A European perspective

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Disclosures

	Employment	Consultant / Advisory	Stock	Honoraria	Research funds	Testimony	Other
Amgen Dompé	no	no	no	no	yes*	no	no
Bayer	no	yes	no	no	yes*	no	no
Glaxo SK	no	yes	no	no	yes*	no	no
ImClone	no	no	no	no	yes*	no	no
Infinity	no	no	no	no	yes*	no	no
Janssen Cilag	no	no	no	yes	Yes*	no	no
Lilly	no	no	no	no	yes*	no	no
Merck SD	no	yes	no	no	yes*	no	no
Molmed	no	no	no	no	yes*	no	no
Novartis	no	yes	no	yes	yes*	no	yes**
Pfizer	no	yes	no	yes	yes*	no	no
PharmaMar	no	yes	no	yes	yes*	no	yes**
Sanofi-Aventis	no	yes	no	no	yes*	no	no
Schering Plough	no	no	no	no	yes*	no	no

yes = myself, compensated
* = funds received by my institution for clinical studies and research activities in which I am involved
** = travel coverages for medical meetings

Alliance for Biomedical Research in Europe

EUROPEAN COUNCIL FOR HEALTH RESEARCH
CONCEPT PAPER

Core Working Group

This Concept Paper has been initiated by a group of multidisciplinary, multi-professional 'opinion-leaders', nominated by the member societies of the Alliance for Biomedical Research in Europe (BioMed Alliance), along with the BioMed Alliance Executive Committee.

EuCHR Core Working Group

BioMed Alliance Executive Committee

Ulf Smith	Julio Celis	Karin Sipido	Laurent Nicod
President	Vice-President	Vice-President	Treasurer

Core Working Group Members	***Proposed by***
Sir George Alberti	EASD
Maciej Banach	ESH
Peter J Barnes	ERS
Laurent Degos	EHA
Wilfried Ellmeier	EFIS
Valentin Fuster	ESC
Silke Mader	ESPR
Michael Manns	EASL/ UEGF
Luis Marti-Bonmati	ESR
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Tomas Zima	FEBS

Advisors

Richard Bergstrom	Liselotte Højgaard
José Mariano Gago	Stella Kyriakidis
Harald zur Hausen	Peter Lange

Alliance for Biomedical Research in Europe

EUROPEAN COUNCIL FOR HEALTH RESEARCH
CONCEPT PAPER

But despite the critical need to advance in health research, **Europe is progressively falling behind as global competition in research becomes stronger**. According to a recent report by the European Commission (EC), innovation performance growth is slowing down and the European Union (EU) is not closing the persistent gap with global innovation leaders such as the United States (US), Japan and South Korea[8]. Many biomedical companies are finding drug development in Europe economically challenging and as a result are moving their operations from the region, mainly to Asia.

Europe is also behind in its investment in research generally. Between 2002 and 2007, European investment in research stagnated[9]; in the same period China increased research and development (R&D) spending by a staggering 160%. This is worrying, as healthcare is a driving factor for different industries in most European countries. Investments in research and innovation related to health will pay off for Europe as new concepts in therapy can be exported worldwide. The UK's Medical Research Council, for example, looked at investment in cardiovascular research, and estimated the return on investment to be up to 39%[10]. Clearly, investment creates employment and improves health, as well as providing innovative cost-saving technologies, thus reducing the growing economic burden Europe faces.

