efpia
European Federation of Pharmaceutical Industries and Associations

Critical impacts of IVDR implementation on patient access to clinical trials






Survey results

Critical negative impact of IVDR implementation to clinical trials

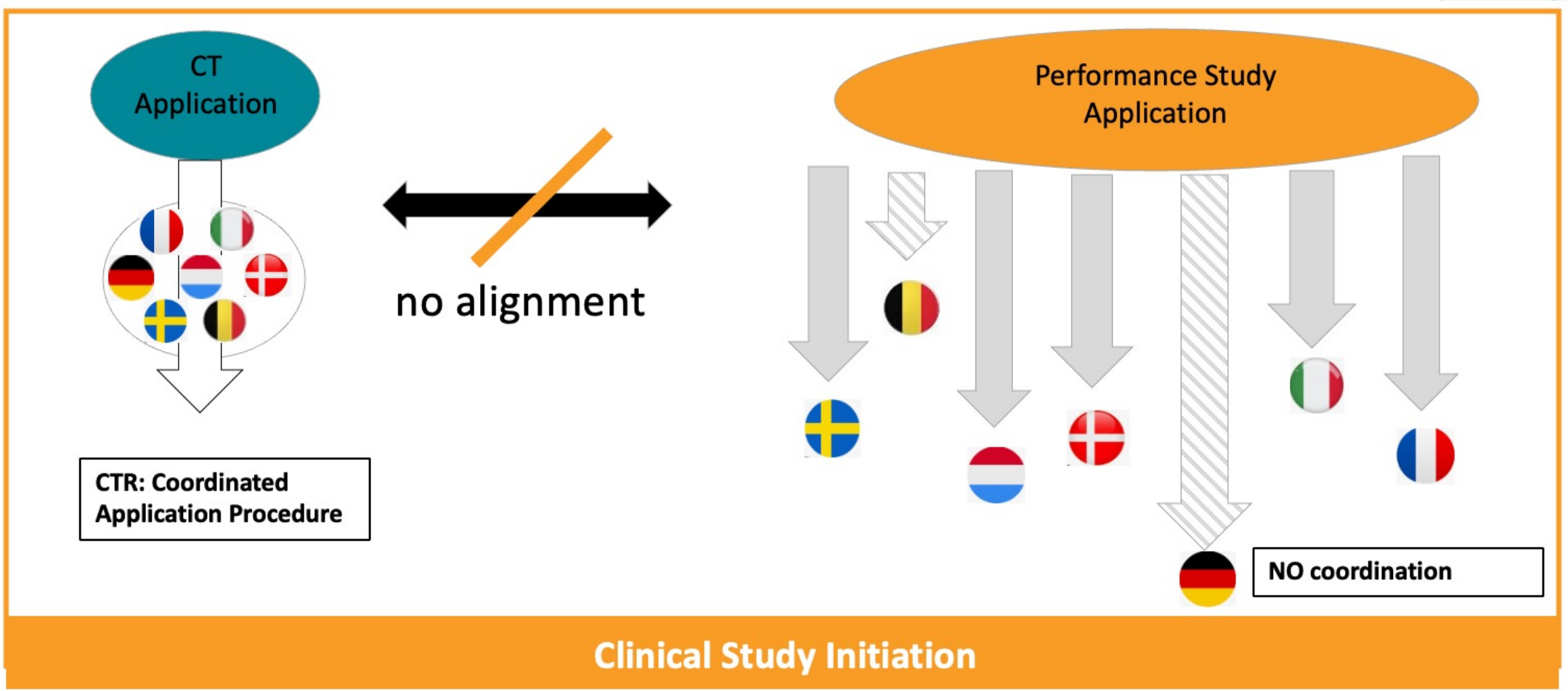
EFPIA fully supports the IVD Regulation aiming at ensuring a high level of public health and patient safety in Europe

However, complex Performance Study Application process leads to:

- **Delayed clinical study initiation and delayed clinical trial launch (6-12 months)**
- **Reduction in access to clinical trials for European patients**
- **Delayed access to novel therapies for European citizens**
- **Adverse impact on other initiatives** e.g. Europe's Beating Cancer Plan, Accelerating Clinical Trials in the EU (ACT EU)

Ability to initiate clinical trials in Europe is severely impacted!

Negative impact of IVDR on clinical trials using an IVD: Lack of coordinated process & clarity for Performance Studies



Ability to initiate clinical trials in Europe is severely impacted!

