Good Clinical Practice Guidelines and the European Directive. How Can Investigator-initiated Research Survive? Current UK Situation-Academic Perspective.

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Scope of Presentation- Personal Perspectives

- Old Scheme
- Current UK Situation
  - NRES
  - MHRA
- Changes and Challenges
  - Reduction in Research Applications
  - Reduction in RECs
  - Industry and CROs
  - Academically Lead Research

Glossary of Terms

NRES:	National Research Ethical Service
IRAS:	Integrated Research Application Service
REC:	Research Ethical Committee
MHRA:	Medicine and Healthcare Products Regulatory Authority
NIHR:	National Institute of Health Research

The Evolving UK Clinical Research Scheme

- Sponsorship (Institute based)
- National Institutes of Health Research (NIHR)
- National Research Ethical Service (NRES)
- Medicines and Health Care Products Regulatory Agency (MHRA)
- Integrated Research Application System (IRAS)
- Research passports

The “Old” Scheme

- Academically Lead Research
  - idea, proposal, funding
- Submit to Local Ethical Committee
  - usually medical school
  - science peer reviewed by funder
- Ethical Committees (up to 2006)
  - no central regulation
  - no training of committee members
- Indemnity
  - local
  - pharma

Sponsorship

- Sponsor no longer the funder

- Sponsor now Institution
  - usually academic institution
  - industry/CRO*

*CRO-Clinical Research Organisation

UK National Institutes of Health Research (NIHR)

- Academic Medicine given supplement by government for Teaching and Research
  - SIFT(R)
- Direct money transfer to hospital (not medical school)
  - large sums of money
    (Culyer Funds for Research)
  - initially non-accountable spend
- Recognition that DH research spend unaccountable
  - money withdrawn from hospital budget
  - NIH(R) Fund established centrally
- Disimbursement of NIHR funding
  - Academic Healthcare Centres
  - Clinical Local Research Network
  - Fellowships

National Research Ethical Service (NRES)

- Protecting the rights, safety, dignity and well-being of research participants
- Facilitating ethical research, which is of benefit to participants, science and society
- National Research Ethical System
  - 111 local committees being tested in UK (2009)
  - REC – 18 volunteers, training
  - 30% lay members
  - 70% expert members (specialist expert co-option)
- "Proportionate Review"