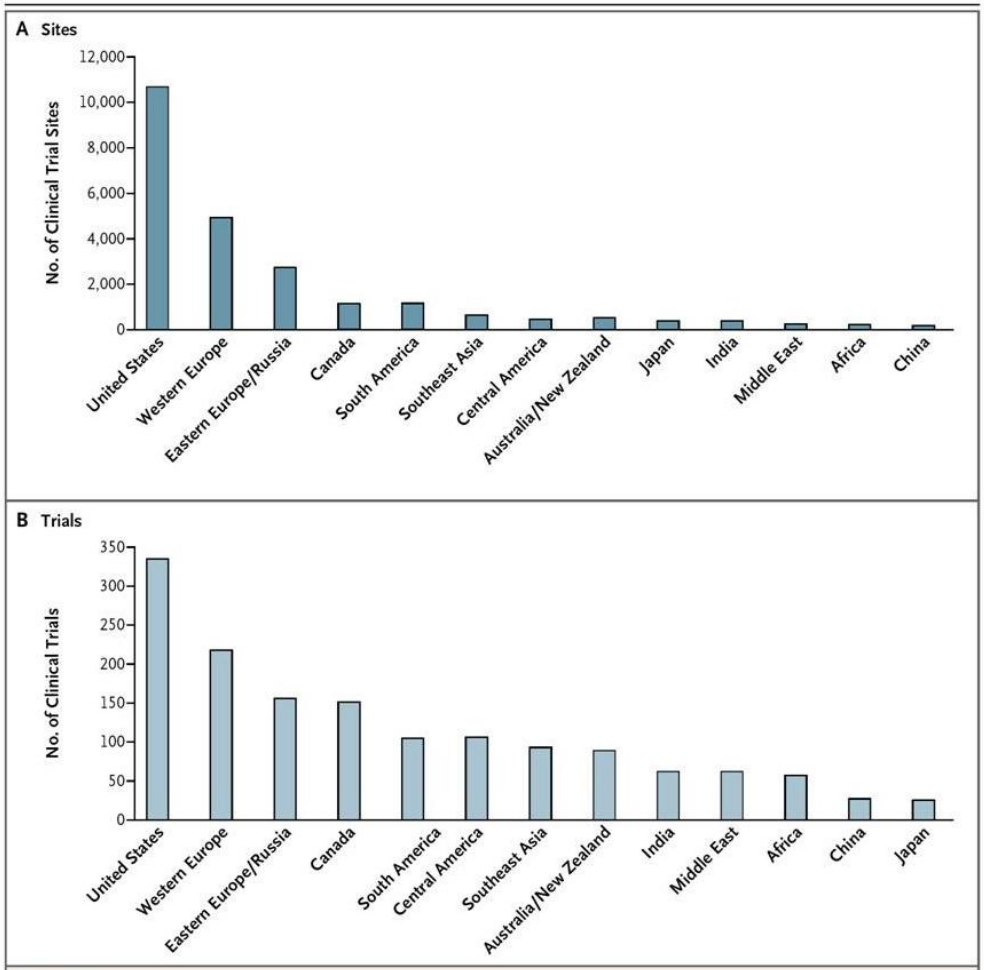


Figure 1. Open Phase 3 Clinical Trials Sponsored by the 20 Largest U.S.-Based Pharmaceutical Companies, as of November 2007.

Table 1. Characteristics of 300 Clinical Trials Reported in the *Journal of the American Medical Association*, the *Lancet*, and the *New England Journal of Medicine* in 1995 and 2005.*

Characteristic	Year	
	1995 (N=150)	2005 (N=150)
No. of countries represented	33	70
No. of patients per trial		
Median	215	661
Interquartile range	75–830	239–1837
Multinational trials — no. (%)	25 (16.7)	44 (29.3)
Information reported about location — no. (%)		
Locations not reported	59 (39.3)	13 (8.7)
Only continents reported	5 (3.3)	8 (5.3)
Only number of countries reported	6 (4.0)	14 (9.3)
Names of countries reported	79 (52.7)	113 (75.3)
Enrollment from each country reported†	1 (4.0)	2 (4.5)
Countries per trial — no. (%)‡		
1	65 (75.6)	94 (72.9)
2–10	17 (19.8)	20 (15.5)
11–20	4 (4.7)	5 (3.9)
>20	0	10 (7.8)
Regions represented — % of trials		
Africa	5.0	8.7
Eastern Europe and Russia	2.5	5.2
Middle East	1.3	3.5
Asia	8.8	6.1
United States	53.8	42.6
Western Europe	40.0	36.5