- Delayed access to novel therapies for European patients
- Reduced access to clinical trials for European citizens
- Adverse impact on other initiatives e.g. European Beating Cancer Plan, Act EU

EFPIA Survey on Impact of IVDR on Clinical Trials

EFPIA surveyed Members anonymously to gather data on the impact of IVDR on clinical trials and delayed patient access to those trials

- More than 2/3 of EFPIA large member companies responded
  - Data gleaned from 21 of 32 large Member companies
- Results represent a **conservative estimate of impact** (more EFPIA & non EFPIA Members)

EFPIA Survey on Impact of IVDR – Trial Delays

82-160 Trials currently delayed

238-420 Trials potentially delayed over next 3 years

6-12 months Most frequently reported length of delay

43% of companies estimated **6-12 months delay** *currently*

48% estimate potential **6-12 months delay** *over next 3 years*

Responses from 21 of 32 EFPIA large Member Companies
Range of numerical responses provided by respondents

EFPIA Survey on Impact of IVDR – Patient Impact

Estimated impact over next three years:

33,815 - 42,200 Patients impacted (patients enrolled, not patients screened)

16,812 - 27,400 Cancer patients impacted

228 - 410 Trials that may enroll fewer EU patients

Responses from 21 of 32 EFPIA large Member Companies
Range of numerical responses provided by respondents

EFPIA Survey on Impact of IVDR - Impact on clinical research in Europe

Impact to Trial Sites

4,984

Number of European sites anticipated to be involved in these trials in the next 3 years

67%

Percentage of EFPIA Members that would consider reducing the number of EU trial sites if IVDR requirements remain the same

Impact to Patients

50,014 to 65,860

Number of European patients anticipated to be enrolled in these trials in the next 3 years