  (Fast Track)
- 30 day max turnaround

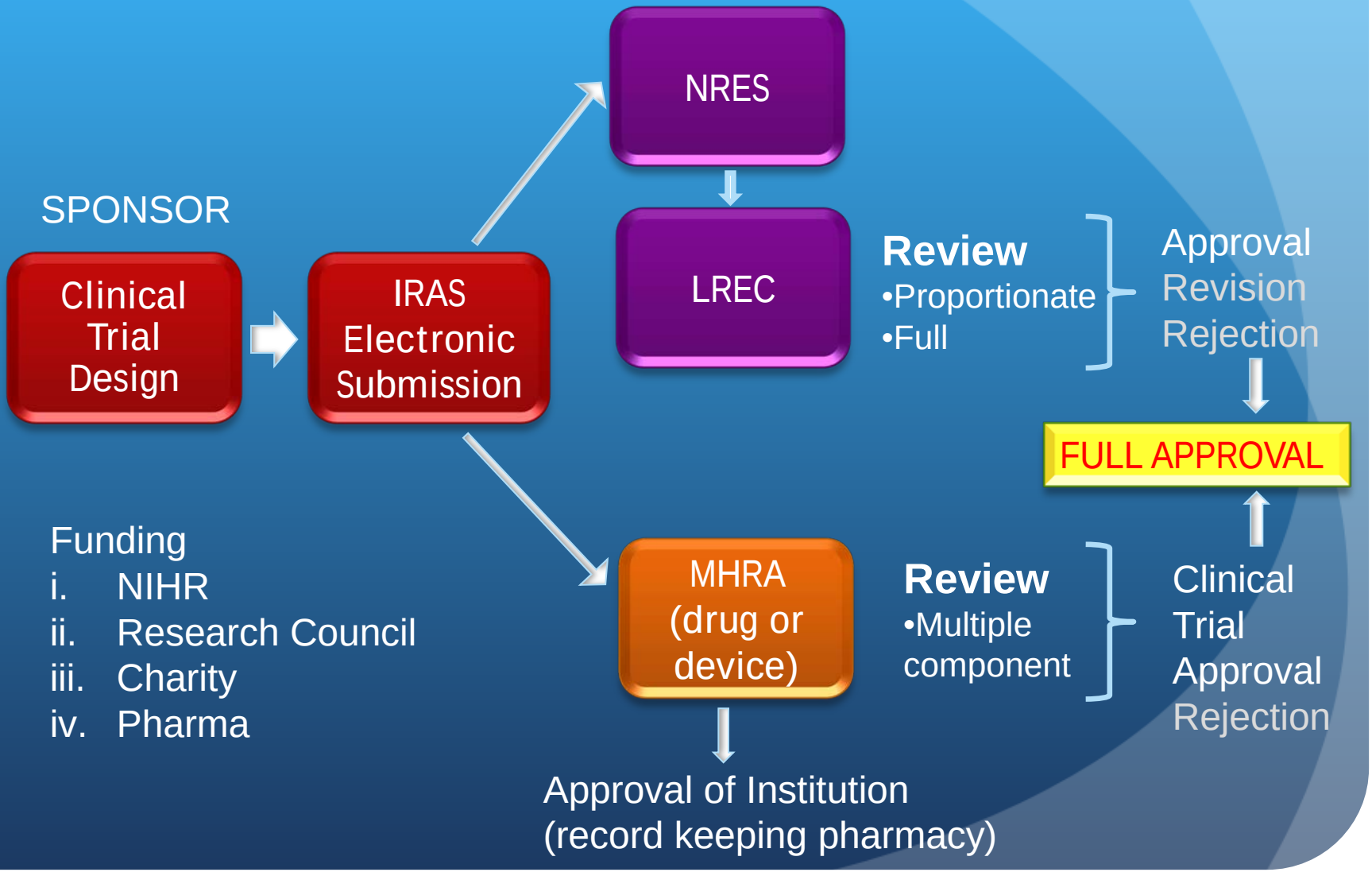
Integrated Research Application Service (IRAS)

- Designed to streamline clinical research application process (April 2008)
- Integrated single electronic system for applying for approval for health and social care/community research in UK
- Designed by NRES
  - Multicomponent
  - Ethical
  - MHRA submission: drug/device
  - Compartmentalised (80 pages!)
  - Cost £3k to £5k per submission

