≥ 2 PGA points from baseline.

Patients who do not meet the above variables will be considered non-responders and their treatment will be discontinued.

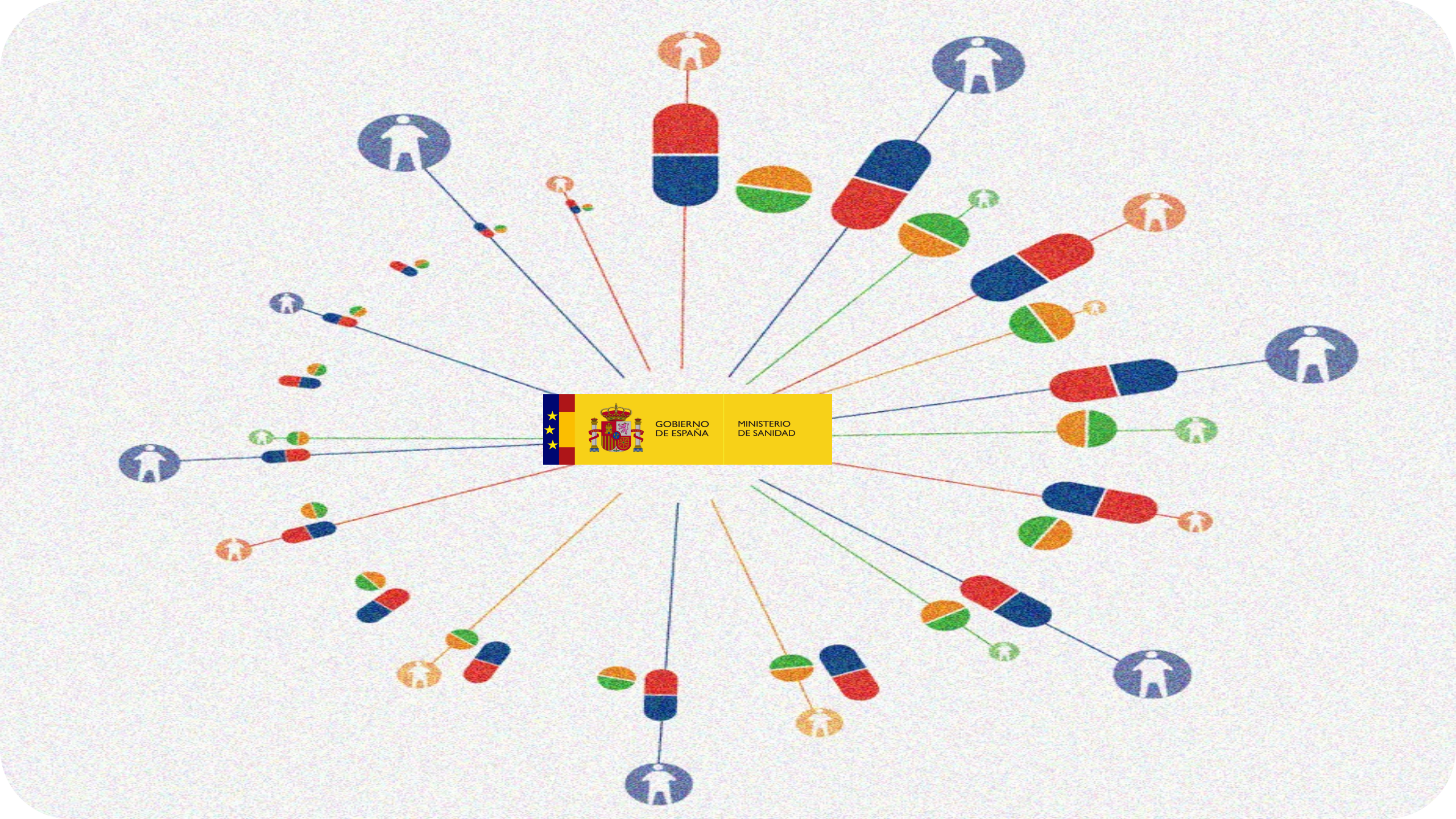
Measurements will be made in week 16, 24 and 52 with a justified deviation of ±2 weeks.

