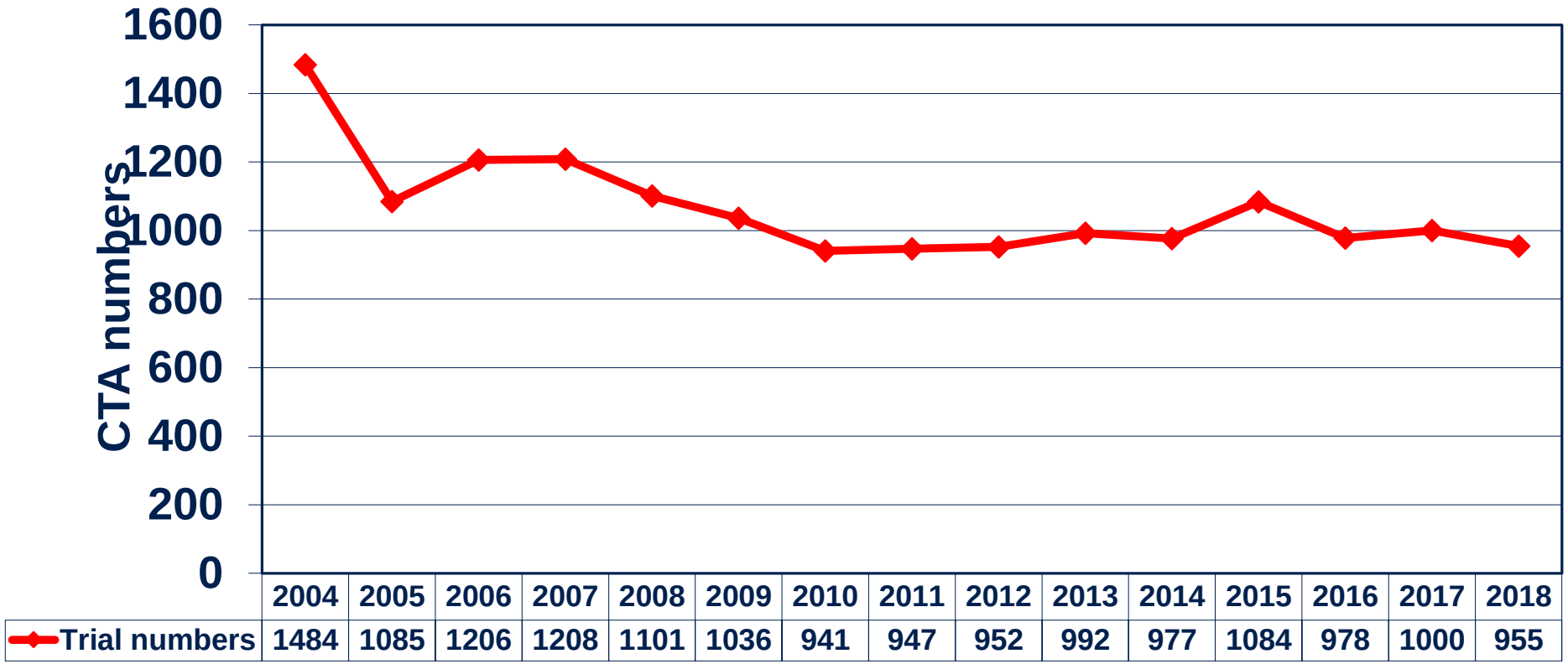
BIA Regulatory Innovation Conference

Session 1: UK global capability for clinical trials – MHRA perspective

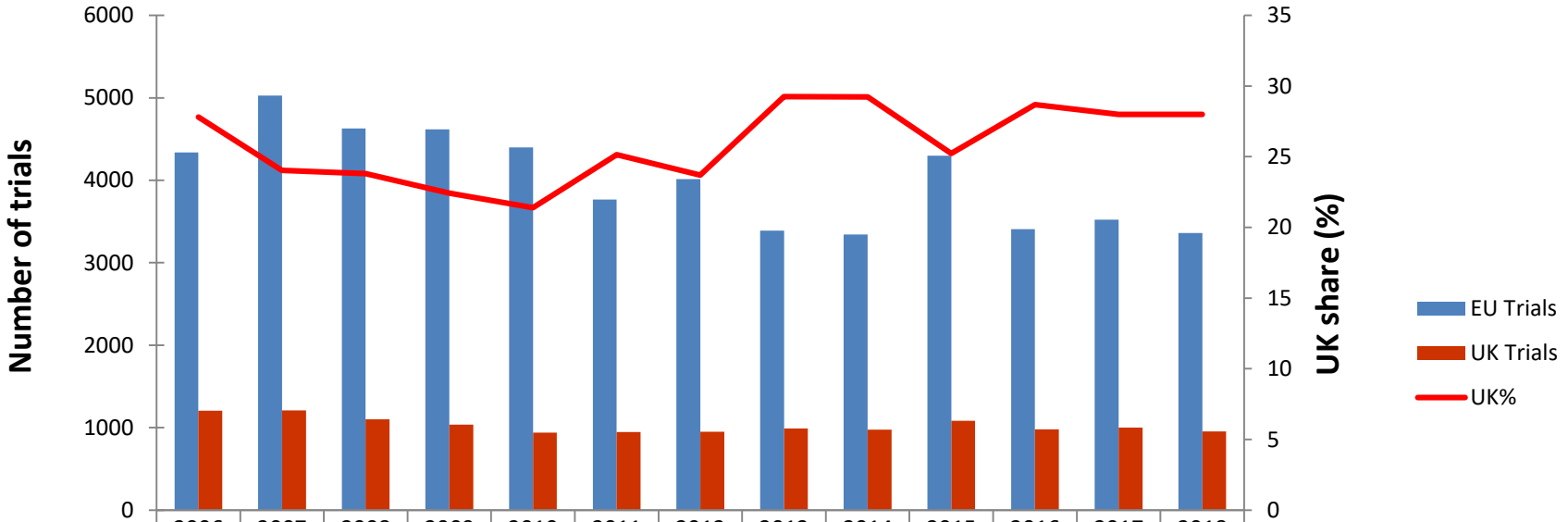
Dr Martyn Ward