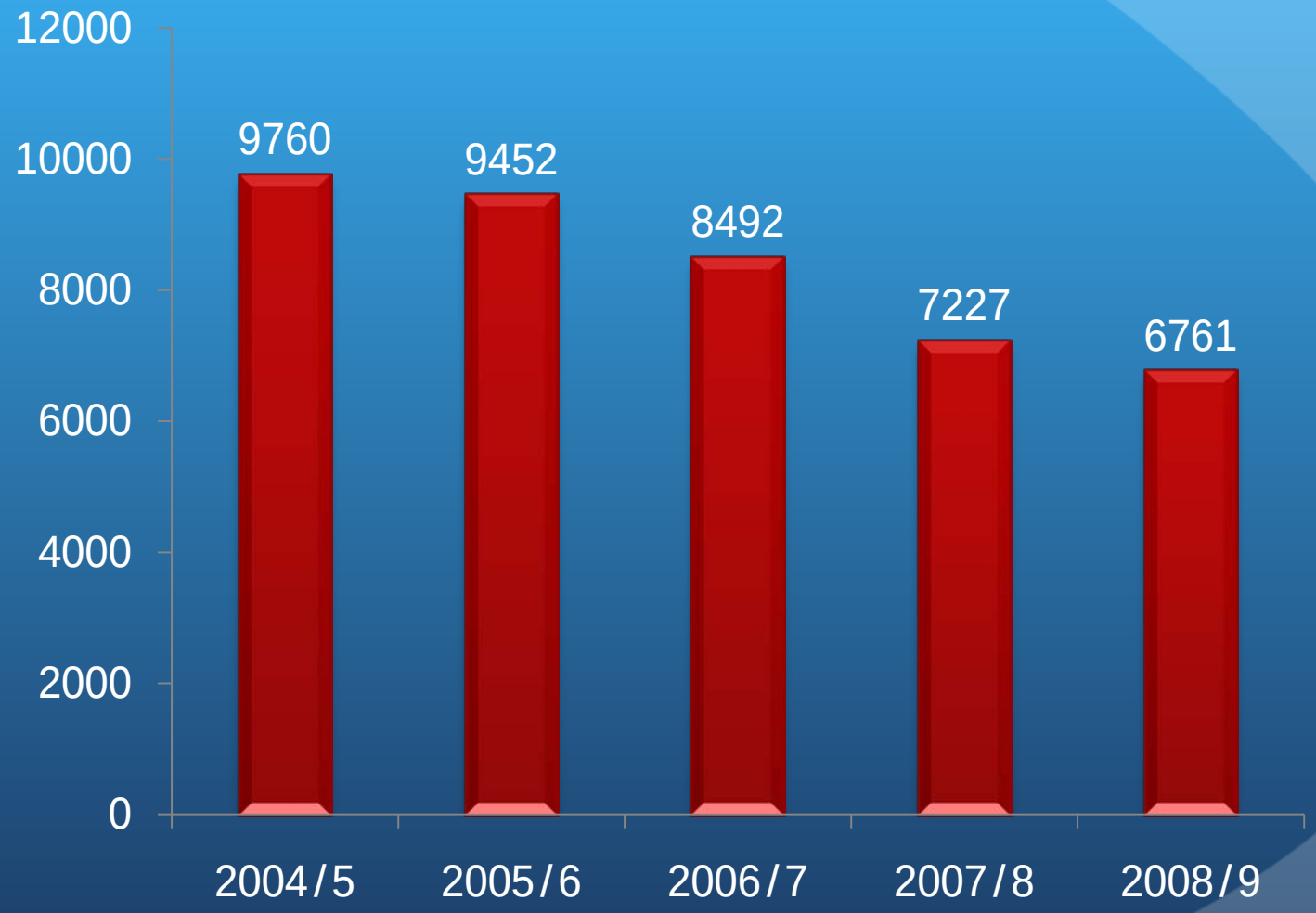
Medicine and Healthcare Products Regulatory Authority (MHRA)

- Replaced Medicine Controls Agency
- Gives permission for Clinical Trials involving DRUGS, DEVICES (Clinical Trial Certificate)
- Monitors record keeping, facilities, pharmacy