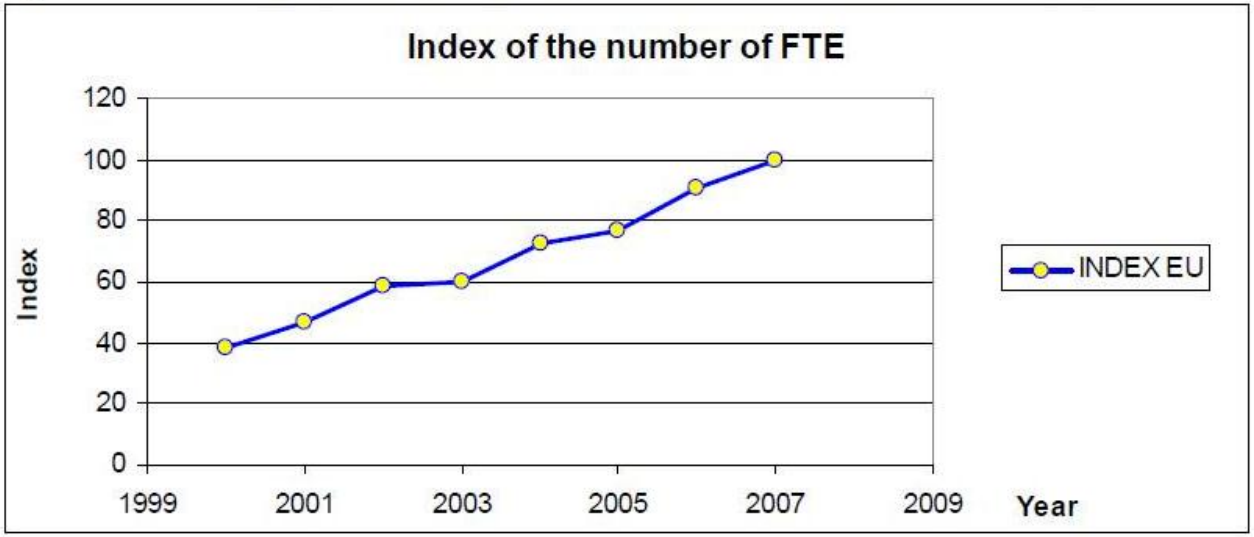
Glickman SW et al, New Engl J Med 2009;360:816

Impact on Clinical Research of European Legislation (ICREL)

Final Report – Second Version

15 June 2009

Figure 18: Index of the number of FTEs for administrative tasks in the EU



Source: Figure CA95 in Statistical Report CA, available on www.efgcp.be/ICREL > Report

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Public Health and Risk Assessment
Pharmaceuticals

Brussels, 09/02/2011
SANCO/C/8/PB/SF D(2011) 143488

REVISION OF THE 'CLINICAL TRIALS DIRECTIVE' 2001/20/EC

CONCEPT PAPER SUBMITTED FOR PUBLIC CONSULTATION

Estimation of costs of insurance per patient per annum for insurance in different Member States (in €):

Belgium	14.50
France	75.00
Germany	75.00
Italy	50.00
The Netherlands	23.00

- **Risk-based approach**
- **Clarity on the scope**
- **Streamlined authorization and assessment of clinical trials**
- **Simplified approval and monitoring requirements**
- **Clearer and detailed guidance**

We welcome the proposal to revise the EU Clinical Trials Directive. We call on the EU institutions, national Governments and others to develop a supportive environment for conducting clinical trials, enabling development and testing of treatment options for patients. Revisions should focus on reducing bureaucracy, which acts as a disincentive to setting up clinical trials. This revision should include streamlining authorisation processes; adoption of a proportionate approach to the regulation of clinical trials; and the provision of clearer guidance. This statement outlines agreement on key issues relating to clinical trials although a more detailed proposal is needed.

These photos show the difference in paperwork needed before and after the implementation of the Clinical Trials Directive

CANCER RESEARCH UK

Supporting Research, Protecting Patients
Cancer Research UK, Feb 2012

DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 4 April 2001

on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

Article 1

Scope

1. This Directive establishes specific provisions regarding the conduct of clinical trials, including multi-centre trials, on human subjects involving medicinal products as defined in Article 1 of Directive 65/65/EEC, in particular relating to the implementation of good clinical practice. This Directive does not apply to non-interventional trials.

2. Good clinical practice is a set of internationally recognised ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects. Compliance with this good practice provides assurance that the rights, safety and well-being of trial subjects are protected, and that the results of the clinical trials are credible.

3. The principles of good clinical practice and detailed guidelines in line with those principles shall be adopted and, if necessary, revised to take account of technical and scientific progress in accordance with the procedure referred to in Article 21(2).

These detailed guidelines shall be published by the Commission.

4. All clinical trials, including bioavailability and bioequivalence studies, shall be designed, conducted and reported in accordance with the principles of good clinical practice.

