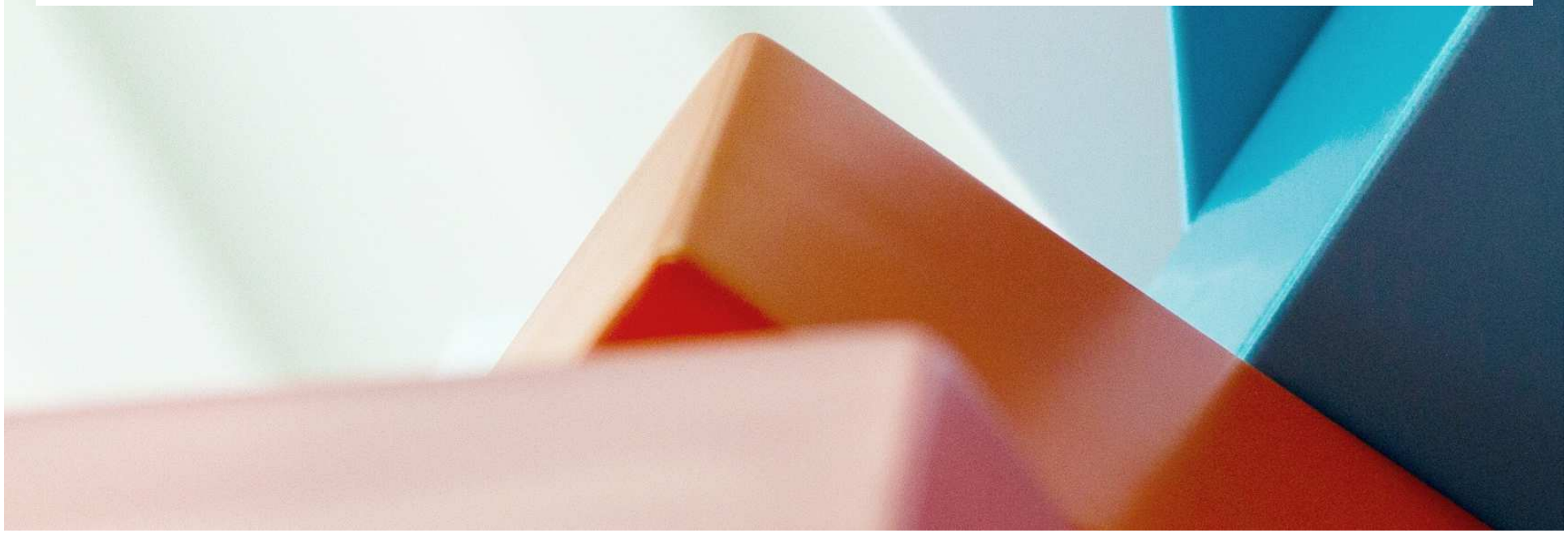
Federal Institute
for Drugs
and Medical Devices

19. DGRA Jahreskongress

23.-24.05.2017, Bonn

View of a national competent authority

Prof. Dr. Karl Broich



Agenda

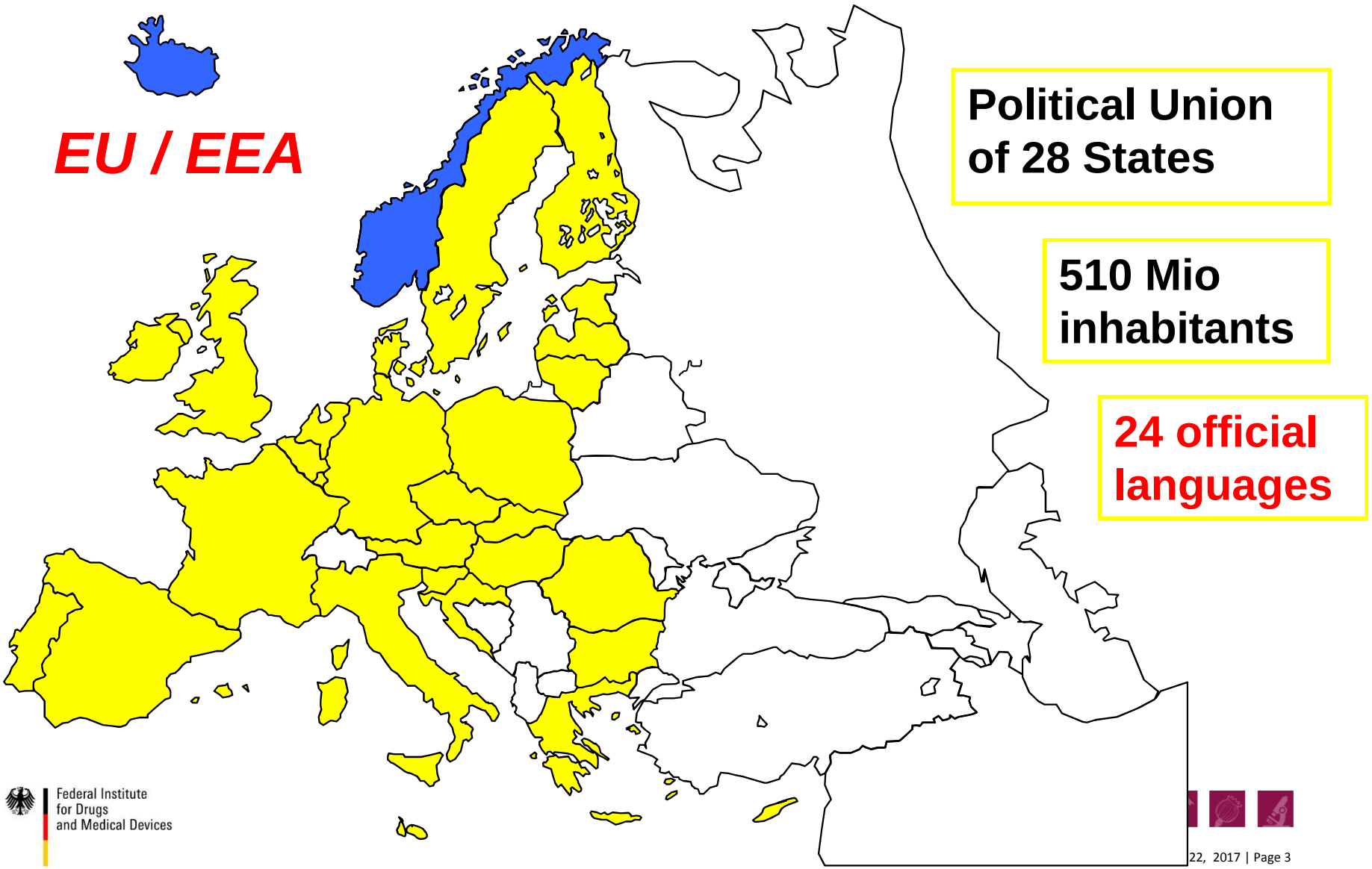
What means Brexit to us?