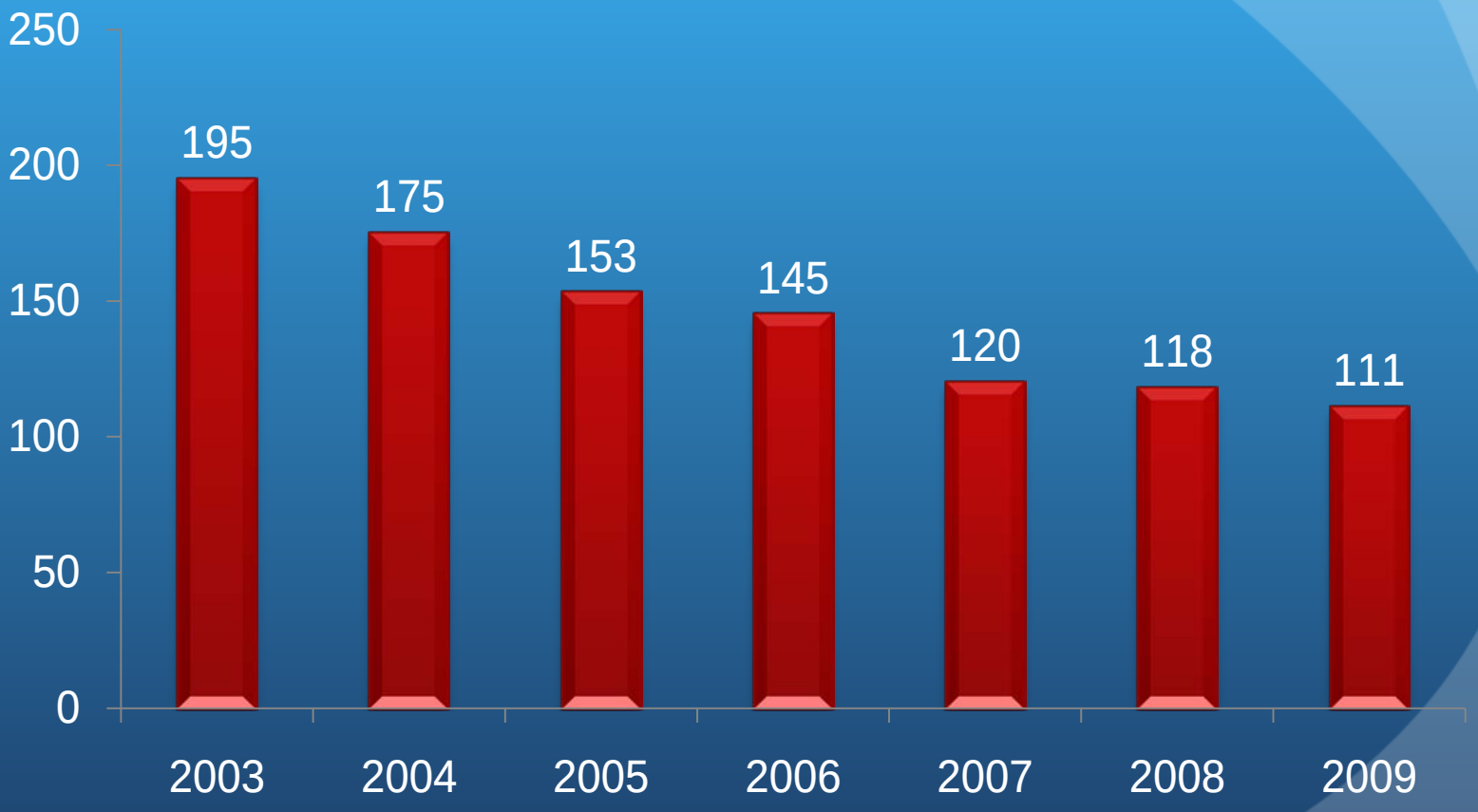
Clinical Trial Application: Simplified Sequence – UK 2010