- data fabrication
- data falsification

STATISTICS IN MEDICINE
Statist. Med. **18**, 3435–3451 (1999)

THE ROLE OF BIOSTATISTICS IN THE PREVENTION, DETECTION AND TREATMENT OF FRAUD IN CLINICAL TRIALS†

MARC BUYSE[1]*, STEPHEN L. GEORGE[2], STEPHEN EVANS[3], NANCY L. GELLER[4], JONAS RANSTAM[5], BRUNO SCHERRER[6], EMMANUEL LESAFFRE[7], GORDON MURRAY[8], LUTZ EDLER[9], JANE HUTTON[10], THEODORE COLTON[11], PETER LACHENBRUCH[12] AND BABU L. VERMA[13]

for the
ISCB SUBCOMMITTEE ON FRAUD

Claims to the contrary notwithstanding, we did not find quantitative evidence that fraud is common in clinical trials. However, fraud is a cause for concern regardless of its prevalence or consequences because the 'habit of truth' is the cardinal value in scientific endeavours.[112,113] Fraud must be fought, but attempts to impose more bureaucracy and heavier monitoring on clinical trials is the wrong answer to an over-rated problem.[114] As the Presidents of the U.S. National Academy of Sciences and of the Institute of Medicine wrote:

> 'If we do not police ourselves, others may step in to do so. The result could be a scientific enterprise that is increasingly constrained by legal strictures, financial oversight, and bureaucratic provisions. […] If scientific research is beset with paperwork and regulation, much of the joy and creativity in doing science could disappear. Such a cultural change would not only impede scientific progress, it would also make our field much less attractive to the dedicated and talented young researchers who represent the future'.[115]

Our view is that fraud can largely be prevented through design of the trial protocol and case report form, and detected by statistical procedures and computerized checks that make use of the unique structure of clinical trial data.

Protocollo 0001

Luglio 1970

ISTITUTO NAZIONALE
PER LO STUDIO
E LA CURA DEI TUMORI

20133 - milano - via venezian, 1 - p.le gorini, 22 - tel. 29.21.76 - 29.21.77 - 29.25.20 - 23.63.940

Partecipanti: G. Bonadonna, S. Monfardini, M. De Lena, F. Fossati-Bellani, G. Beretta, E. Bajetta.

Somministrazione di adriamicina in tumori solidi mediante un nuovo schema terapeutico.

A) SCOPO: determinare (con il G.W.C.C.S.G.) la tossicità e l'efficacia dell'adriamicina in vari tumori solidi dell'adulto e dell'infanzia mediante un nuovo schema terapeutico intermittente.

B) SCELTA DEI PAZIENTI: sono candidati tutti i pazienti con linfoma o neoplasia solida in fase avanzata. Sono esclusi i casi trattati con chemioterapici nelle tre settimane precedenti la somministrazione dell'adriamicina, i casi con riserva midollare compromessa, con iperazotemia e con anamnesi di malattie coronariche o aritmia cardiaca.

C) ESAMI DI LABORATORIO: emometria completa, creatininemia, uricemia, SGOT, SGPT, fosfatasi alcalina, BSF, elettroforesi, ECG, CPK; ove possibile, mielogramma. L'emometria va ripetuta 2-3 volte la settimana (con particolare attenzione attorno al 14° giorno), mentre gli altri esami verranno ripetuti prima di ogni ciclo terapeutico.

D) DOSE PIENA: 25 mg/m^2/die x 3 i.v. (G.B. 5000; PP 150.000)
DOSE RIDOTTA: 20 mg/m^2/die x 3 i.v. (G.B. 3-5000; PP 100-150.000)
Il dosaggio può essere modificato nel tempo usando le seguenti dosi in base ai valori minimi dell'emometria ottenuti nelle tre settimane di intervallo:

15 - ~~20~~ 25 - 30 - 35 (mg/m^2/die x 3)

dose iniziale piena

G.B.		PP	Dose seguente
5000	e	150.000	aumentare di un livello
3-5000	o	100-150.000	invariata
2-3000	o	50-100.000	diminuire di un livello
2000	o	50.000	diminuire di due livelli

dose iniziale ridotta

G.B.		PP	Dose seguente
3-5000	e	100-150.000	aumentare di un livello
2-3000	o	50-100.000	invariata
2000	o	50.000	diminuire di un livello

E) DURATA DEL TRATTAMENTO: se vi è risposta obiettiva, proseguire ogni tre settimane fino alla ripresa della neoplasia. Se vi è arresto della crescita della neoplasia, la terapia può essere proseguita a discrezione del ricercatore. Se vi è progressione della malattia, il trattamento viene proseguito fino produrre mielodepressione. Se il tumore a questo punto continua a proliferare il trattamento viene interrotto.