Successes

- Good collection of data per disease/condition: e.g. atopic dermatitis
- This allows use as real-world comparator for new drugs for the same condition
- An agreed protocol with a follow-up commission at an Autonomous Communities level including the manufacturer
- Availability of epidemiological lacking data: e.g. Budget Impact Analysis
- Valtermed is a modular information system: Quality of life module to be added shortly
- All Protocols are translated into English
- Publication of results: evidence generation

Hurdles

- Collection difficulties due to clinicians workload: double entry
- Balancing: “ease of use for clinicians” and “ease of data analysis”
- We expect to address this in the following evolutionary developments:
  - Web services to send large amounts of data
  - Application programming interfaces linked to electronic medical records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Evidence of patient benefit: the importance of patient organizations' involvement

Jean-Pierre THIERRY

RWE4Decisions REAL WORLD EVIDENCE

Public Webinar Series: National health data initiatives in Finland, Spain and France

May 3 2022

- Senior medical advisor

France Assos Santé is the name chosen by the National Union of Registered Associations of Health System Users (89) (l'Union nationale des associations agréées d'usagers du système de santé) to publicize its activities as the organization of reference representing and defending the interests of patients and health system users. With a mission officially recognized by its inclusion in the public health code via the law of 26 January 2016, France Assos Santé was created in March 2017 building on more than 20 years of advocacy aimed at establishing and gaining recognition for robust interassociative user representation.

- Member of the "Transparency Committee" of the French HTA body "Haute Autorité de Santé"

Assess medicinal product with prior to inclusion in the list of reimbursable medicines (after or before a market approval by EMA/ANSM with the French Early Access Procedure formerly ATU.

- I have no conflict of interest to disclose

PUBLIC AND PATIENT INVOLVEMENT IN HTA

Objectives

- Give a voice to patients and public
- Use relevant information in the HTA process
- Collect and use balanced information
- Representativity (e.g. Including vulnerable groups)
- Transparency and fairness, ethical issues
- Adressing the Conflicts of Interest
- Increasing public confidence and trust in the healthcare system

PUBLIC AND PATIENT PARTICIPATION IN EUROPE HTA

2017

	England	Canada	Scotland	France	Germany
	NICE	CADTH	SMC	HAS	G-BA
Board membership					
member of Policy strategy meetings					
Committee membership				*	***
contribution by patients org and patients				**	
Patient experience formalized				**	
Training of participants					
Assessment of PPI				**	
	* 1 membre titulaire et 1 suppléant				
	** expérimental				
	*** ne vote pas				

PUBLIC AND PATIENT PARTICIPATION IN EUROPE HTA

2022

	England	Canada	Scotland	France
	NICE	CADTH	SMC	HAS
Board membership				*
member of Policy strategy meetings				
Committee membership				**
contribution by patients org and patients				
Patient experience formalized				
Training of participants				
Assessment of PPI				

* 1 Membre du college de la HAS

** 3 membres représentant des associations de patients (2 titulaires et 1 suppléant)
Sur 21 membres titulaires et 7 suppléants

PPI IN EUROPE HTA : future of Effectiveness studies ?

QUALITY OF LIFE and PPI

OECD Paris Meeting February 2017

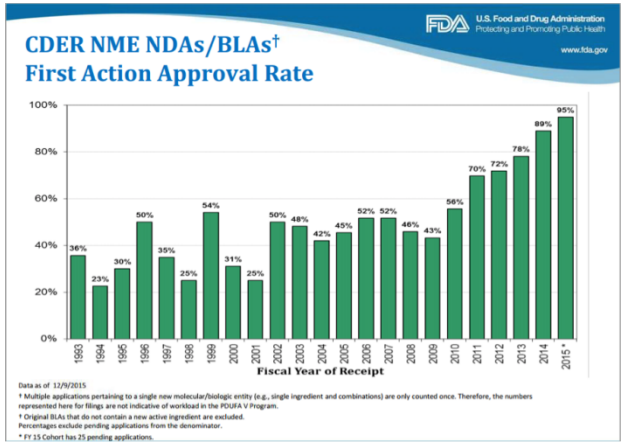
Reliance on **mortality rates and clinical indicators gives only a partial view of the value of health care**, they concluded. What people really care about is its impact on their wellbeing and their ability to play an active role in society, so that's what we should be measuring. And, of course, **the only way to do this is to ask patients themselves**.