UK Clinical Trial numbers



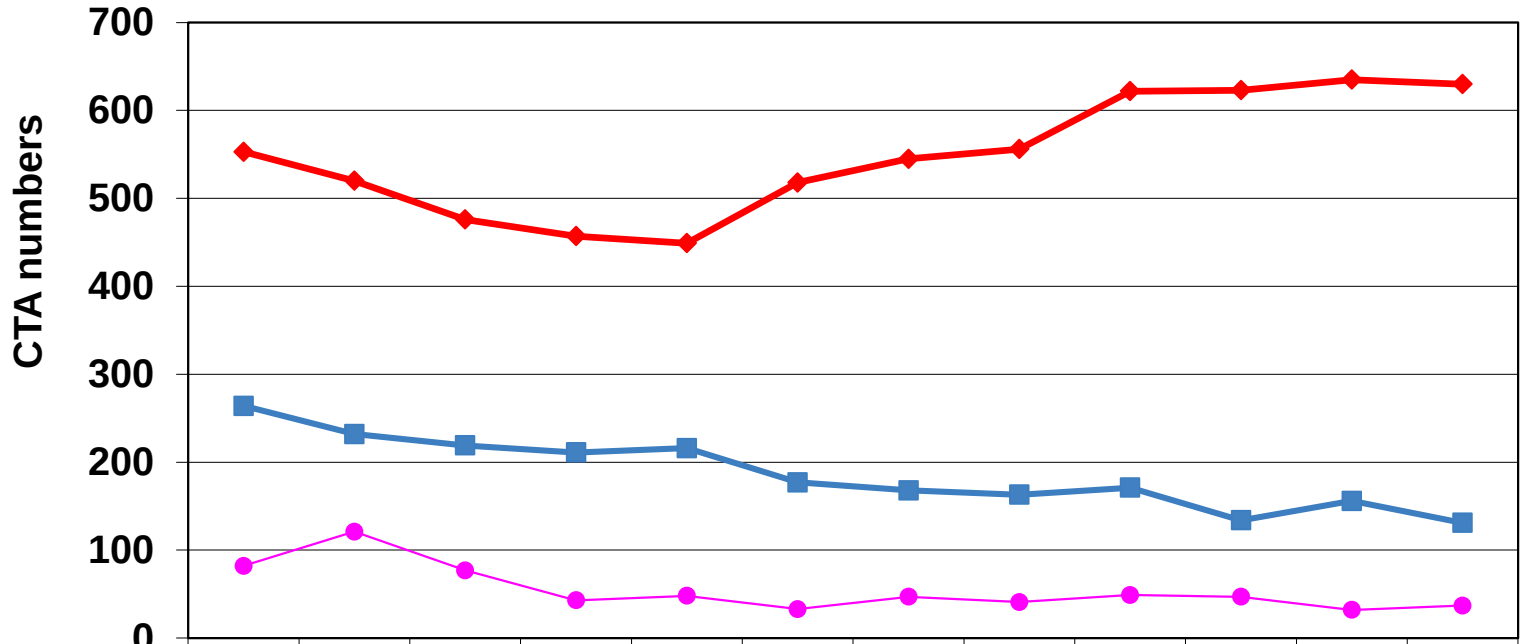
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Trial numbers	1484	1085	1206	1208	1101	1036	941	947	952	992	977	1084	978	1000	955