Il trattamento viene considerato adeguato se l'adriamicina viene somministrata per un minimo di due cicli. Per ogni tipo istologico è necessario trattare 15 pazienti in modo adeguato per poter determinare una risposta terapeutica del 20% o più.

COMITATO ETICO INDIPENDENTE (CEI) DELL'ISTITUTO

[redacted]

[redacted]

Notifica del cambiamento dell'inchiostro utilizzato per apporre il marchio sulle compresse di [redacted] (farmaco sperimentale) [redacted]

Spettabile Comitato Etico,

per quanto riguarda lo studio in oggetto, a causa di un recente cambiamento da parte della Società produttrice del farmaco sperimentale, ci è stato richiesto di notificare a Codesto Comitato Etico che l'inchiostro utilizzato per apporre il marchio sul nuovo lotto di compresse di [redacted] verrà cambiato. Invece del tipo di colore rosso opacode S-1-15038, verrà utilizzato il rosso opacode S-1-15095. Il nuovo inchiostro per apporre il marchio è una sostanza approvata. Il Sommario delle Caratteristiche del Prodotto aggiornato relativo al farmaco sperimentale, verrà inviato non appena disponibile.

Si invia tale informazione come notifica, e non come emendamento sostanziale, sulla base di considerazioni di carattere etico, dal momento che la fornitura delle compresse sopra menzionate, prodotte utilizzando la precedente composizione di inchiostro, è quasi esaurita. Dal momento che non si desidera il verificarsi di una interruzione della fornitura di medicinale ai pazienti mentre si attende l'approvazione, i pazienti verranno provvisti del farmaco sperimentale sopra citato, fabbricato con la nuova composizione di inchiostro. Si prega di farci pervenire eventuali obiezioni a questa notifica.

Si allega alla presente una copia della dichiarazione, da parte dello Sponsor, che si ritiene che questo cambiamento, nell'inchiostro utilizzato per apporre il marchio, non metterà a repentaglio la sicurezza dei pazienti coinvolti nello studio [redacted]