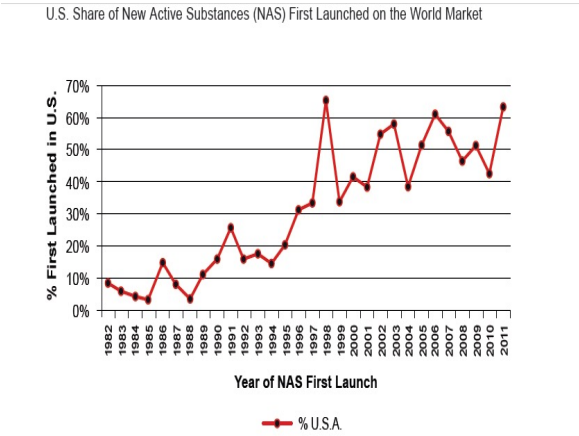
This groundbreaking ministerial statement endorsed plans for a major programme of work on **patient reported indicators of health system performance. Patient Reported Experience Measures (PREMs) and Patient Reported Outcome Measures (PROMs)** seem set to become the **new currency for comparative performance assessment, but they may have an even more important role in clinical care**.

Angela Coulter, PhD ***Measuring what matters to patients*** *(20 February 2017) BMJ 2017;356:j816*

RWD/RWE rationale and drivers

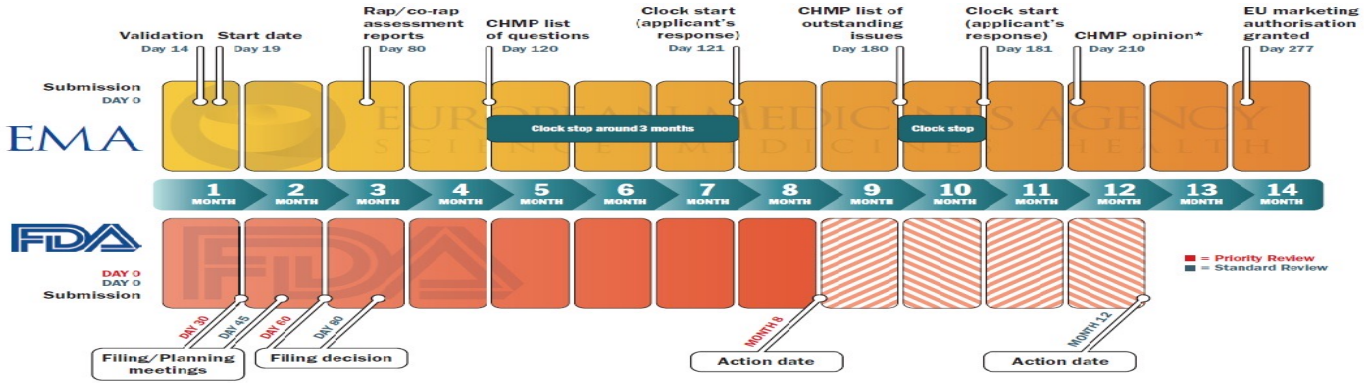
USA 21st Century Cures Act





EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EU Medicines Adaptive Pathways to Patients (MAPPS)