UK vs EU New Trials by Year – All Phases



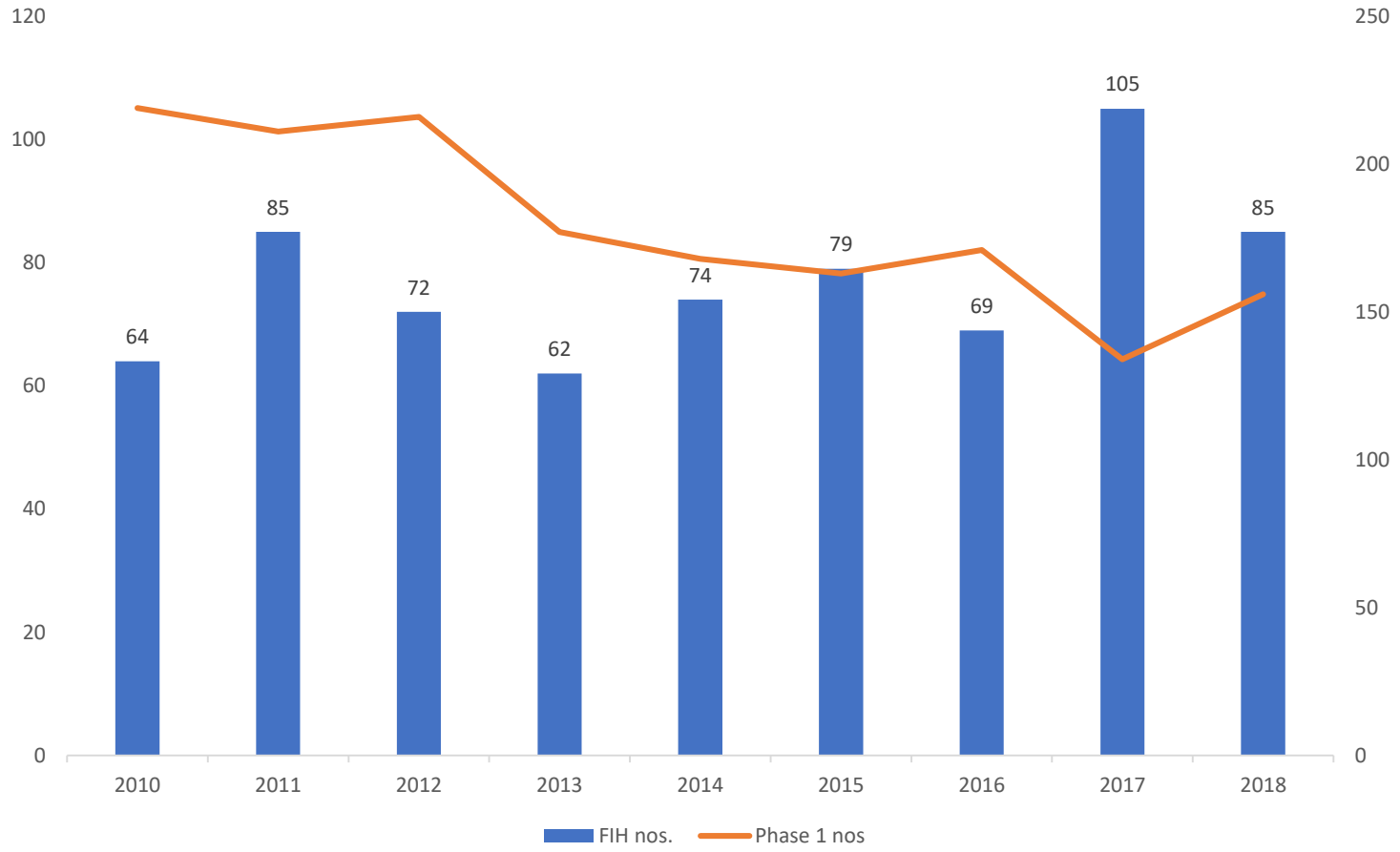
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
EU Trials	4336	5028	4627	4619	4400	3766	4016	3391	3343	4297	3409	3521	3361
UK Trials	1206	1208	1101	1036	941	947	952	992	977	1084	978	1000	955
UK%	28	24	24	22	21	25	24	29	29	25	29	28	28