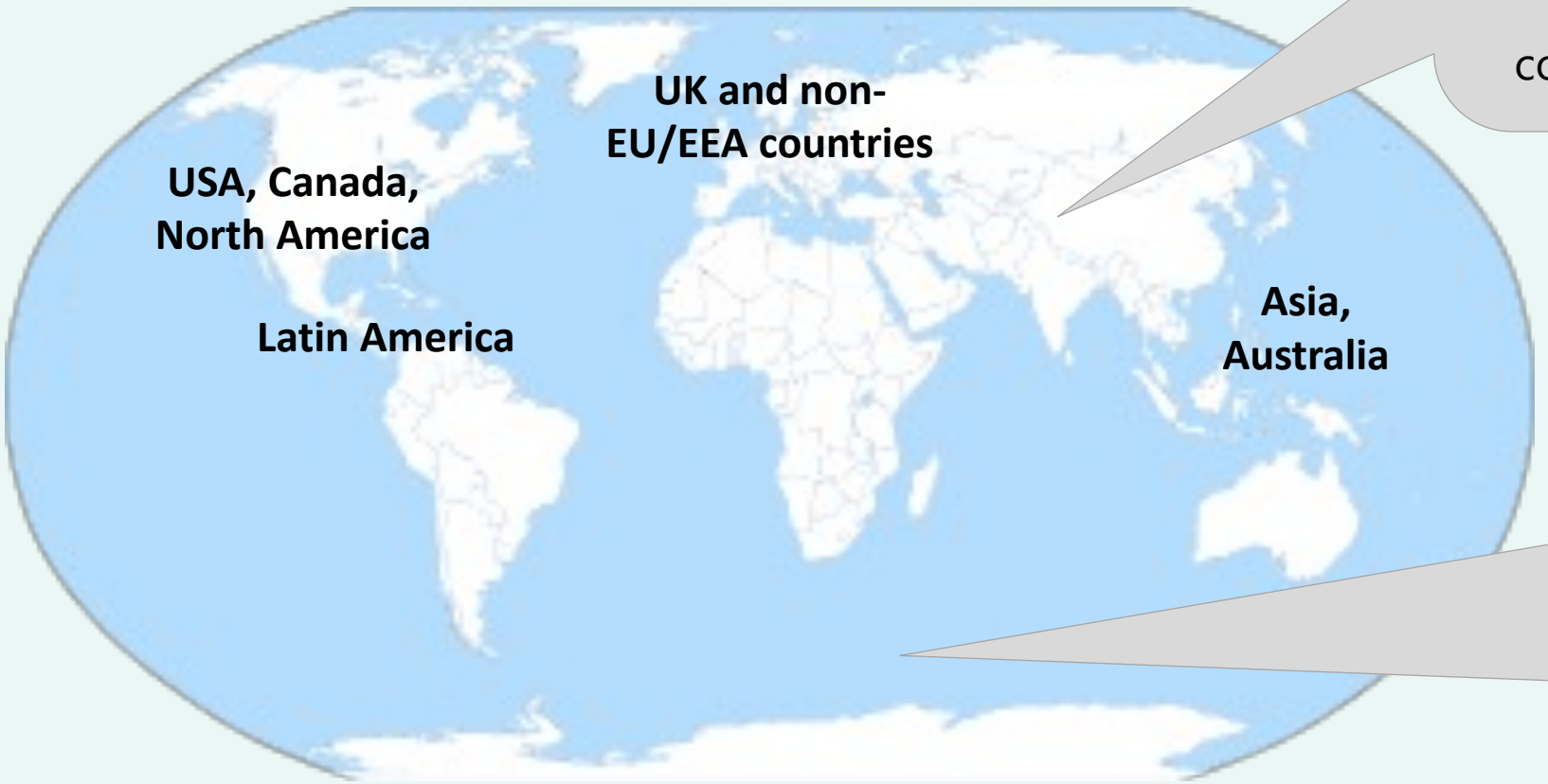
71%

Percentage of EFPIA Members that would consider reducing the percentage or number of EU patients if IVDR requirements remain the same

Responses from 21 of 32 EFPIA large Member Companies

EFPIA Survey on Impact of IVDR
Impact on Clinical Research in Europe

Where will the trials be conducted instead of European sites?

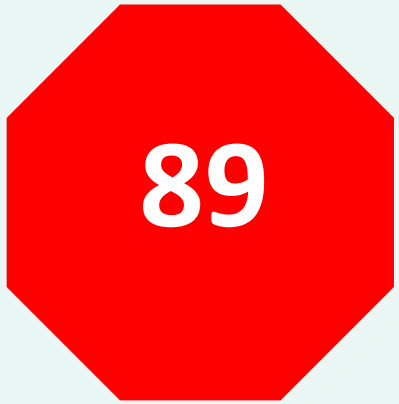


"**It is already occurring** now that trials are shifted away from Europe to US and Asia. This movement will be getting stronger upon the experience with IVDR adding more complexity to CTAs in Europe."

"The regulatory burden under the IVDR is large and **in rare disease**, the low testing volume could be challenging for clinical trials in the EU. The process as it currently stands is putting access to novel medicines for EU patients at risk."

EFPIA Survey on Impact of IVDR - Impact on Access to Innovative Medicines in Europe

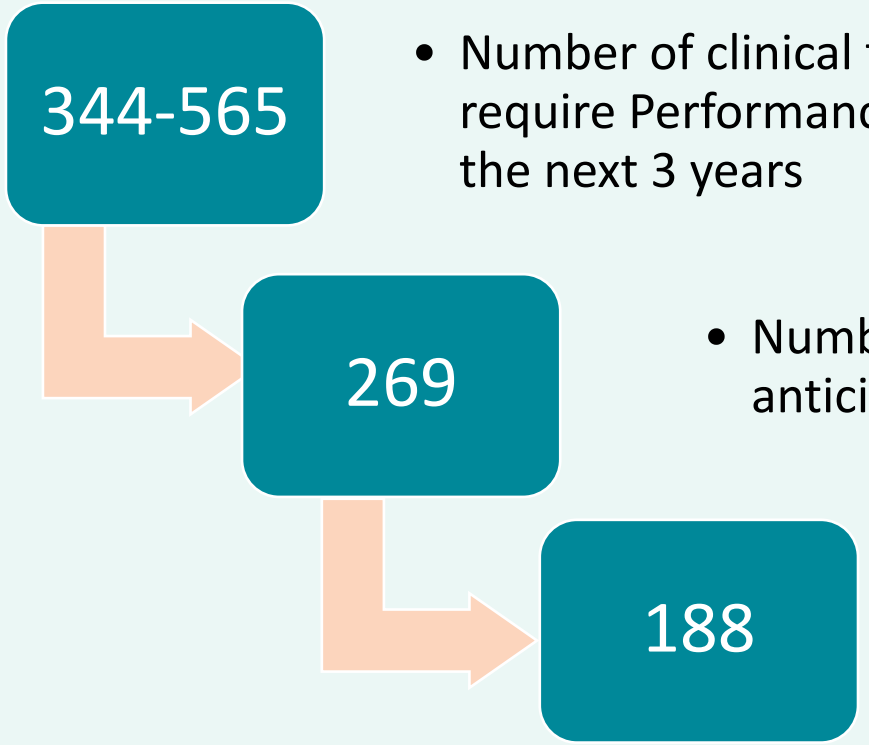
Therapies that could face delayed launch in Europe if clinical trials are delayed…



