GA2LEN : an European Network of Excellence for Clinical Trials in Allergic and Immunologic Diseases

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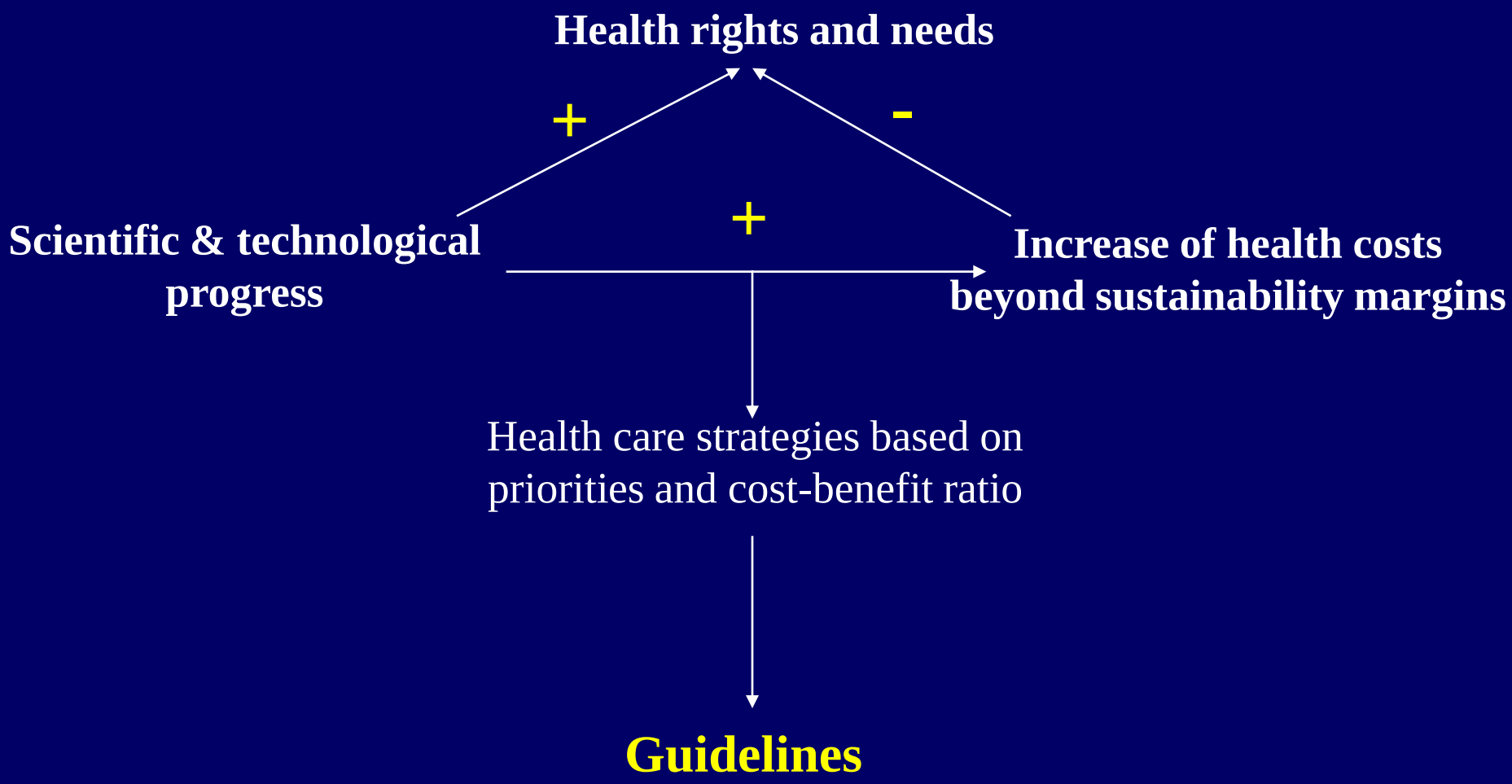
Health need and policy