Preparedness in general

Workload and Procedures

Collaboration EMA and NCAs

“United in Diversity“



Political Union of 28 States

510 Mio inhabitants

24 official languages

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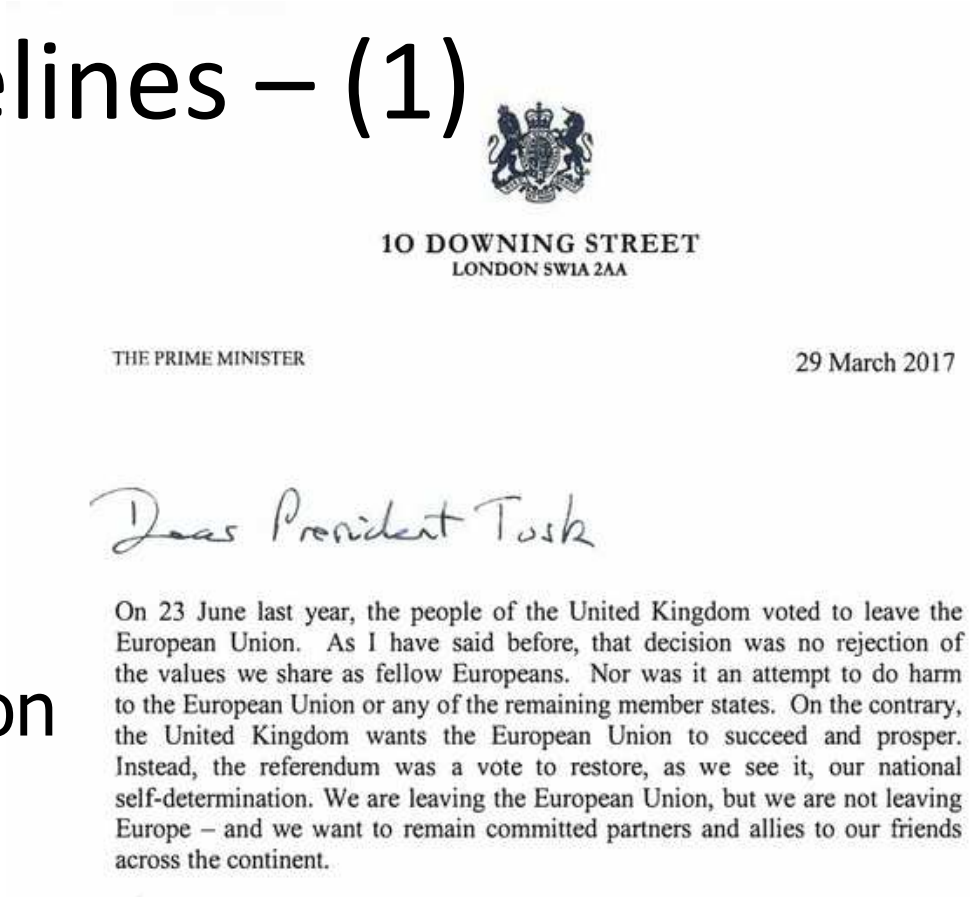
Timelines – (1)

- ✓ European Union (Notification of Withdrawal) Bill 2016-17
- ✓ Article 50 Notification 29th March 2017