UK Commercial applications received

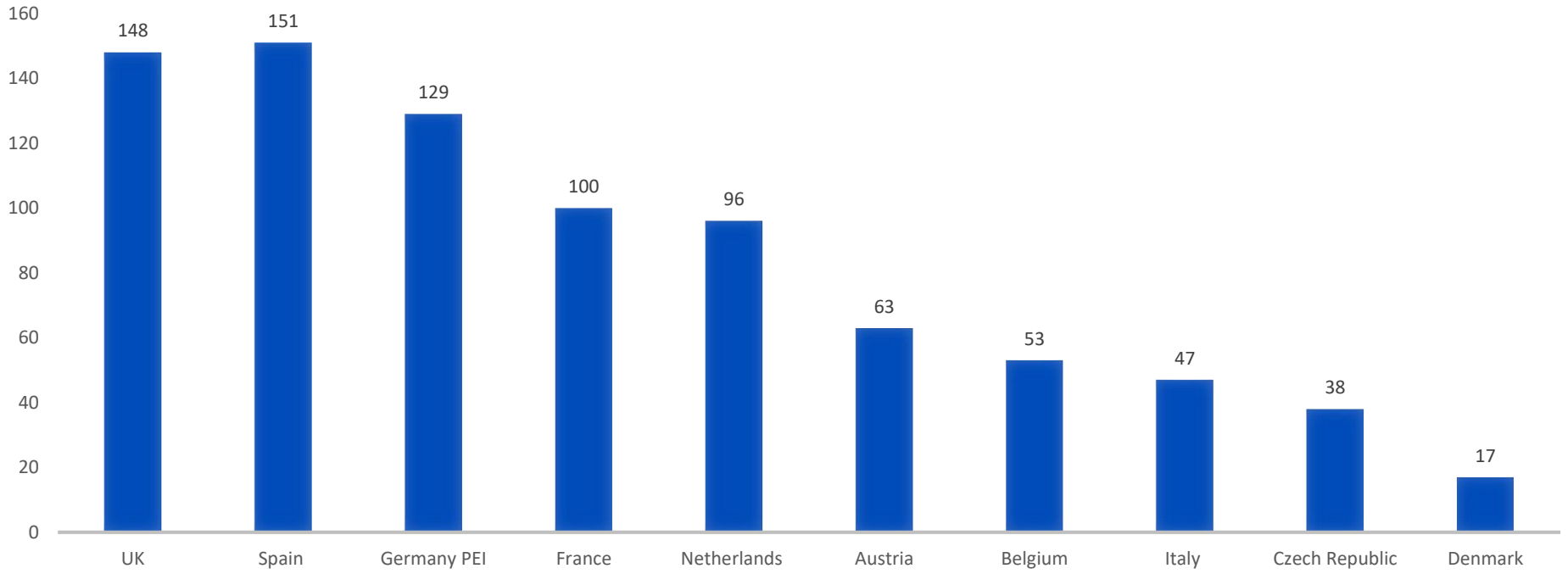


	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Commercial Phase 2-3	553	520	476	457	449	518	545	556	622	623	635	630
Commercial Phase 4	82	121	77	43	48	33	47	41	49	47	32	37
Commercial Phase 1	264	232	219	211	216	177	168	163	171	134	156	131