Clinical studies

Clinical studies

Clinical studies

Clinical studies

Clinical studies

Clinical studies

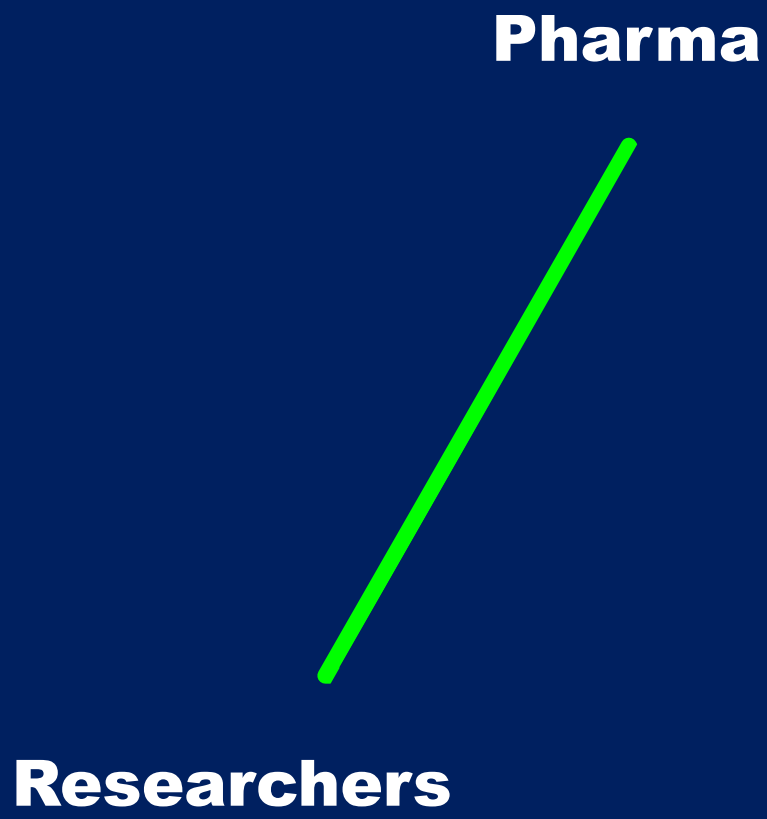
Industry-supported studies

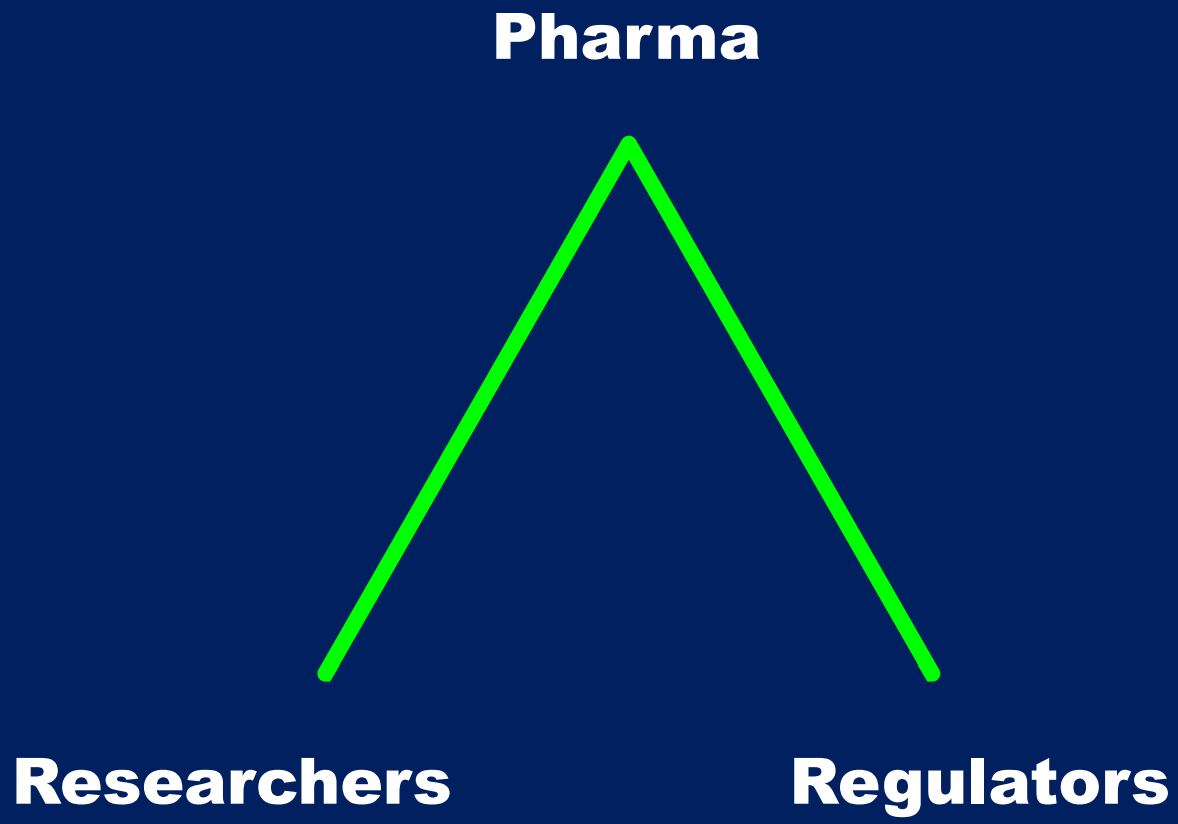
- study conduct
- data analysis
- translational science
- .....

Industry-supported studies

- study design
- study conduct
- data analysis
- translational science
- .....

R


Pharma
Researchers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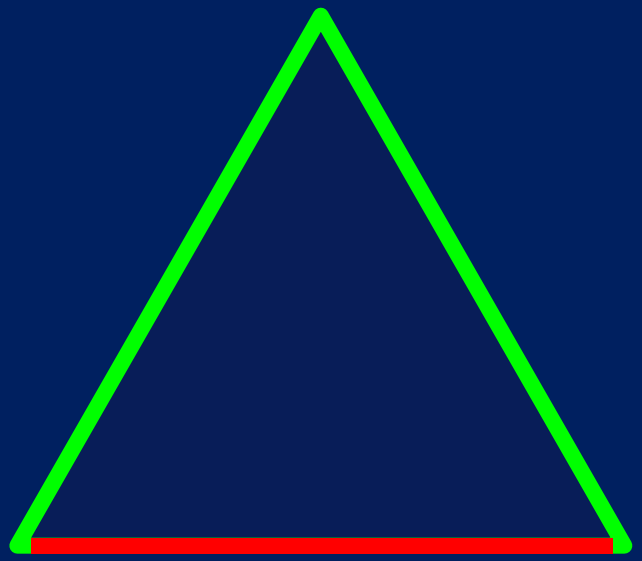
Regulators