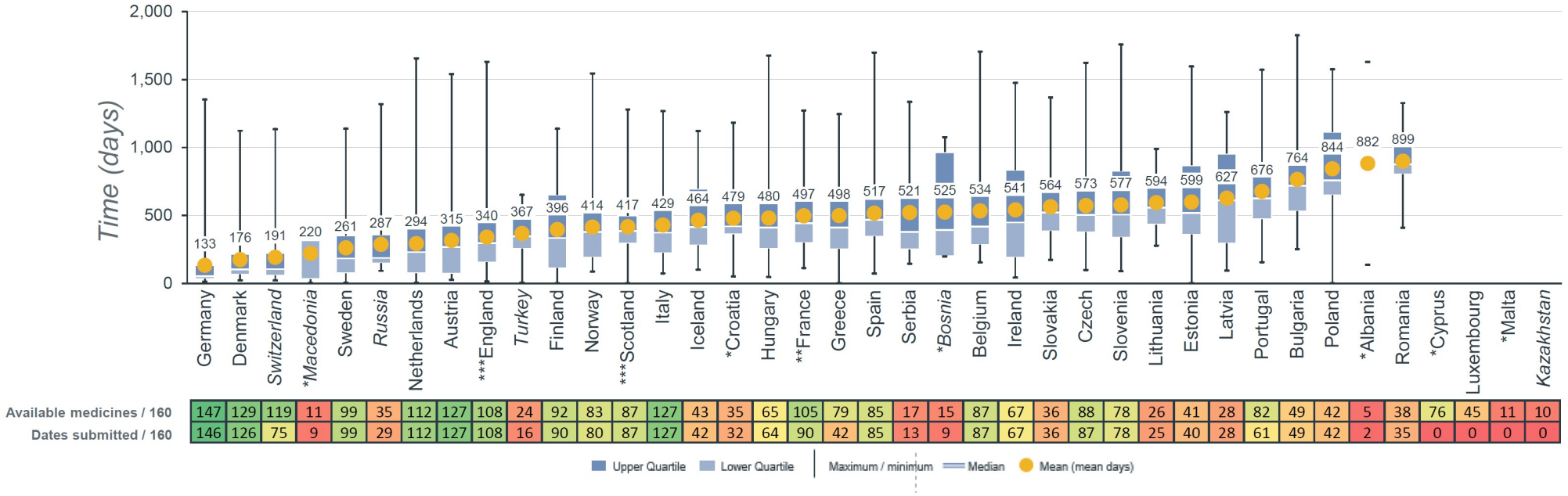
On average the EMA takes around six months more than the FDA to approve a new drug or new indication for a drug. This is mainly due to time lost to clock stop and the delay between getting a positive CHMP opinion and approval from the European Commission. Furthermore, in the US almost all cancer drugs are approved under priority review, whereas accelerated assessment is rarely used by the EMA

Source: CDER 21st Century Review Process (www.fda.gov); User Guide for Micro, Small and Medium-sized Enterprises (www.ema.europa.eu)

*Day 150 for accelerated assessment; Rap – Rapporteur

Time to availability (2017-2020)

The **time to availability** is the days between marketing authorisation and the date of availability to patients in European countries (for most this is the point at which products gain access to the reimbursement list†). The marketing authorisation date is the date of central EU authorisation in most countries, except for countries shown in italics where local authorisation dates have been used. Data is correct to 1st January 2022.