- 2 year negotiations – 29th March 2019



10 DOWNING STREET
LONDON SW1A 2AA

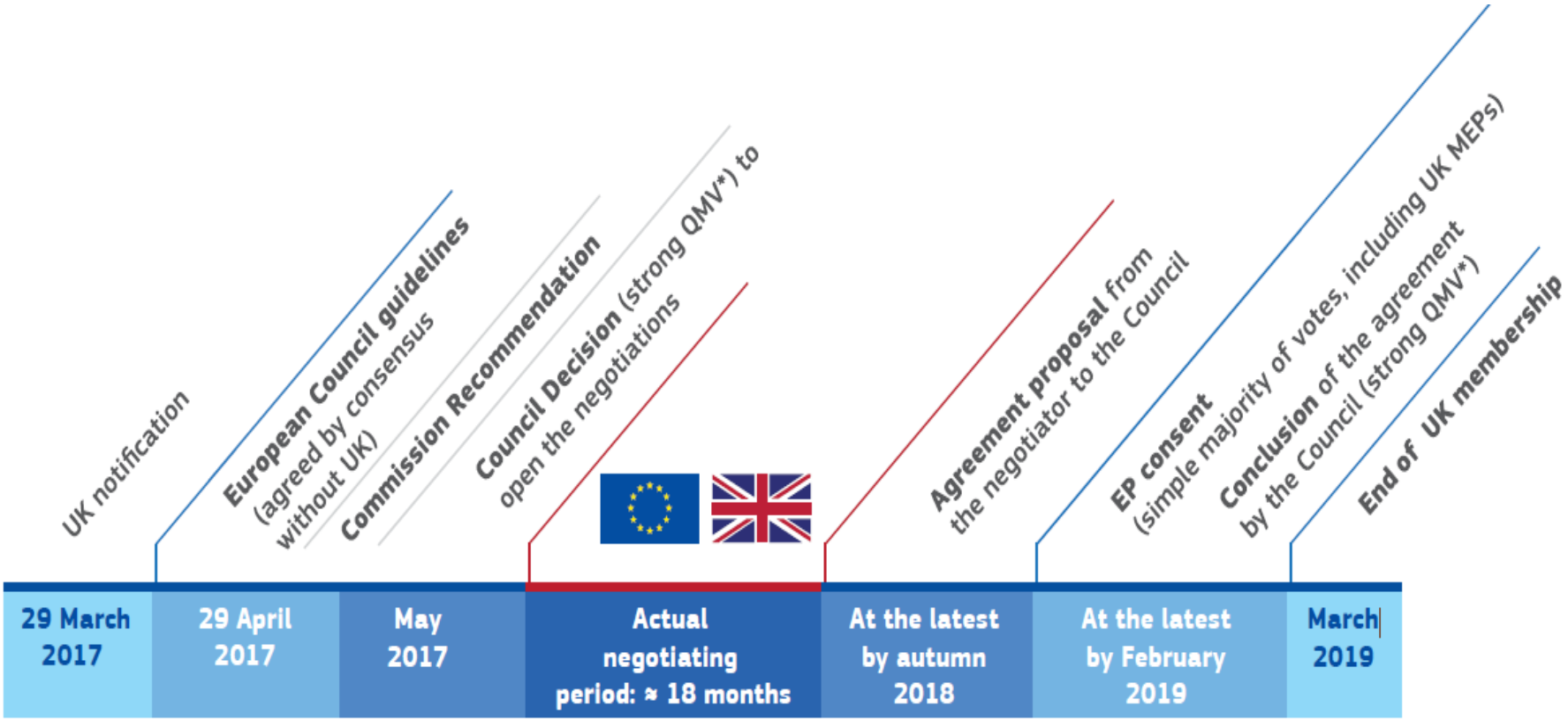
THE PRIME MINISTER

29 March 2017

Dear President Tusk

On 23 June last year, the people of the United Kingdom voted to leave the European Union. As I have said before, that decision was no rejection of the values we share as fellow Europeans. Nor was it an attempt to do harm to the European Union or any of the remaining member states. On the contrary, the United Kingdom wants the European Union to succeed and prosper. Instead, the referendum was a vote to restore, as we see it, our national self-determination. We are leaving the European Union, but we are not leaving Europe – and we want to remain committed partners and allies to our friends across the continent.

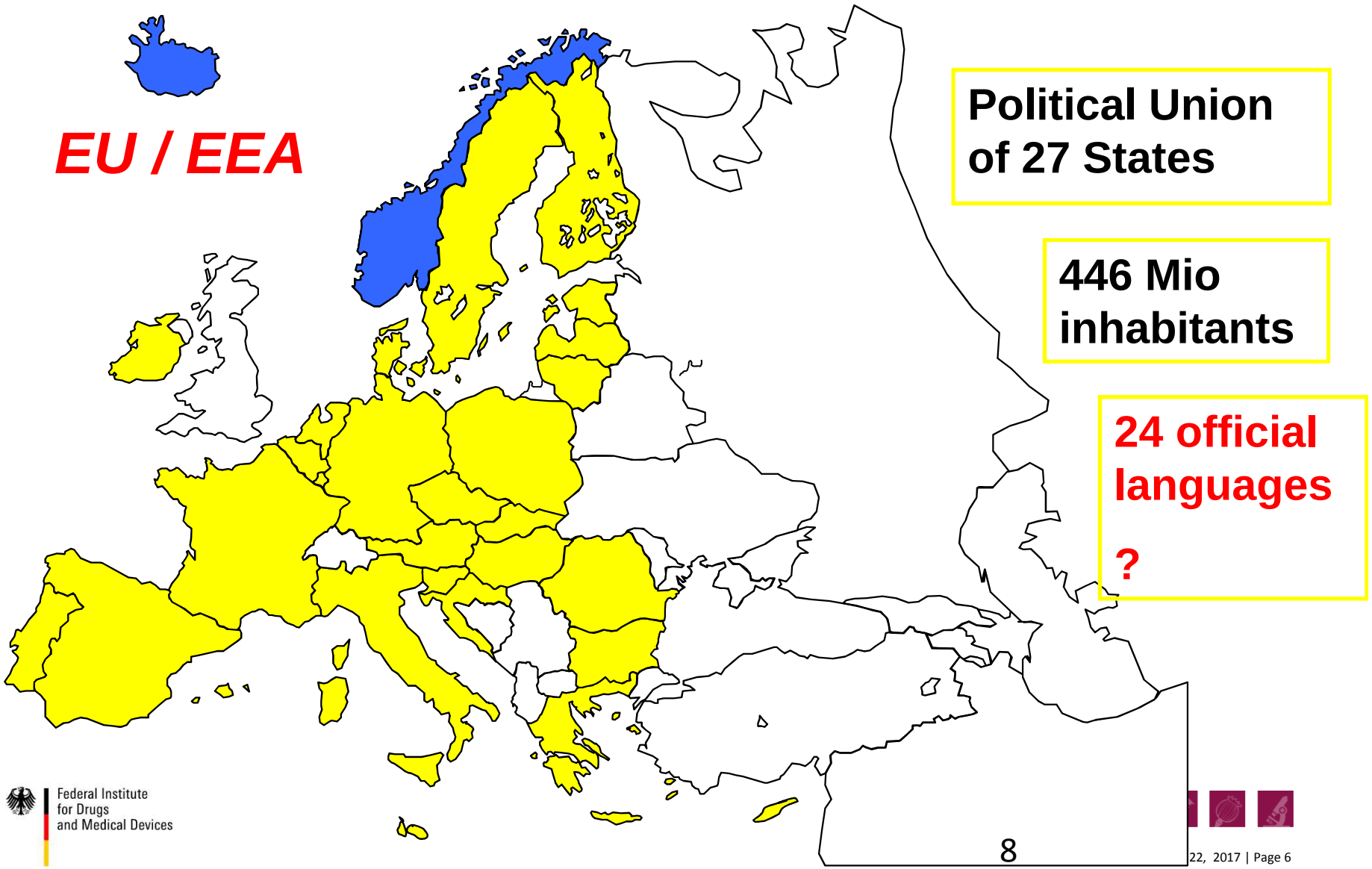
Timelines – (2)