…In the following therapeutic areas (Respondents asked to select all that apply)

Therapeutic Area	Percentage of Respondents
1. Oncology	84%
2. Rare Disease	58%
3. Neuroscience	42%
4. Inflammation	37%
5. Cell & Gene Therapy	32%
6. Pediatrics	26%
7. Cardiovascular	25%

EFPIA Survey on Impact of IVDR - Impact on Clinical Research in Europe



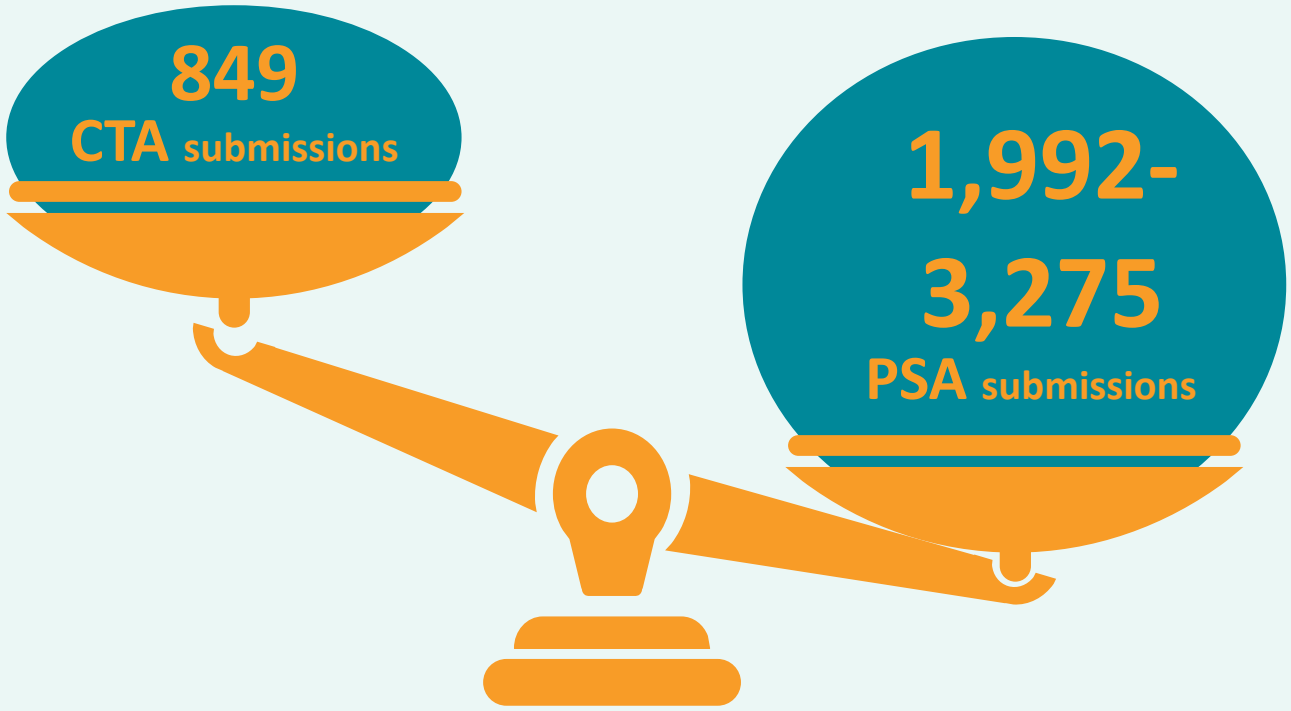
- Number of clinical trials in Europe that would require Performance Study Application within the next 3 years
- Number of these trials anticipated to be registrational
- Number anticipated to be non-registrational trials

In Which Therapeutic Areas?	Percentage of Respondents
1. Oncology	86%
2. Rare Disease	57%
3. Cell & Gene Therapy	48%
4. Neuroscience	43%
5. Pediatrics	33%
6. Inflammation	29%
7. Cardiovascular	24%

(Respondents asked to select all that apply)

EFPIA Survey on Impact of IVDR - Burden of Performance Study Applications (PSA)

Anticipated submissions to Member States over the next 3 years, assuming no coordinated process



Which Member States are you Engaging with on Performance Study Submissions?