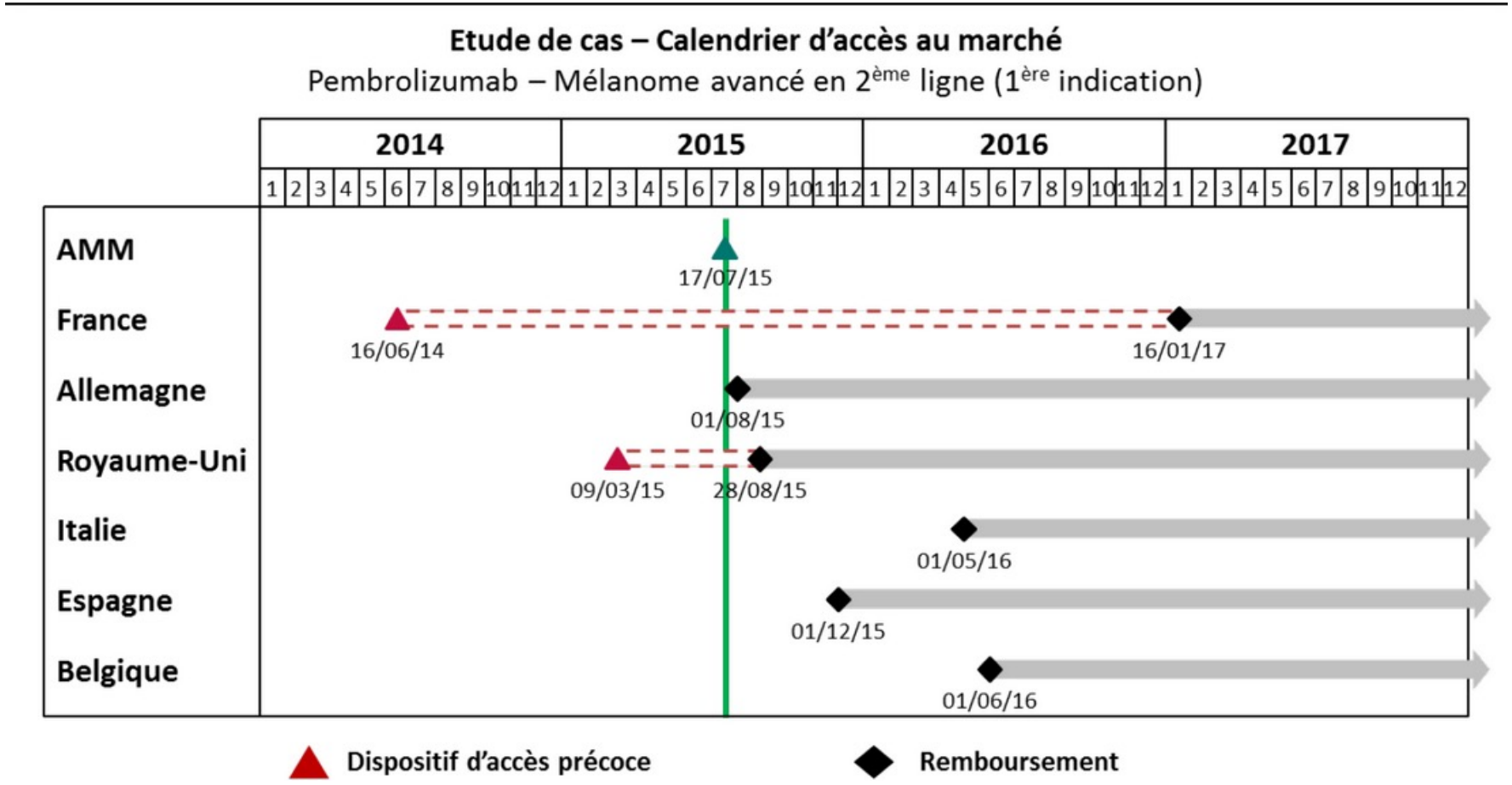


European Union average: 511 days (mean %) †In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative **For France, the time to availability (497 days, n=105 dates submitted) includes products under the ATU system (n=44 dates submitted) for which the price negotiation process is usually longer. If one considers that products under the ATU system are directly available (time to availability = 0), the average time to availability is 240 days. ***In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorisation but is not included within this analysis, and would reduce the overall days for a small subset of medicines.

IQVIA

EFPIA Patients W.A.I.T. Indicator 2021 Survey *Published April 2022 https://www.efpia.eu/media/636821/efpia-patients-wait-indicator-final.pdf*

Early access to cancer drugs



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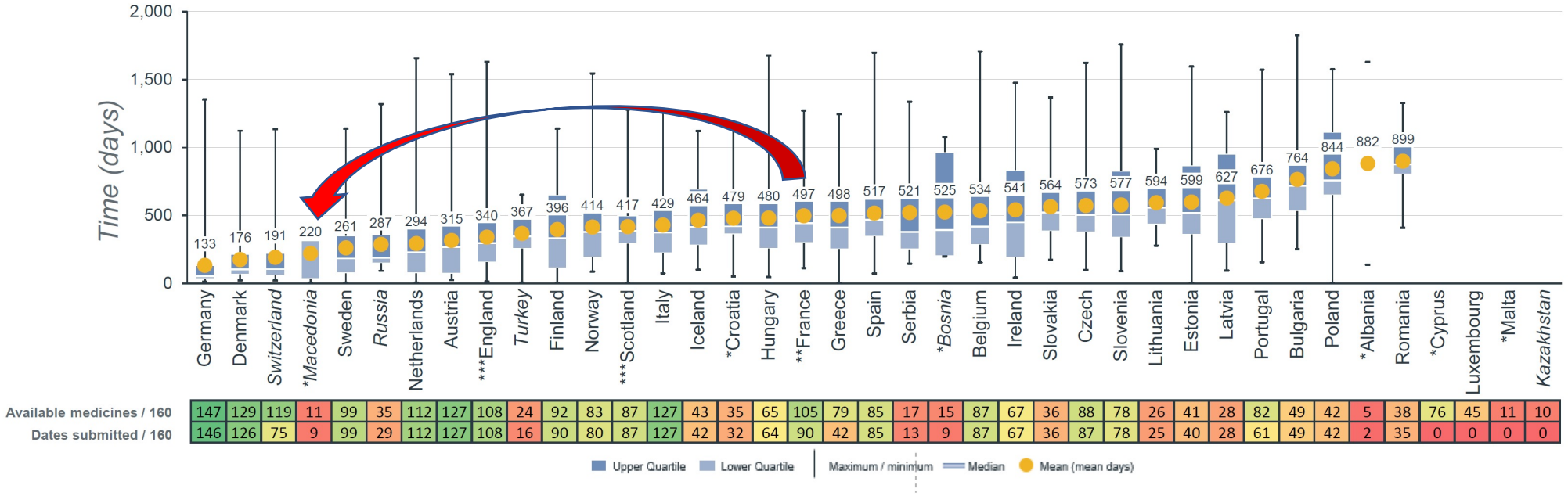