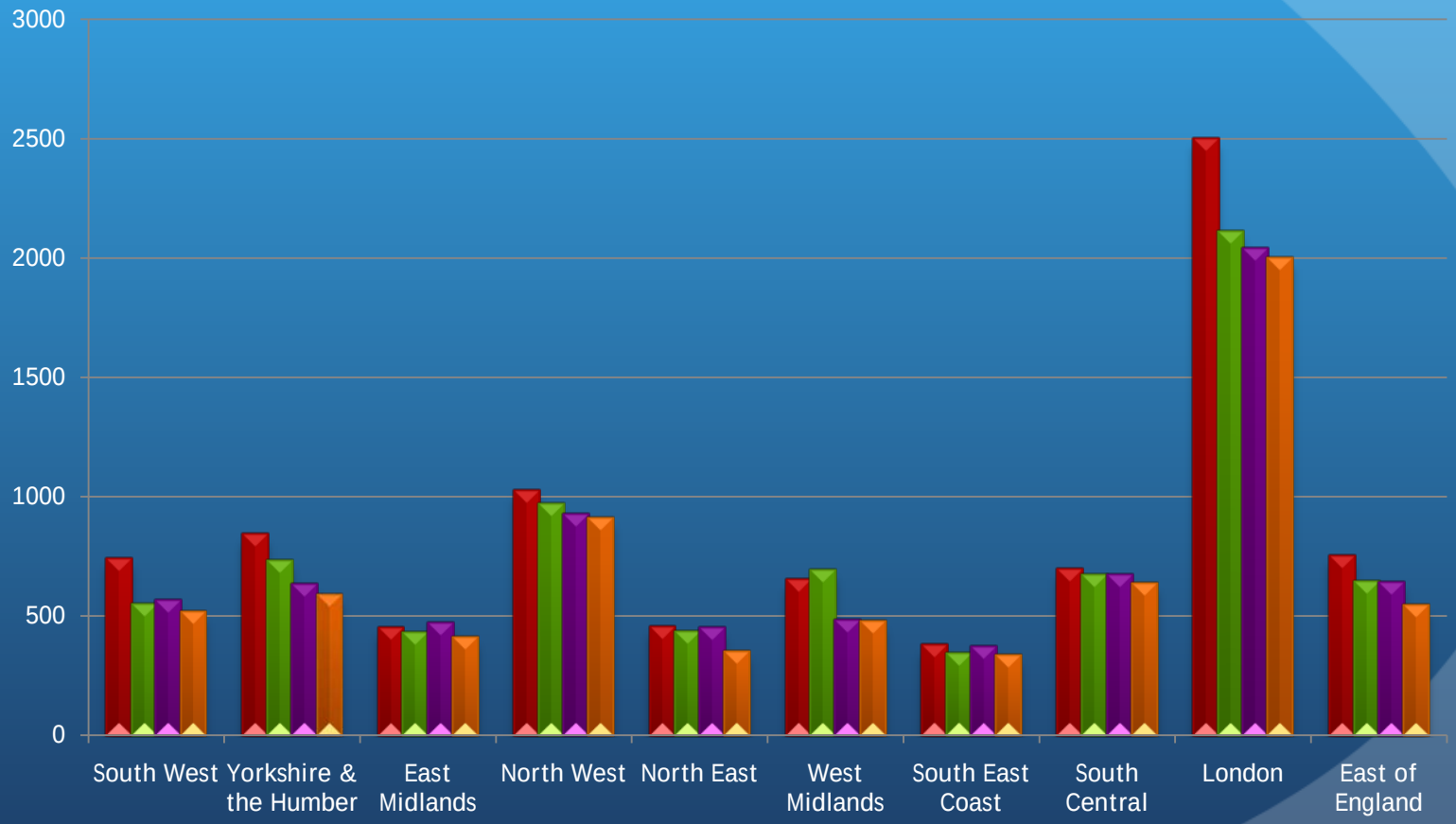
IRAS applications (England)