* **Strong QMV** = 72% of the 27 Member States, i.e. 20 Member States representing 65 % of the EU 27 population.

Source: European Commission

“United in Diversity“



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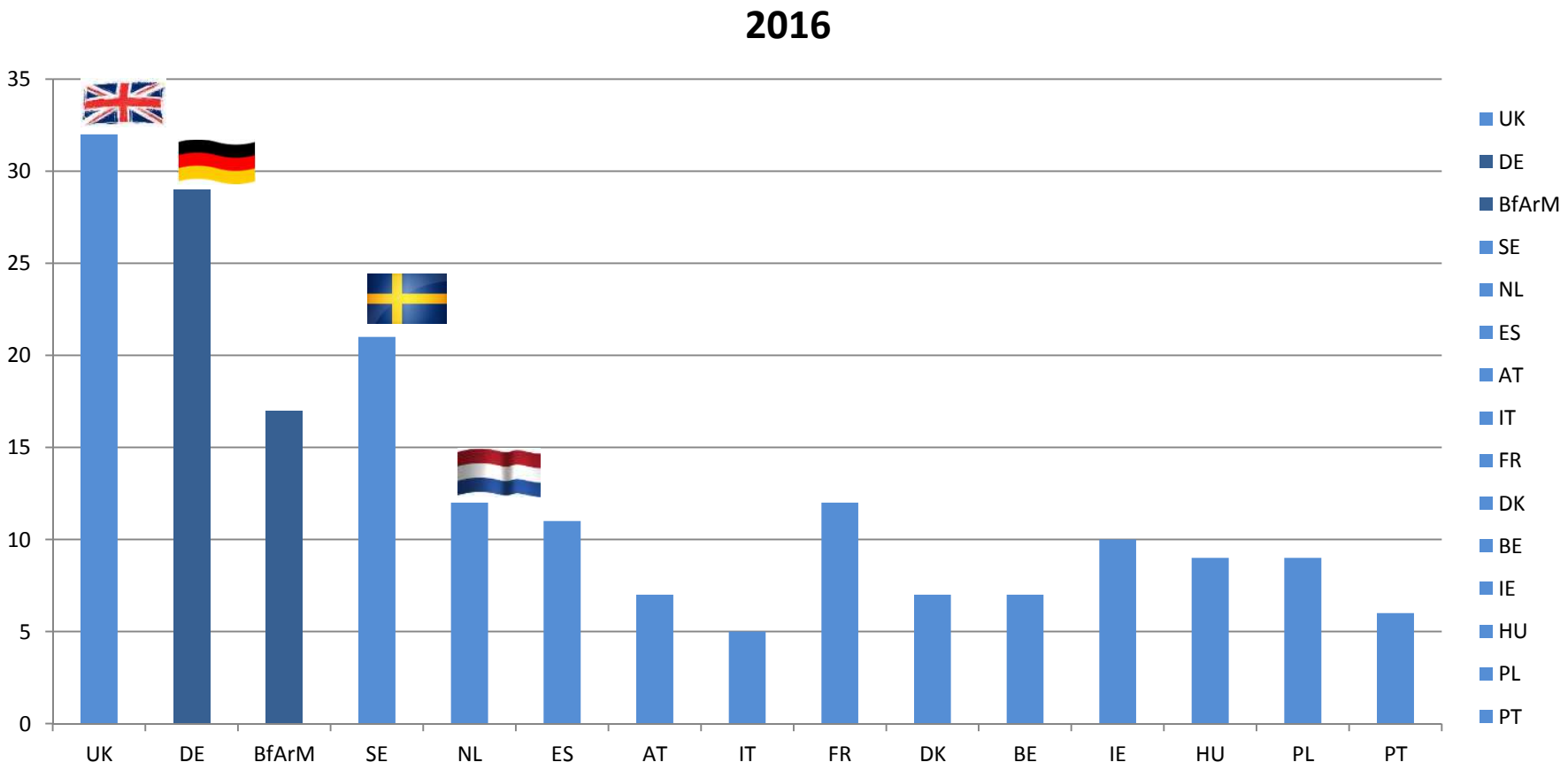
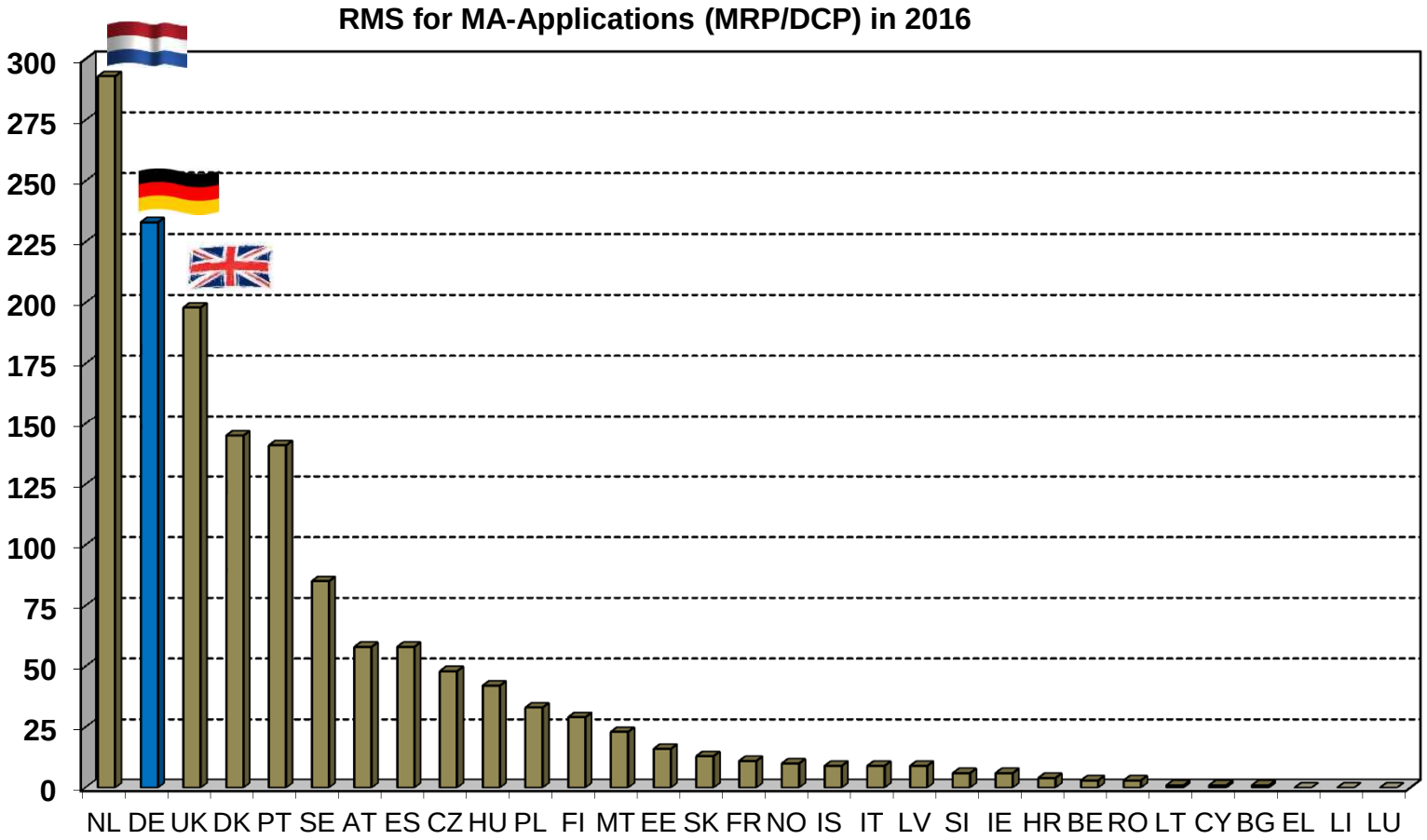
We prepare for the worst case scenario
… and hope for a miracle