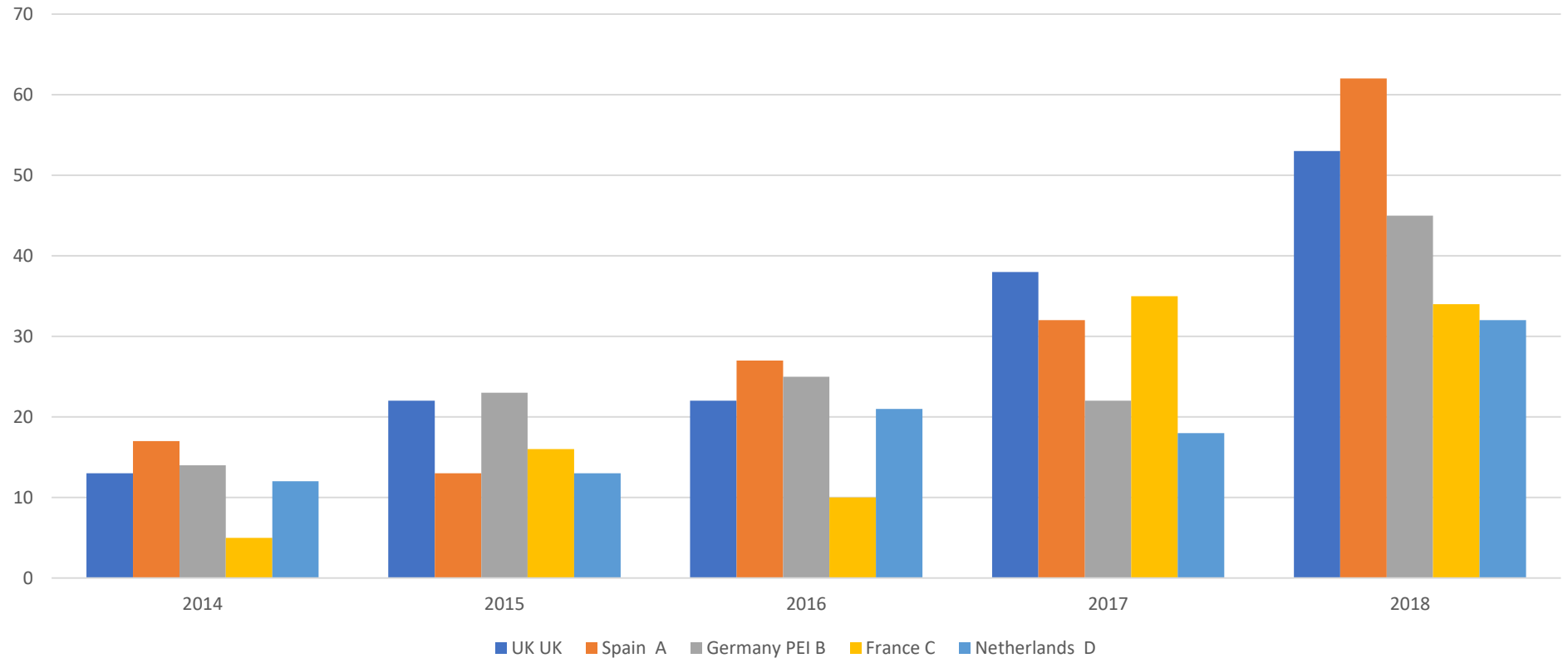
UK Phase 1 and FIH totals by year



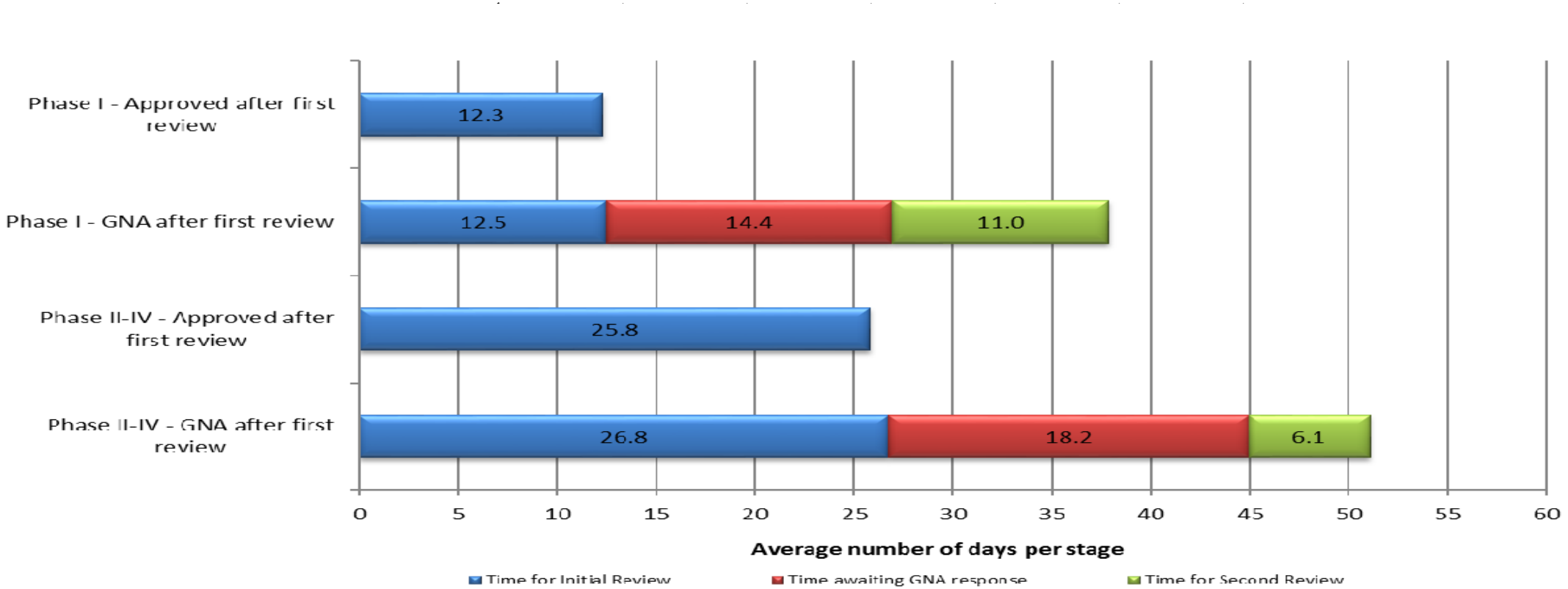
Total ATMP CTAs in EU over past 5 years



Top 5 EU Member States ATMP trial numbers



Timelines: Clinical Trial Assessment Performance



Current UK clinical trials status

- MHRA largest single regulator in EU (since 2013) and is (joint) largest authority for advanced therapy trials

- The proportion of UK CTA applications is approximately **25-29%** of total EU CTA applications.

- Clinical trials numbers have been stable since 2009 (approx. 950 - 1000 trials per year; ~5000 amendments)

- Increased Phase 2/3; low, stable Phase 4; decreased Phase 1 - but First-in-human and ATMP numbers have increased.

- Competitive Assessment Timelines
  - Phase 1: Average 12.5 days (no GNA); 36.9 days (with GNA)
  - Other trials: Average 25.8 days (no GNA); 50.9 days (with GNA)

Looking forward

- Goal is for UK to remain an attractive and competitive location for research within the global environment and build from current successes
- MHRA as regulator has been and continues to be in listening mode re stakeholder views on what is needed
- Within wider government looking at potential for relationships outside of UK and EU
- MHRA within UK working with HRA, NIHR and Devolved Administrations to explore options for future scenarios

Post Brexit

- Post Brexit current legislation will continue to apply in UK
- It will still be possible for UK sponsors to run multistate trials involving the EU and RoW
- Data generated in UK trials will be admissible to support marketing authorisations in EU and globally
- Currently planning to implement or to align with the Clinical Trials Regulation (536/2014)

Brexit Planning

- Planning for multiple scenarios:
  - ‘Deal’
    - depends on agreed EU relationship and capacity for any wider global relationships
    - planning to implement CTR
      - UK legislation (implementing SI)
      - IT systems/processes (EU Portal)
      - communications/training
  - ‘No Deal’
    - depends on EU relationship and any wider global relationships
    - planning to align with CTR (IRAS Portal)
    - UK legislation ready (‘no deal’ SI)
    - IT systems/processes (European Systems contingency/ current IRAS)
    - communications/training