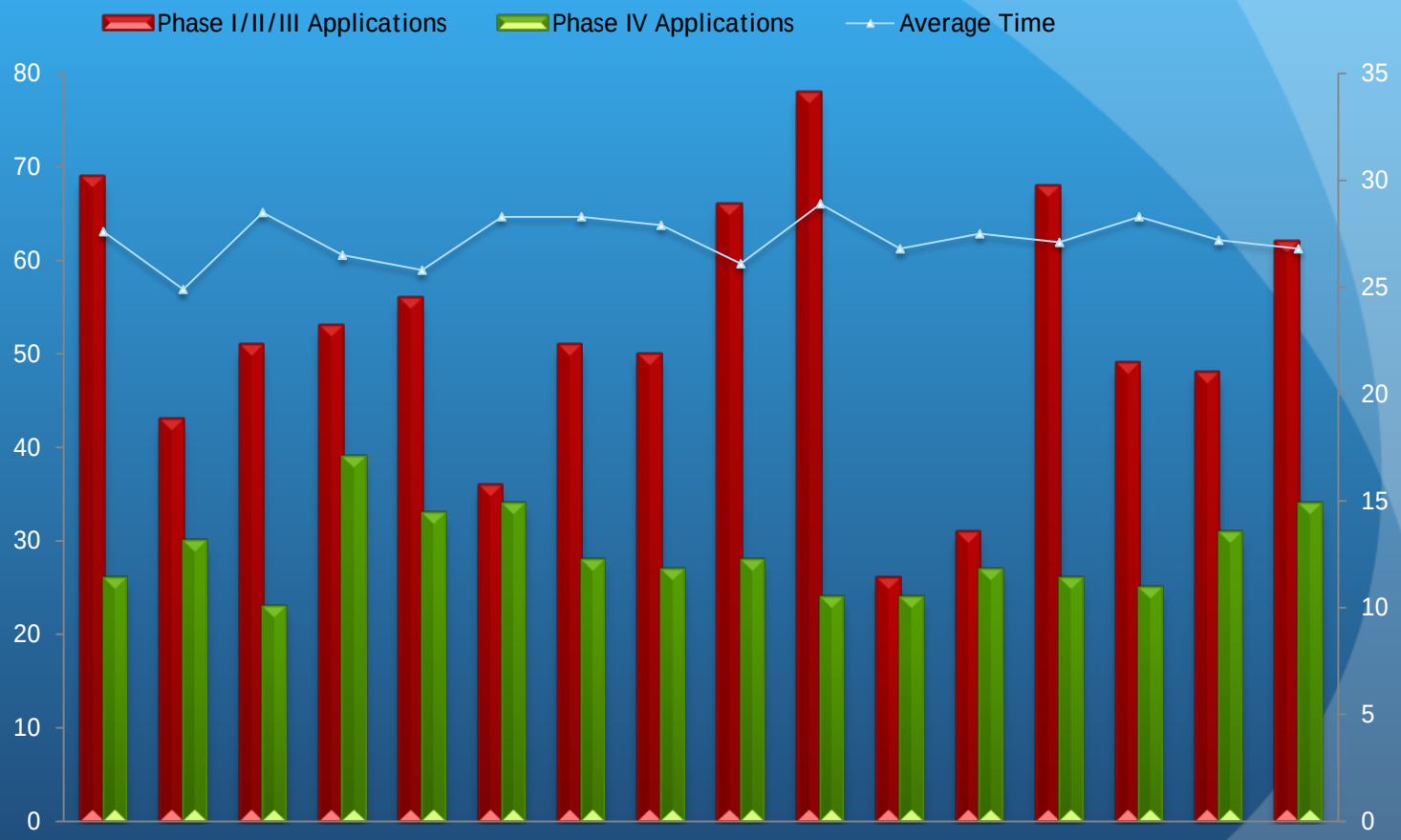
Research Ethical Committees (England)