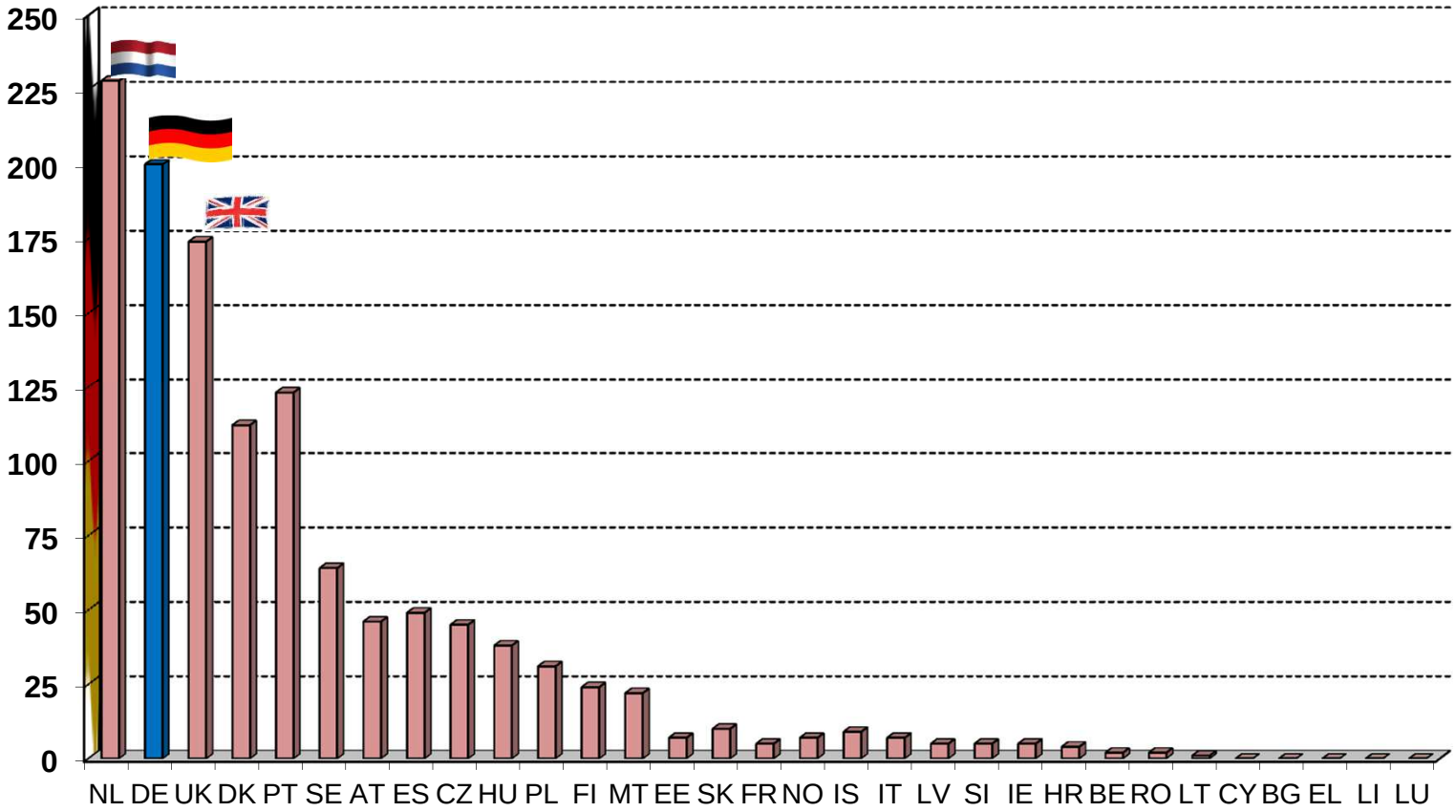
Centralized Procedures*: Rapporteur-/CoRapporteurships