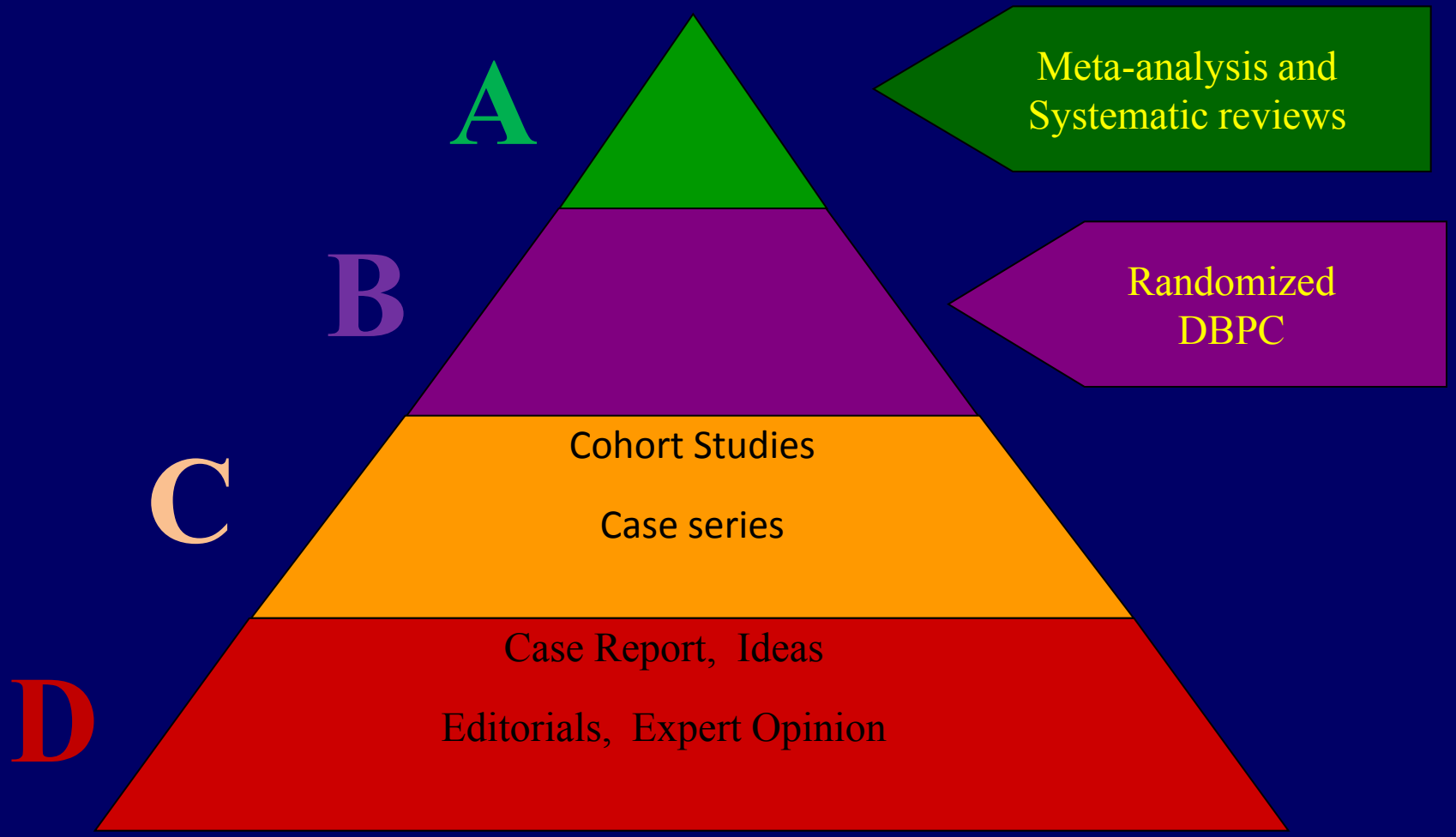
Guidelines in Allergology

Rhinitis	**ARIA www.whiar.org**
Asthma	**GINA www.ginasthma.com**
Conjunctivitis	**http://www.worldallergy.org/**
Urticaria	**EAACI/GA2LEN/EDF guideline: definition, classification and diagnosis of urticaria. Allergy 2006; 61:316-20** **EAACI/GA2LEN/EDF guideline: management of urticaria. Allergy 2006; 61: 321-31**
Anaphylaxis	**The diagnosis and management of anaphylaxis: an updated practice parameter. Joint Task Force on Practice Parameters; AAAAI; ACAAI; JCAAI. J All Clin Immunol 2005 ;115: S483-523.**

Guidelines
should be based on evidence
derived from research

Clinical Research

Observational studies	Interventional studies
Only observe associations (correlations) between the treatments experienced by participants and their health status or diseases	The investigators manipulate the administration of a new intervention and measure the effect of that manipulation
Provide less compelling evidence than controlled trial	Provides the most compelling evidence of a causal relationship between the treatment and the effect