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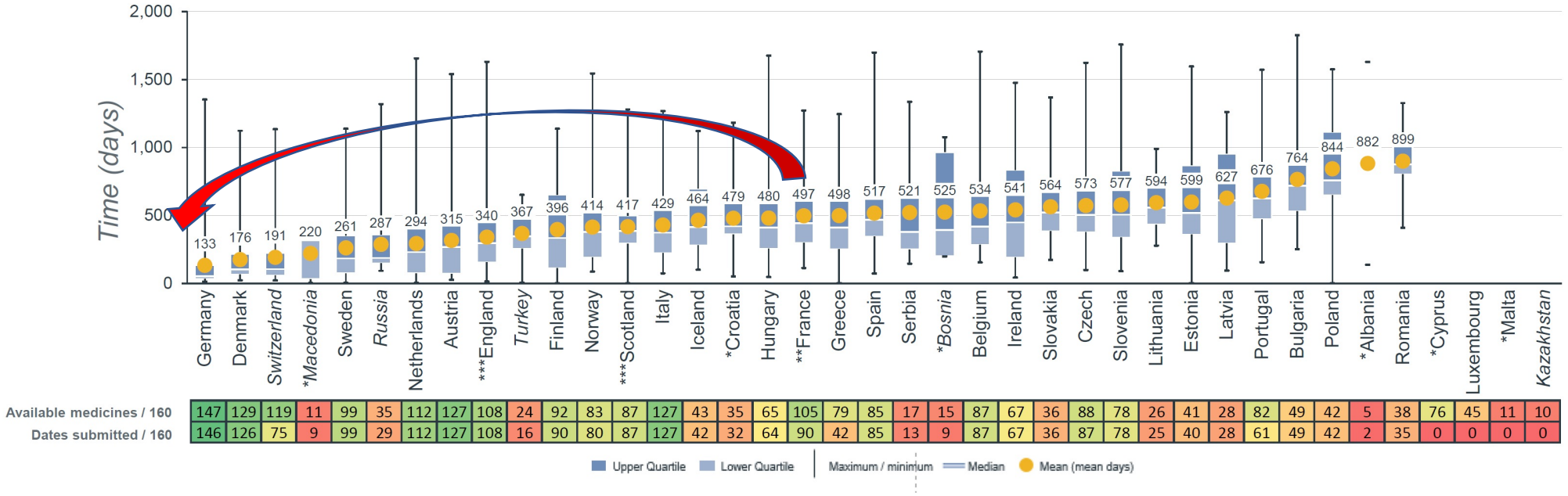
The **time to availability** is the days between marketing authorisation and the date of availability to patients in European countries (for most this is the point at which products gain access to the reimbursement list†). The marketing authorisation date is the date of central EU authorisation in most countries, except for countries shown in italics where local authorisation dates have been used. Data is correct to 1st January 2022.



European Union average: 511 days (mean %) †In most countries availability equates to granting of access to the reimbursement list, except in DK, FI, NO, SE some hospital products are not covered by the general reimbursement scheme. *Countries with asterisks did not complete a full dataset and therefore availability may be unrepresentative **For France, the time to availability (497 days, n=105 dates submitted) includes products under the ATU system (n=44 dates submitted) for which the price negotiation process is usually longer. If one considers that products under the ATU system are directly available (time to availability = 0), the average time to availability is 240 days. ***In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorisation but is not included within this analysis, and would reduce the overall days for a small subset of medicines.