- *Innovative Medicinal Products only
- *without Generics and informed consent applications

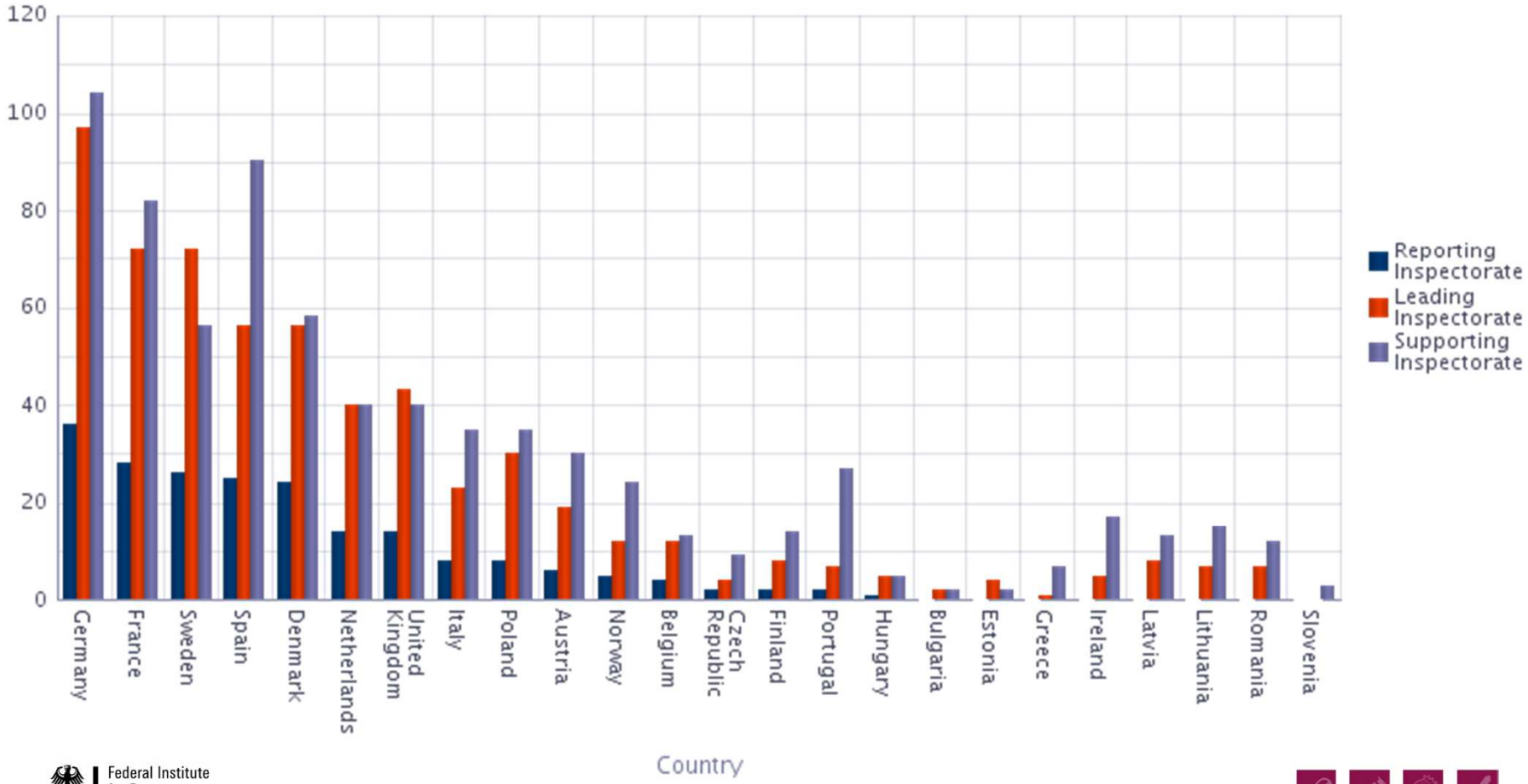

RMS for MA-Applications (MRP/DCP) in 2016
300
275
250
225
200
175
150
125
100
75
50
25
0
NL DE UK DK PT SE AT ES CZ HU PL FI MT EE SK FR NO IS IT LV SI IE HR BE RO LT CY BG EL LI LU

RMS for DCP-Applications in 2016



Involvement in GCP Inspections by Member State and role

Overview of EMA strategic aspects



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Agencies are prepared!