All Member States being engaged across respondents.

Member States where 50% or more of respondents are engaging: France, Belgium, Czech Republic, Germany, Denmark, Austria, Hungary, Italy, Netherlands, Poland, Portugal, Spain, Sweden.

Member States where 80% or more of respondents are engaging: Spain, Italy, Germany, France

Inconsistency of Approach and Lack of Infrastructure

What are the key hurdles you are experiencing at the Member State level? Select all that apply.

Challenge	% of Respondents
Performance study application submission **process is not consistent** across Member States	100%
Inconsistent interpretations of which studies require performance study applications under the IVDR	89%
Performance study application **documentation is not consistent** across Member States	83%
Timing of **Ethics Committee** reviews is not consistent and poses challenges for planning	67%
Member States have **inconsistent positions** regarding the **timing** of performance study applications relative to clinical trial applications under the Clinical Trial Regulation	61%
Performance study application documentation expectations are too **burdensome**	61%
Review of performance study applications is **not meeting IVDR timelines**	50%

Inconsistency of Approach and Lack of Infrastructure

What are the key hurdles you are experiencing at the Member State level?

Other challenges reported in free text:
Member state stating that **IVDR does not apply to them**.
Authorities taking **conservative approaches** in terms of requests of performance study application. It is unclear whether authorities are checking if the performance studies fall in the scope of the IVDR.
Absence of harmonized guidance document (across member states) for determining the need a Performance Study application.
Member states **do not know how to review the performance study**…some member states do not have paperwork or process in place to review PS.
Study risk is not taken into account: All clinical trials studies involving investigational tests for medical decision making would require PSA, because there is no risk impact assessment procedure.
IVDR does not set clear bounds on the maximum allowable **time for Ethics Committee** to review and issue opinions.
Where PSA and CTA are submitted at the same, more than one **ethics committee** may be assigned to review. The reviewers **do not coordinate** making incorporating feedback challenging.

Challenges at Member States level

Experiences with IVDR in the different Member States

to help identify the issues and

work together on improving the situation

Challenges at Member State Level

Which Member States are Currently Posing or Expected to Pose the Most Challenges?

Member States Cited by >25% of Respondents	Percentage of Respondents
Germany	74%
France	47%
Italy	32%
Czech Republic	32%
Spain	26%
Poland	26%
Austria	26%

EFPIA Survey on Impact of IVDR - Challenges & Inconsistencies at Member State Level (Free Text Responses)

 **Bulgaria**	National Ethics Committees (EC) that is slow to respond and/or do not adhere to IVDR review timelines, paper copy/wet ink signature requirements
 **Czech Republic**	Unstable Submission Portal, little to no information for IVDR PSA available on website, requesting notifications for PS using left-over samples when all requirements in IVDR Annex XIV are met, paper copy/wet ink signature requirements; no separate process for CDx performance study notification; NCA slow to respond; sequential EC then CA process extends study approval time significantly vs parallel submissions
 **France**	Unstable Submission Portal, Does not have database ready to allow same Ethics Committees to review IVD and Medicinal Product study protocols; different interpretation than all other countries of which studies require a PSA
 **Romania**	No published PSA-IVDR submission guidance and review timelines, little to no information for IVDR PSA available on website; no separate process for CDx performance study notification and are applying a burdensome approach per full performance study authorization; administrative issues resulting in delayed processing of PS application
 **Slovakia**	No published PSA-IVDR submission guidance and review timelines, said they will not follow IVDR until EUDAMED database is fully functional, paper copy/wet ink signature requirements
 **Spain**	Unstable Submission Portal that has delayed submissions, States with no clear Ethics Committee procedure for multicenter studies , requesting notifications for PS using left-over samples when all requirements in IVDR Annex XIV are met; sequential EC then CA process extends study approval time significantly vs parallel submissions

EFPIA Survey on Impact of IVDR - Challenges & Inconsistencies at Member State Level (Free Text Responses)

Belgium

List of submitted documents has to be a word file, pdf is not accepted

Germany

Decentralised Ethics Committee (EC) review for multicenter studies (each site EC reviews); in many cases, deficiencies raised are not consistent across sites, sequential EC then NCA process extends study approval time significantly vs parallel submissions, timeline and additional requirements beyond Art. 76 IVDR, MPDG training required for all PI from Pharma sites, not consistently handled across ECs