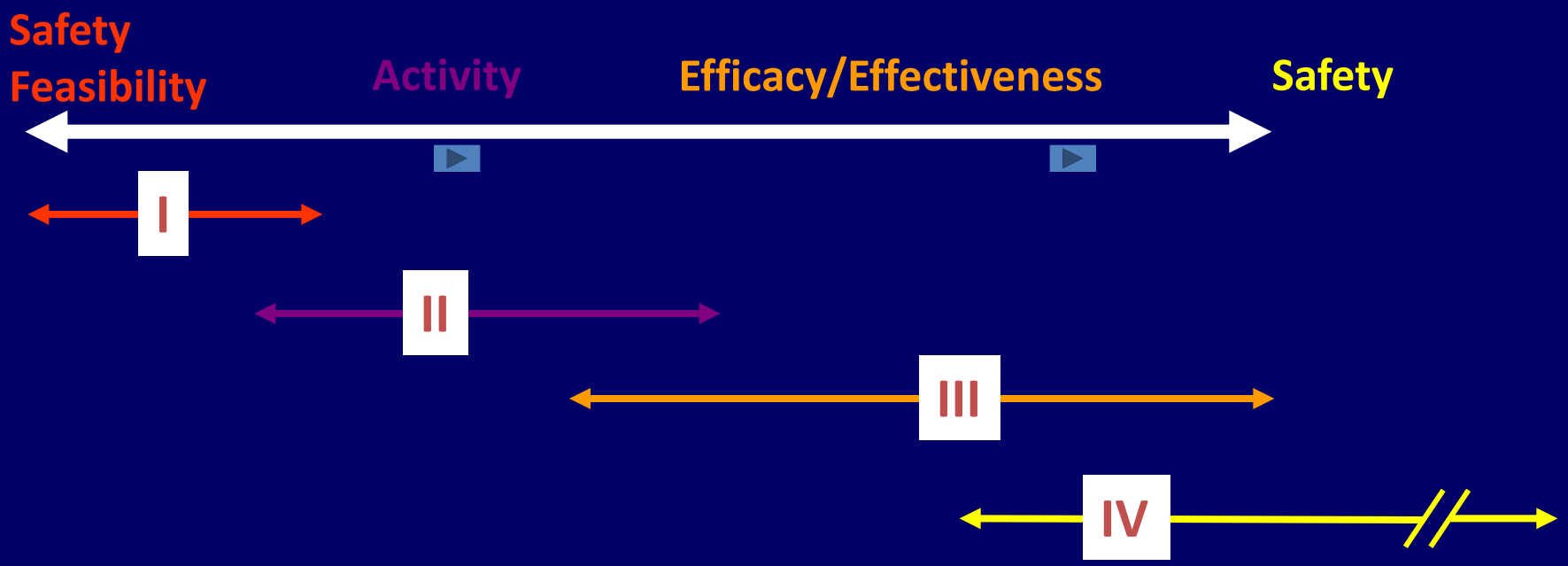
Evidence-Based Medicine Hierarchy

Shekelle BMJ 1999; 318; 593-596

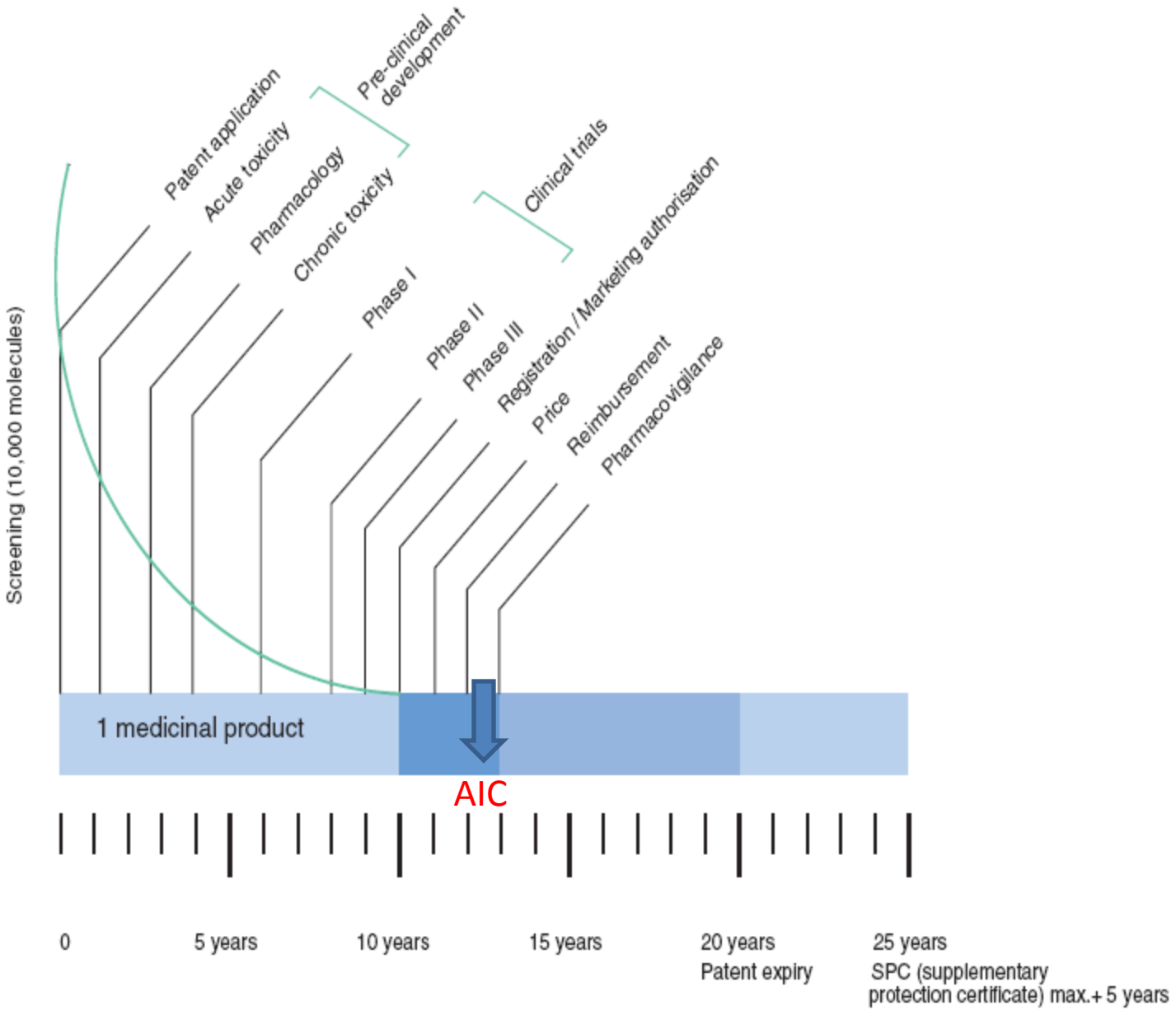
Clinical Trials

Phase 0	**Pre-clinical. Animal and in vitro studies to obtain preliminary pharmacological information**
Phase I	**In man (20-80 healthy subjects) Aimed at evaluating safety, pharamacokinetics and pharmacodynamics of the drug**
Phase II	**200-300 patients and healthy volunteers Aimed at evaluating the efficacy of the treatment IIA – optimal dosage IIB – efficacy**
Phase III	**300-3000 patients RCT aimed at evaluating the efficacy of the drug vs placebo or the actual golden standard**
Phase IV	**Post-marketing pharmacovigilance aimed at evaluating safety of and rare adverse events**