- Activities of HMA and EMA as much as possible aligned in order to avoid duplication of work
- HMA, NCAs and CMDh/v are dealing with MRP/DCP, EMA with CAPs
- EC, EMA and CMDh have already published information on Brexit
- Other WP also involved in necessary preparations
- Close cooperation with UK esp. wrt running affairs

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/04/news_detail_002738.jsp&mid=WC0b01ac058004d5c1

General principles on workload distribution

- Ensuring business continuity
- Maintaining the quality and robustness of the scientific assessment
- Continuing to comply with legal timelines
- Ensuring knowledge retention, either by building on existing knowledge, or through knowledge transfer
- Assuring an easy implementation and medium- and long-term sustainability

Capacities

- Reprioritize ressources within NCAs
- NCAs are increasing capacities by employing additional staff
- Processes are further streamlined in the network
- Better cooperation in the network

- We have to do it now to use the transition period!

Are MAHs/applicants prepared?

Brexit is Vigilance

- to identify the risk
- to mitigate the risk
  - for your marketing authorization
    'risk management plan'
  - for your company
    'vigilance masterfile'
- not to be prepared is a risk
- NCAs can't rescue MAs not in line with legal requirements

EU Legislation

- no derogation from the current EU-Legislation for UK during the Brexit-negotiation
- the current EU-Legislation applies to the EU (including UK) until 29 March 2019, 23:59 h (CET)

Is the CMDh prepared?

Yes !

CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

London, Februar 2017
Doc Ref.: rev1

Subject: **CMDh Brexit White Paper**

A paper to start the discussion and to collect tasks to be addressed
– should be kept confidential and is definitively not for publication –

CMDh Press release on 29th March 2017

CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

Report from the CMDh meeting held on 20-22 March 2017

Revision of the CMDh procedural advice on changing the RMS

Following the triggering of Article 50 of the Treaty on the European Union by the United Kingdom and in preparation of Brexit, the CMDh, in liaison with HMA, has agreed an update of the CMDh procedural advice on changing the RMS. "The RMS has triggered Article 50 of the Treaty on the European Union" has been added as a justifed reason to request a change of the RMS. No changes to the usual procedure have been introduced. Agreement of both current and future RMS needs to be sought by the MAH as outlined in the document. As already stated in the paper, switches can only be performed when no pending procedures are outstanding. Applicants intending to switch should confirm that all procedures submitted are finalised before the switch. The updated document will be published on the CMDh website under "Procedural Guidance, General Information".

CMDh PROCEDURAL ADVICE ON CHANGING THE REFERENCE MEMBER STATE

Doc. Ref.: CMDh/039/2002/~~Rev4~~Rev5
~~December 2011~~
March 2017

"MS have furthermore agreed upon that a justified reason is "RMS has triggered Article 50 of the Treaty on European Union". In that connection agreement has also been reached by MS that a switch back to that MS who has triggered Article 50 will also be allowed if there will be an exemption agreed as a result of the negotiations between that RMS and the EU."

RMS switch

- Recommended as early as possible
- Switch back to UK is possible
- BUT: All ongoing procedures have to be finalised before the switch!!!

⇨ 900 renewals with UK as RMS outstanding…

Agreed Variation-Grouping

"After a member state has triggered an Art. 50 procedure of the Treaty on European Union several changes to the finished product might be necessary, e.g. changes to MAHs, manufacturers for batch release, new summary of pharmacovigilance system in case of MAH transfers or changes in the product names etc. While the transfer of the MA to a new MAH is an independent purely national application all other **changes related to the consequences of this Art. 50 procedure, may be grouped in one application** according to the highest variation type for the single changes."

European Regulatory Network

28 April 2017
EMA/271635/2017
Media and Public Relations

Press release

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA and heads of national competent authorities discuss consequences of Brexit

Key principles and working methodology established

The European Medicines Agency (EMA) organised an information meeting yesterday with members of its Management Board and heads of the National Competent Authorities (NCAs) of the EU/EEA Member States. The goal was to start discussing how the work related to the evaluation and monitoring of medicines will be shared between Member States in view of the United Kingdom's (UK) withdrawal from the European Union.

Commission/EMA and CMDh on 2 May 2017

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH
AND FOOD SAFETY

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use

The United Kingdom submitted on 29 March 2017 the notification of its intention to

CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

Notice to marketing authorisation holders of national authorised medicinal products for human use

Doc. Ref.: CMDh/360/2017
02 May 2017

Federal Institute
for Drugs
and Medical Devices

The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw

The Notice to MAH …

CMDh
Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

Notice to marketing authorisation holders of national authorised medicinal products for human use

Doc. Ref.: EMA/CMDh/278559/2017
02 May 2017

The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless the withdrawal agreement establishes another date or the period is extended by the European Council in accordance with Article 50(3) of the Treaty on European Union, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET). The United Kingdom will then become a 'third country'.