IQVIA

EFPIA Patients W.A.I.T. Indicator 2021 Survey *Published April 2022 https://www.efpia.eu/media/636821/efpia-patients-wait-indicator-final.pdf*

RWD / RWE rationale

The case of cancer drugs

Traditional gold standard studies (randomized Phase III) have been replaced by phase II or more recently by Single arm trials starting with the most refractory patients.

RWD / RWE

Evaluate effectiveness of drugs (« postmarket »)

Effectiveness in the general population

Toxicity

Patient-centered indicators (PROMS, QoL)

Evaluate performance in the healthcare system

Access
Patient journey
Resources/organization
Evidence-practice gap

RWD/RWE

RCTs	Population-based studies
Precise measures of efficacy under ideal conditions	Difficulty in eliminating bias and confounders of effect
Poor measure of effectiveness under real life conditions	Can estimate effectiveness in the general population
Limited information on toxicity	Assess toxicity under real life conditions
Applicability to clinical practice can be limited	Evaluate uptake of treatment in general population

Booth & Tannock Brit J Cancer 2014

RWD/RWE

Going back to the Gold Standard may be an option

To Pazdur, the habit of starting with the most refractory patients has more to do with drugmakers' "love affair" with single-arm trials. And dilly-dally with entrant into an earlier treatment line "may actually be doing harm to the field."

"There is no reason to do a phase 2 trial of 100 patients other than getting an approval by the FDA on accelerated approval"
"After 30 patients [in a phase 1 trial], people should be moving to a randomized setting."

https://www.fiercebiotech.com/biotech/fda-oncology-chief-eyes-accelerated-approval-earlier-cancer-treatment-under-planned-project
April 6, 2022

RWD/RWE is a challenging endeavour

- Methodological issues vs RCTs
- Long life cycle (IT projects)
- Secondary use of relevant data when available
- Interoperability issues
- Investment in Big Data infrastructure
- Workload issues (now critical in the post-pandemic, era)
- Avoidance of duplication, fragmentation and wastes.
- Independance and transparency
- GDPR and data trajectory (cloud)

RWE should remain a priority of Public Health Policy and not only for the validation – or invalidation – of expedited approved drugs but to ensure a better quality and safety of care.

Thank you

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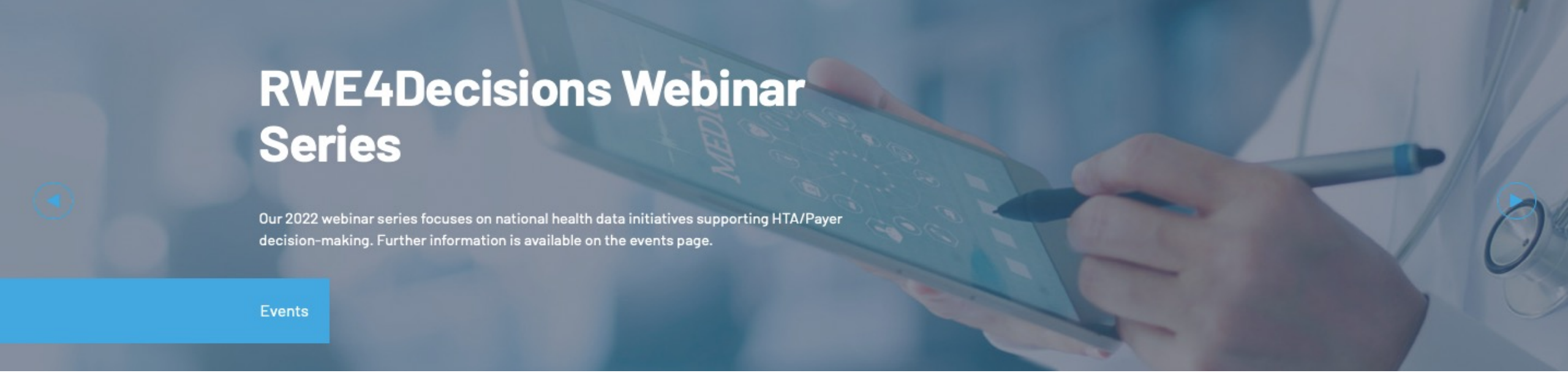

Thank you for your attention!

The recording & webinar report will be available on the website: www.rwe4decisions.com

For any questions or suggestions, please email secretariat@rwe4decisions.com

Next Public Webinar in September 2022

RWE Symposium on 24 November 2022 (in-person, Brussels)

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