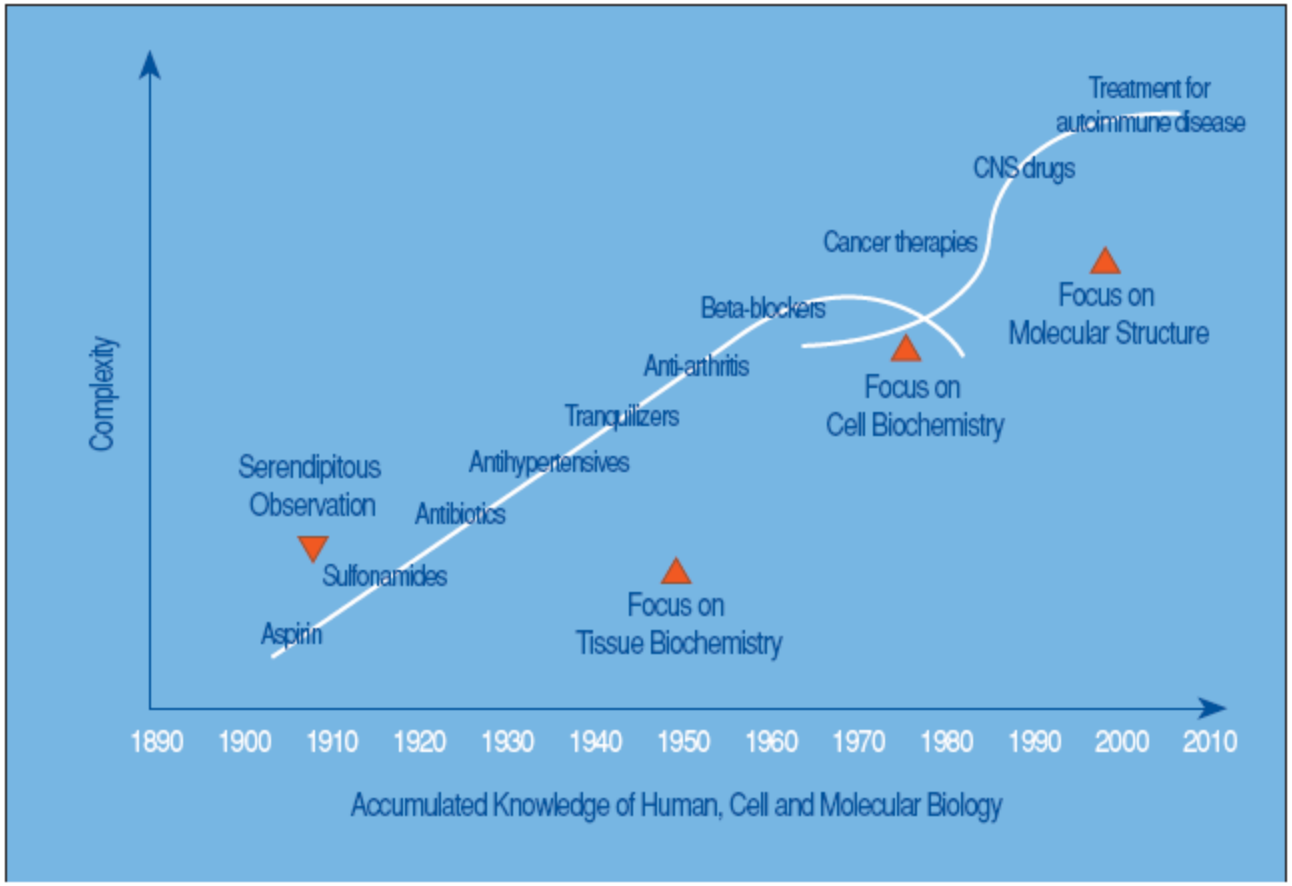
Clinical trials phases:
a continuum



PHASES OF THE RESEARCH AND DEVELOPMENT PROCESS



CHRONOLOGY OF DRUG INNOVATION



Source: Boston Consulting Group

How to obtain marketing authorization of a new drug in Europe

- Centralized
- Mutual recognition
- Decentralised
- National

Mandatory scope Art. 3 (1) and Annex

Indent 1	Indent 3	Indent 4
"Biotech products" **•Recombinant DNA technology** **•Controlled gene expression** **•Monoclonal Antibobies**	**"Therapeutic classes"** New active substance for: **•AIDS** **•Cancer** **•Neurodegenerative disorders** **•Diabetes** **•Autoimmune diseases** **•Viral diseases**	**Orphan designated products**