In this regard, marketing authorisation holders of national authorised medicinal products for human use are reminded of certain legal repercussions, which need to be considered:

- EU law requires that marketing authorisation holders are established in the EU (or EEA);
- Some activities must be performed in the EU (or EEA), related for example to pharmacovigilance, manufacturing, import etc.

Preparing for the withdrawal is therefore not just a matter for European and national administrations, but also for private parties. Marketing authorisation holders may be required to adapt processes and to consider changes to the terms of the marketing authorisation in order to ensure its continuous validity and exploitation, once the United Kingdom has left the Union.

Marketing authorisation holders will need to act sufficiently in advance to avoid any impact on the continuous supply of medicines for human use within the European Union.

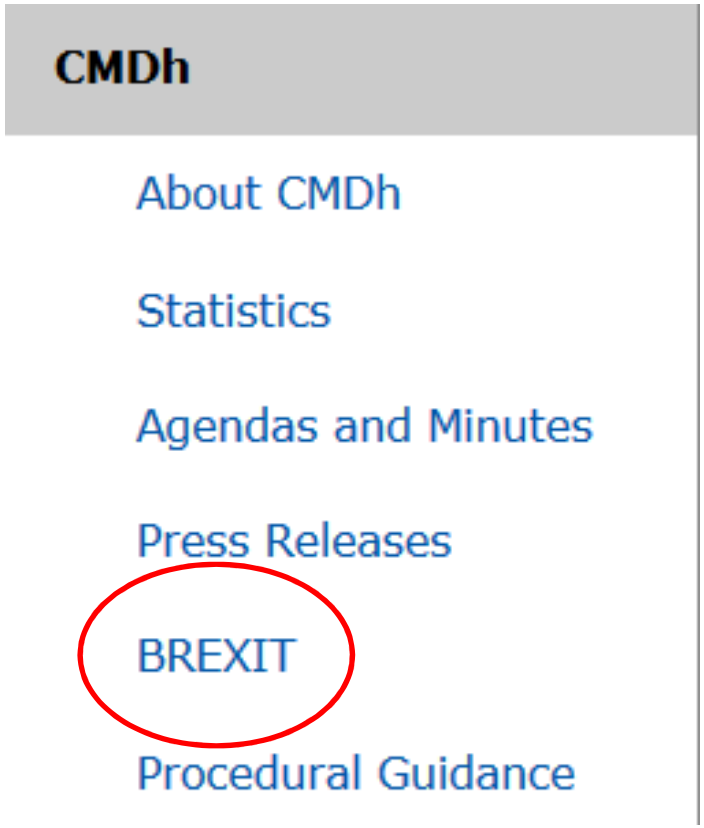
In particular, the CMDh expects marketing authorisation holders to prepare and proactively screen authorisations they hold for the need for any changes. The necessary transfer or variation requests will need to be submitted in due time considering the procedural timelines foreseen in the regulatory framework.

The CMDh stands ready to support marketing authorisation holders and will provide a series of Q&As on a dedicated page of the CMDh website. This page will be updated with further practical information and relevant Q&As, from May 2017 and will be subsequently expanded, where necessary.

For products authorised in the centralised procedure the information will be provided through the websites of the Commission and the European Medicines Agency.

Federal Institute for Drugs and Medical Devices

The Notice to MAH



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MRP/DCP – in the planning

- There is only one evaluating MS = RMS
  ⇨ without a RMS there is no procedure!
- It is up to the applicant to choose the RMS
- The applicant chooses the 'risk'

MRP/DCP – with granted MA

1. UK as CMS
   - deletion from the procedure

2. UK as RMS
   - need to find a new RMS
   - ongoing procedures (renewal, variations, repeat-use procedures) have to be finalized before transfer to a new RMS

MRP/DCP – ongoing procedures

1. UK as CMS
   - deletion from the procedure

2. UK as RMS
   - finalisation is highly recommended before Brexit is effective
   - fate of open procedures?

     ⇨There is no procedure without a RMS!

Implications for Pharmacovigilance

- Location of the QPPV
- Location of the PSMF

must be inside the EU/EEA

Good news:

This is 'only' a change to the Article 57-database, but you have to find a new QPPV or to move him inside the EU/EEA

Implications for the MAH/Applicant

- MAH/Applicant need a legal establishment in the EEA
- The legal construct of a MAH must be in line with EEA requirements – Ltd.?
- A new legal entity is a new MAH and result in a transfer of a MA
- Transfer of a MA is a non-harmonised process among MS
- A new MAH needs a new summary of the PharmVigSystem – no submission via Article 57 database, but variation

Further implications to be discussed

- Is a medicinal product authorised in UK a valid reference medicinal product for a generic/hybrid application after the Brexit?
- Are BE studies against authorised UK reference products acceptable after the Brexit?
- Is a BE study done with an authorised UK product after the Brexit acceptable for a repeat use procedure?
- Can the MAH, batch release, QP, QPPV still be located in the UK?
- Will a GMP/GCP-Inspection performed by UK still be acceptable after the Brexit?

Implications for European Committees

e.g. CMDh:

- Voting members are from EU-MS
- Non-voting members are the three EFTA-MS Norway, Iceland and Liechtenstein
- Chair and Vice-Chair are elected from the voting MS
- Change of quorum or majority – No!

Relocation of EMA

- Longlasting uncertainties will increase loss of staff
- Planning reliability and acceptability of new location might decrease loss of staff and opens new opportunities
- Planning reliability key for all stakeholders
- Negative impact on health care not acceptable

- NCAs must prepare to help EMA in
  - Scientific work
  - Administrative work
  - Logistical Work

Thank you very much for your attention!

Contact

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