Number of IRAS applications per Strategic Health Authority

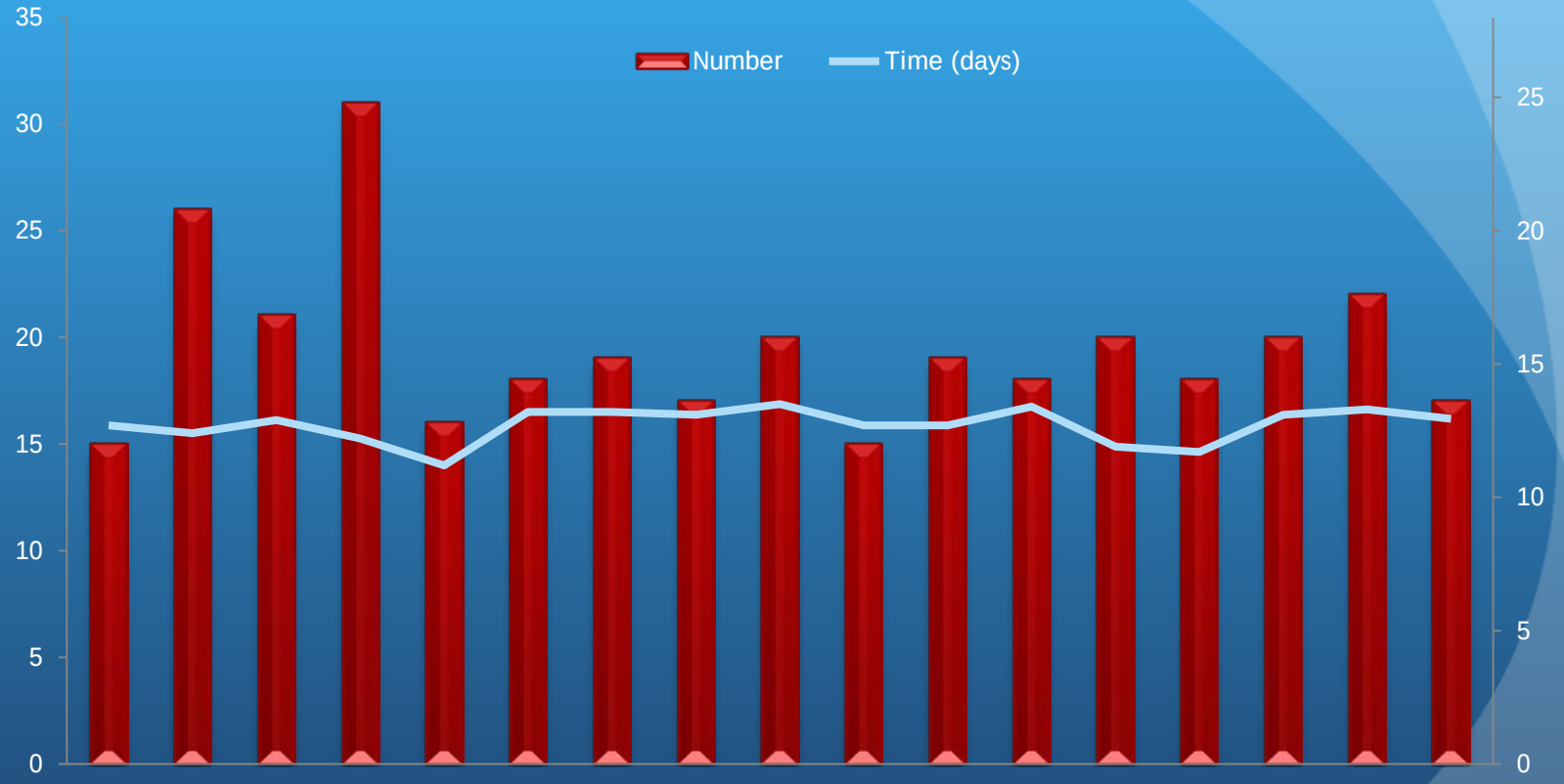


Clinical Trials (Phase I – IV)
MHRA Assessment Time (April 08-July 09)



	apr-08	mei-08	jun-08	jul-08	aug-08	sep-08	okt-08	nov-08	dec-08	jan-09	feb-09	mrt-09	apr-09	mei-09	jun-09	jul-09
Phase I/II/III Applications	69	43	51	53	56	36	51	50	66	78	26	31	68	49	48	62
Phase IV Applications	26	30	23	39	33	34	28	27	28	24	24	27	26	25	31	34
Average Time	27,6	24,9	28,5	26,5	25,8	28,3	28,3	27,9	26,1	28,9	26,8	27,5	27,1	28,3	27,2	26,8

Healthy Volunteer Trials
MHRA Assessment Time



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Number	15	26	21	31	16	18	19	17	20	15	19	18	20	18	20	22	17
Time (days)	12,7	12,4	12,9	12,2	11,2	13,2	13,2	13,1	13,5	12,7	12,7	13,4	11,9	11,7	13,1	13,3	12,94

Challenges

- Time, expense difficult for academics/institutions
  - Trials in developing countries (e.g. TB)
- Growth of CROs
  - May compromise clinical excellence
- Integrated system not yet fully operational
  - Proportionate Review likely to be implemented
- ? EU Regulation for non-drug trial Clinical Research

Summary

- Clinical academe initially compromised by EU directive
  - Increased bureaucracy, time
  - Under resourced research support
  - Increased costs
- Ethical approval has been enhanced in the UK
  - Professional well trained members
  - Enhanced lay representation
  - Proportionate review
- Inspection of facilities heavy handed

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