"Guideline on therapeutic areas within the mandatory scope of the centralised procedure for the evaluation for marketing authorisation applications with reference to article 3 and point 3 of Annex of Regulation (EC) No 726/2004" (EMEA/ 282954/2005)

"Scientific aspects and working definitions for the mandatory scope of the centralised procedure" (May 2008) EMEA/CHMP/121944/2007

Optional scope Art. 3 (2)

Indent a	Indent b
New active substances	**"Significant innovation (Therapeutic, scientific, technical)** **OR** **"Interest of patients at community level**

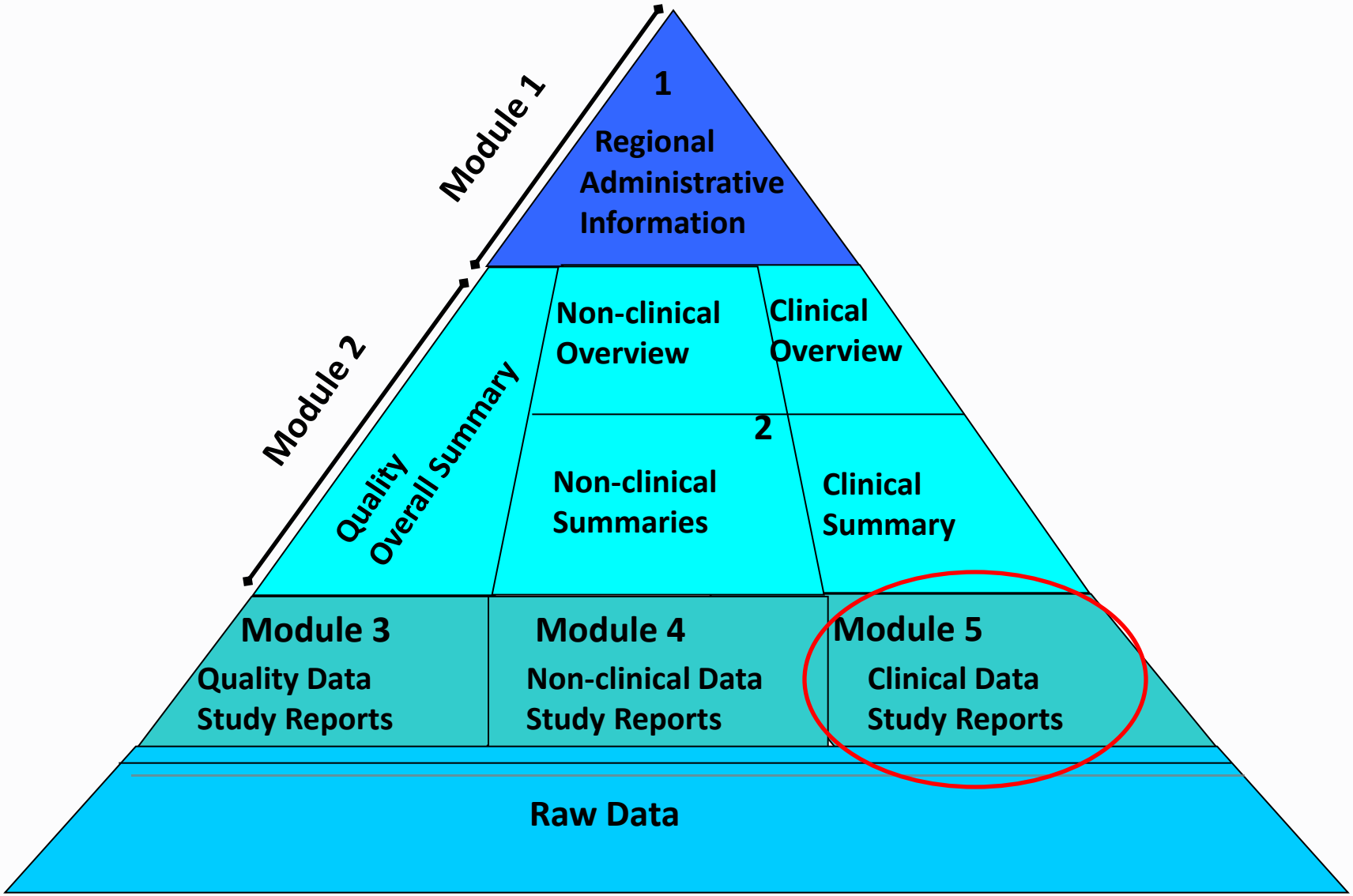
Art. 3 (3) Generic/Hybrid medicinal product