Pharma



Researchers

Regulators

Sharing
of clinical trial databases

Retrospective clinical research

DIRECTIVE 2002/58/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 12 July 2002

concerning the processing of personal data and the protection of privacy in the electronic communications sector (Directive on privacy and electronic communications)

EUROPEAN COMMISSION

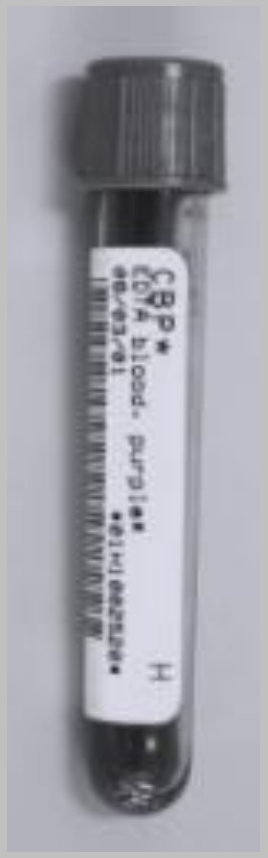
Brussels, 25.1.2012
COM(2012) 11 final

2012/0011 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)


CBP*
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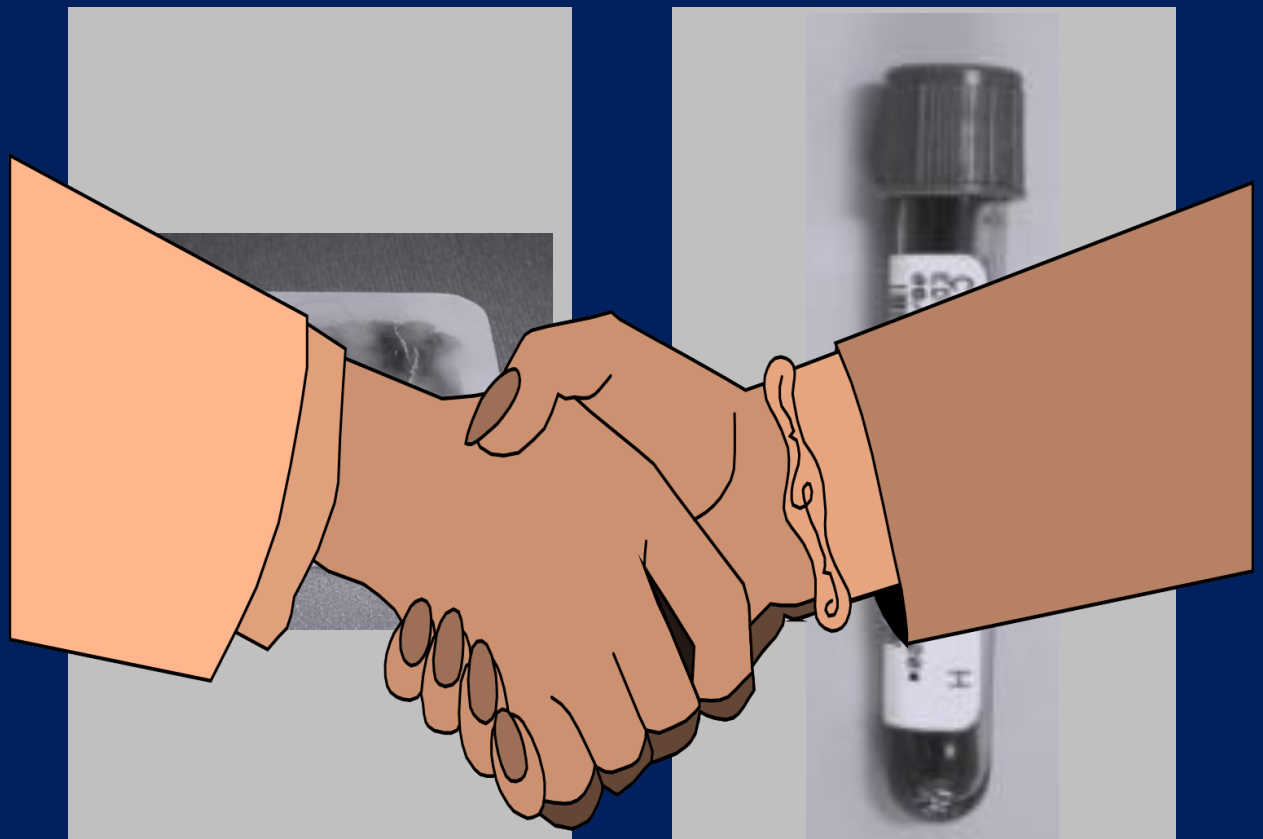