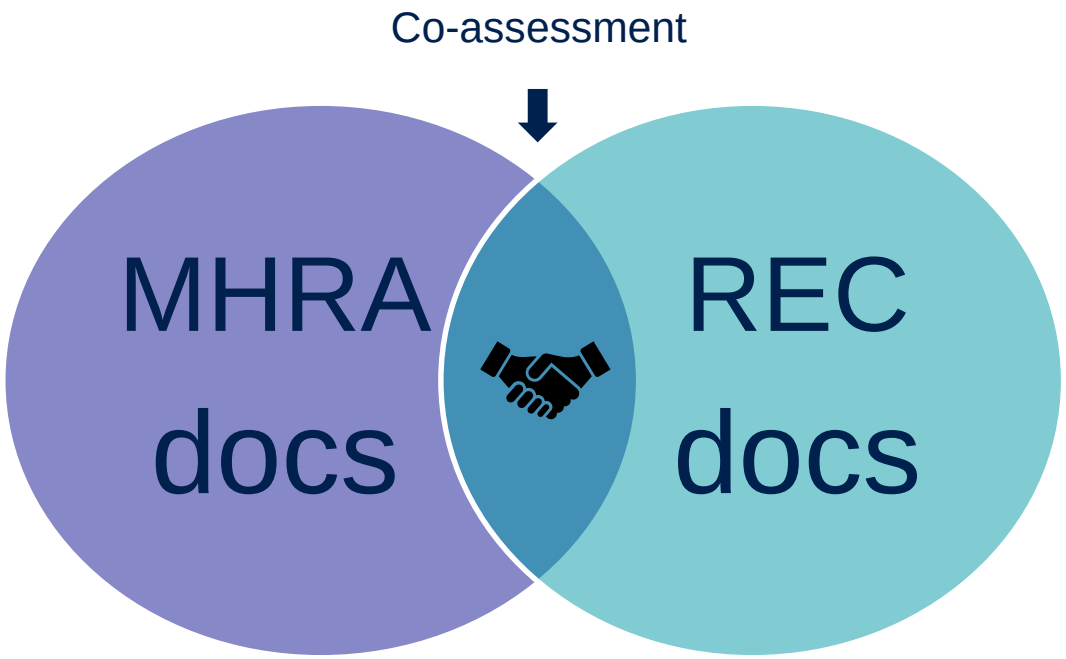
MHRA IT Developments

New MHRA IT systems

- Work Package 1 – Sentinel replacement
  - Completed April 2019
- Work Package 2 – MHRA/HRA integration
  - Work underway – Go Live planned early 2020
- Work Package 3 – CT Safety systems upgrade
  - Work planned – Go Live 2020
- Work Package 4 – Full EU or IRAS integration
  - Planning underway

MHRA/HRA Combined Ways of Working

- A new process that will pilot a single clinical trial application route resulting in a single UK decision on a clinical trial (ethics opinion plus MHRA clinical trial authorisation).



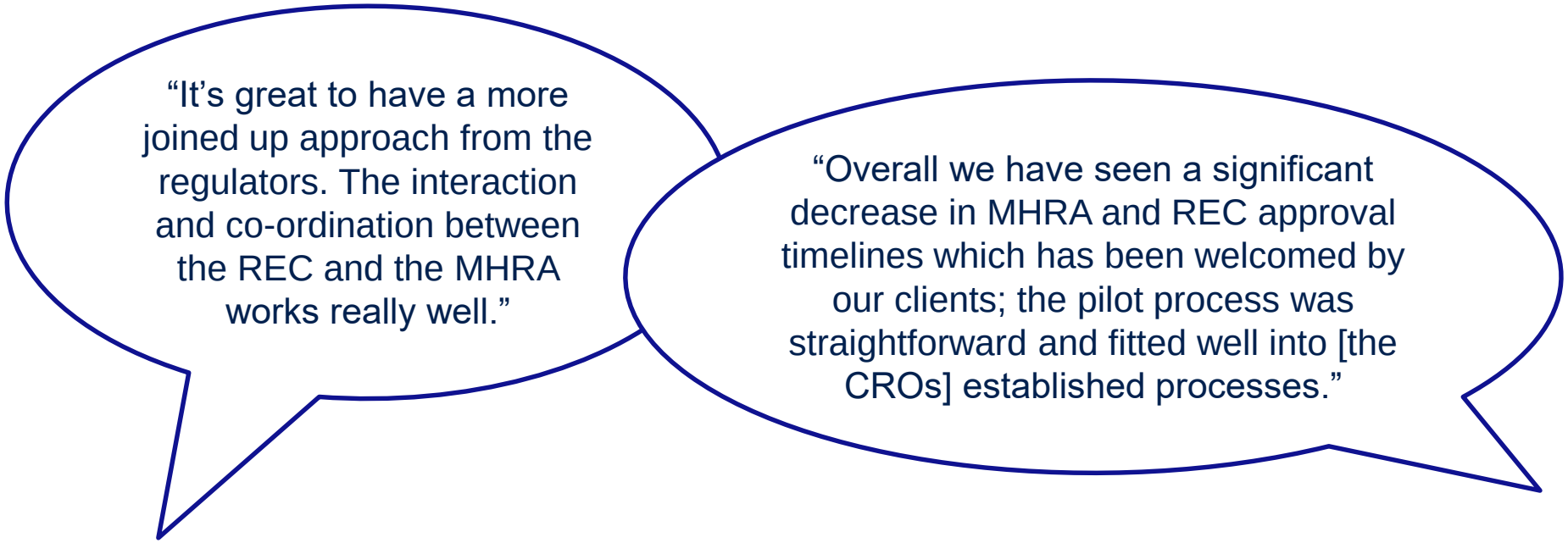
Pilot launched in April 2018; First application 29th May 2018