Greece

No published PSA-IVDR submission guidance and review timelines, National Ethics Committees that is slow to respond and/or do not adhere to IVDR review timelines

Hungary

National Ethics Committees that is slow to respond and/or do not adhere to IVDR review timelines. No clear EC procedure for multicenter studies, said they cannot approve a Dx performance study for a Dx that is not already approved; does not have a clear process or documentation in place to handle review of a Dx performance study; Administrative issues resulting in delayed processing of PS application; require wet signatures and packages to be mailed in, not electronically submitted

Iceland

National Ethics Committees that is slow to respond and/or do not adhere to IVDR review timelines; Administrative issues resulting in delayed processing of PS application

Lithuania

State with no clear Ethics Committee procedure for multicenter studies; Administrative issues resulting in delayed processing of PS application

EFPIA Survey on Impact of IVDR - Challenges & Inconsistencies at Member State Level (Free Text Responses)

Austria

Same day Clinical Trial Application (CTA)/Performance Study Application (PSA) Requirements,
"We are not submitting CTAs with IVDs in Austria because known to be challenging"

Poland

Decentralised Ethics Committee review for multicenter studies (each site EC reviews); in many cases, deficiencies raised are not consistent across sites, little to no information for IVDR PSA available on website, requesting notifications for PS using left-over samples when all requirements in IVDR Annex XIV are met, paper copy/wet ink signature requirements and certified translations; sequential EC then CA process extends study approval time significantly vs parallel submissions, do not have a clear process or documentation in place to handle review of a Dx performance study, do not have a separate process for CDx performance study notification and are applying a burdensome approach per full performance study authorisation

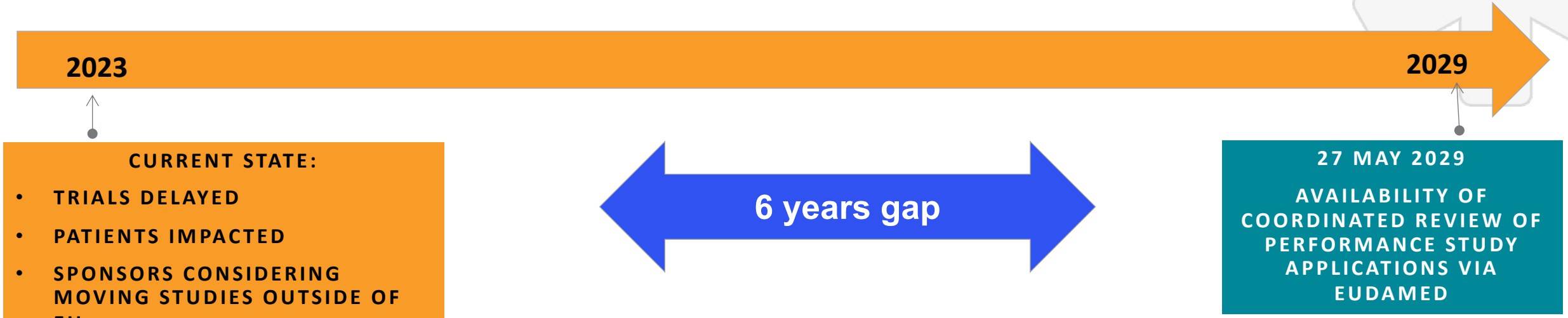
Sweden

Providing a large number of very detailed questions, lack of understanding of the device and how it is being used in a combined study

Italy

National Ethics Committees that is slow to respond and/or do not adhere to IVDR review timelines; Decentralised Ethics Committee review for multicenter studies (each site EC reviews); in many cases, deficiencies raised are not consistent across sites; little to no information for IVDR PSA available on website, requesting notifications for PS using left-over samples when all requirements in IVDR Annex XIV are met; sequential EC then CA process extends study approval time significantly vs parallel submissions; requiring Principal Investigator (PI) to submit PS-EC application, instead of Study Sponsor; requires detailed personal information of company representatives.

How do we keep clinical research and innovation in Europe?



Proposed EFPIA solutions:

- **Voluntary coordination pilot** across MS for Performance Study Application
- **New guidance on common set of principles** for Performance Study Submission and Reviews
- **Risk-based approach** to Performance Studies
- Under **Article 92**: Temporary **accept nonconformity to** PSA requirements
- **Clarify definitions of in-house test** to broaden scope
- **Delay application of IVDR** to IVDs used in clinical trials

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Thank you