Draft "Guideline concerning the optional scope of the centralised procedure in accordance with Article 3(2) of Regulation (EC) No 726/2004"

Anche vecchi medicinali ma con una innovazione significativa (nuova indicazione, nuovo meccanismo di azione, nuova forma farmaceutica) ad es. Aspirina per il morbo di Alzheimer

Canary Wharf – Docklands London

Common Technical Document (CTD)



Clinical Trials in Allergy & Clinical Immunology

Background I

- The idea of creating a platform to facilitate clinical trials in A&CI was born within GA2LEN, an European Network of Excellence (NoE) funded by the EU for 14.4 M Euro for the period 2004-2009 to favour research and education networking in allergy and asthma
- One of the ultimate goals of EU NoEs is to generate permanent platforms which may assure sustainability of the network even beyond the period funded by the 6th EU Framework Program

Clinical Trials in Allergy & Clinical Immunology

Background II

Why a platform on Clinical Trials?

- **Clinical Trials are the basis for an optimal medical care and regulatory decisions**
- **There are several unmet needs lamented both by sponsors and centers involved in clinical trials:**
  - **Limited expertise in GCP standards**
  - **Unadequate inventory of performed and ongoing clinical trials**
  - **Lack of peer-review and publication of negative results**
  - **Burocratical and insurance issues**
  - **Lack of standardized outcome measures, reference material, etc.**

Clinical Trials in Allergy & Clinical Immunology

Background IV

Aims of the Clinical Trials Platform

- **Making an inventory of international and national regulations**
- **Keeping a list of CROs and centers with experience, personnel, structures and patients to perform CT in A&CI, certified on the basis of standard requirements**
- **Providing technical support and legal/insurance advice in defining protocols and contracts, as well as in facilitating contacts with ethic committees, sponsors, CROs, hospitals**
- **Keeping a secondary registry of all CT in A&CI**
- **Training personnel on how performing CT in GCP**
- **Exploring opportunities of fund raising by offering the added value of a structured network vs potential of individual centers**

1.Has your Unit experience in clinical trials?