MHRA/HRA Combined ways of Working

- Based on need to implement Clinical Trial Regulation
- Agencies explored how to create a single application/single decision process for UK stakeholders
- Pilot started in April 2018 – supported by manual processes
  - Limited ‘front end’ work so far
  - More extensive ‘back end’ work on Ethics Committee training and assessment collaboration
- Work underway to develop IT systems to support new processes
  - Based on IRAS as a UK submission Portal
  - New system to allow interactive assessment of applications
- Plan to expand pilot early 2020
  - Test IT systems
  - Allow UK stakeholders to develop own internal processes

Status of pilot

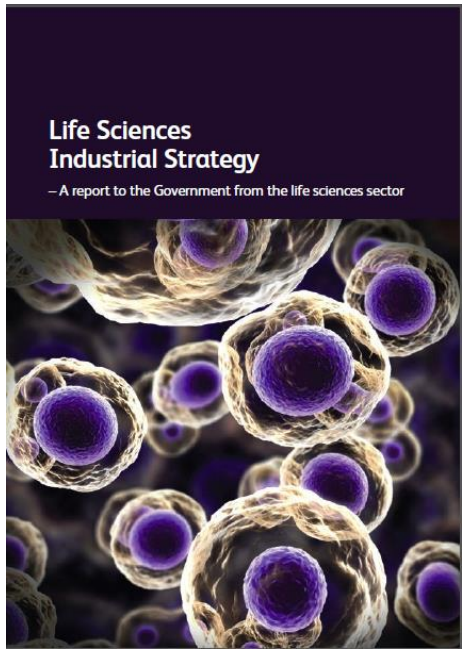
- 75 initial applications, 63 amendments and 8 end of trials received to date (29 July 2019)
- Time for initial assessment:17 to 36 days (target 30 days); final approvals issued between 20 and 69 days (target 60 days).
- Ethics opinions delivered in average of 51 days (range 34-62 days) under pilot versus 81 days (range 17-263 days) outside pilot



Life Sciences Industrial Strategy 2017 report to the UK Government:

"As the UK seeks to do more **complex and innovative trials**, MHRA needs to continue engaging with sponsors to **assist with innovative protocol designs** and should facilitate efficient approval of complex trials and amendments to such trials, for example, to add new arms.

The **UK should attempt to lead the innovation** in clinical trial methodology, such as basket trials, and should also attempt to embed routine genomic analysis to make trials more targeted, smaller and more likely to deliver high efficacy."



Supporting innovative trial designs

- Already see and approve many novel trial designs throughout all phases of study.
- Working at national and EU level to develop guidance for novel trial designs: integrated, umbrella, basket, matrix, use of companion diagnostics etc
- Also working with sponsors to help with adaptive design studies and supporting modifications to ongoing trials
  - *The biggest barrier to innovation from our perspective is not engaging with the regulator early enough (or at all!)*
- UK workshop planned for 2019

Sources of advice from MHRA Clinical trials Unit

- Scientific / Regulatory advice
  - 75-100 meetings per year.

- Dedicated Clinical Trial Helpline
  - Approx. 3500 emails + 5000 phone calls per year
    - 14 day target response (currently ~4 days)

- Access to assessors
  - Direct phone number/email address provided in Request for Information letters

Contact: Clintrialhelpline@mhra.gov.uk

Summary

- UK continues to be attractive for clinical research with no significant ‘Brexit’ effect so far. In fact – increase in innovative trials!
- Brexit preparations in place and ready to go, regardless of scenario
- MHRA/HRA working to further streamline the UK trial approval process and where possible reduce the regulatory burden
- MHRA has an objective to support innovation and a key message is we want to see early engagement from stakeholders developing in this area