100% Yes
2005 = 259 (1 to 45)
2006 = 267 (1 to 50)
2007 = 302 (1 to 65)

2. WHAT KIND OF CLINICAL TRIALS ARE PREFERENTIALLY PERFORMED IN YOUR UNIT/CENTRE?

- Phase I 31.4 % (dal 5% al 50%)
- Phase IIA 45.7 % (dal 5% al 45%)
- Phase IIB 62.8 % (dal 5% al 45%)
- Phase III 96 % (dal 5% al 100%)
- Phase IV 68.5 % (dal 5% al 70%)

3.INDICATE THE PERCENTAGE DISTRIBUTION ACCORDING TO SPONSORS OF CLINICAL TRIALS PERFORMED IN YOUR UNIT/CENTRE?

- **Indipendent:**

  26/35 centres (74% of all)

- **Industry:**

  34/35 centres (97.1 of all)

26 Galen Units 57 Collaborating Centres = 83 Centres

35 sent questionnaire

46.5 % of Galen Units

40,3 % of Collaborating Centres

42 % of total Centres

4. IS THERE A SPECIFIC DEPARTMENT, TEAM FOR CLINICAL TRIALS IN YOUR UNIT/CENTRE?

- Yes 22/35 Centres - 62.8%

5. IS THERE DEDICATED PERSONNEL FOR CLINICAL TRIALS?

- Yes 23/35 Centres - 65.7%

6. DO YOU USUALLY REGISTER CLINICAL TRIALS?

- Yes 22/32 centres 68.7%

ClinicalTrials.gov
EUDRACT
EMEA
Controlled-trials.com / ISRCTN.org

National registers 4 centres (CCMO; BfArM; ecc)
Local registers 3 centres

7. PLEASE, PROVIDE INFORMATION ON YOUR ETHICS COMMITTEE ?

Members : 5 to 110

8.HOW LONG DOES IT TAKES FOR HAVING A REPLY FROM YOUR ETHICS COMMITTEE?

< 15 days	11.7%
15-30 days	47%
30-45 days	26.4%
45-60 days	17.6%
More	0%

9. HAVE YOU STANDARD MATERIAL FOR CLINICAL TRIALS ?

Yes: **88.3 %**

10. HOW DO YOU JUDGE THE KNOWLEDGE OF GPC REGULATIONS IN PEOPLE PARTECIPATING IN CLINICAL TRIALS AT YOUR U/C?

Excellent	**60.7% (20/33 Centres)**
Good	**33.3% (11/33 Centres)**
Fair	**3% (1/33 Centre)**
Unsatisfactory	**3% (1/33 Centre)**
Very limited	**0%**

12. WHAT KIND OF PATIENTS ARE REFERRED TO YOUR U/C?

13/34 Centres only adults 38.2%

4/34 Centres only children 11.7%

15/34 Centres both 44.1%

1/34 Centre did not answer 2.9%

1/34 Centre does not see patients 2.9%

13. WHAT KIND OF DISEASE/ALLERGIC CONDITION YOU HAVE EXPERIENCE OF AND MIGHT REPRESENT THE PREFERENTIAL TARGET FOR CLINICAL TRIALS TO BE PERFORMED BY YOUR UNIT/CENTRE?

- Asthma 57.385 patients/year
- Rhinitis/Rhinosinusitis 67.439 patients/year
- Conjunctivitis 25.294 patients/year
- Urticaria/angioedema 15.676 patients/year
- Atopic Dermatitis 25.098 patients/year
- Anaphylaxis 3.393 patients/year
- Food allergy 13.296 patients/year
- Drug allergy 8.875 patients/year
- Others (ITS 2500p/y, Chronic lung diseases >2000, Polyposis 1150 p/y, Hymenoptera allergy >1000p/y)

Clinical Trials in Allergy & Clinical Immunology

WAO Special Committee

To extend the GA²LEN initiative to a global level