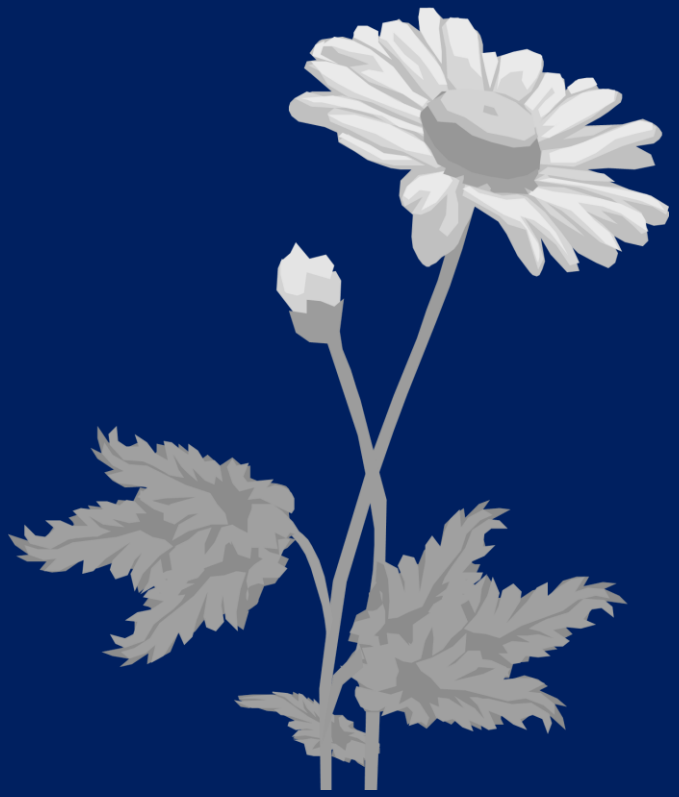



CRP

“Donation” of tissues, and data!



Data protection: what to hope for...

Epidemiological research (Cancer Registries, etc.)

- ***Derogation from informed consent request***

Retrospective clinical research

- ***Derogation from informed consent request***
- ***Broad consent ("donation" of data)***

Prospective clinical trials

- ***Specific consent liable to cover also retrospective use of data***

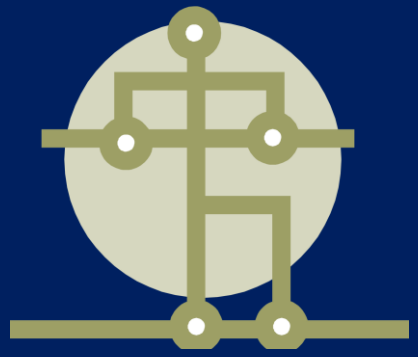
Biobanks

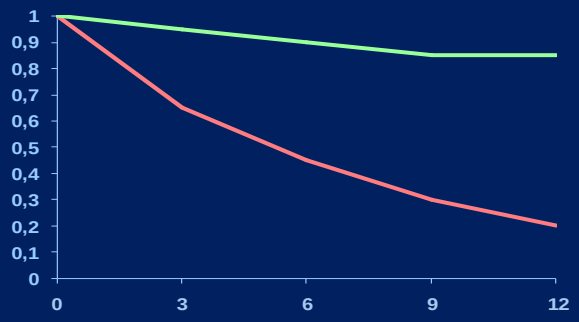
- ***Broad consent ("donation" of tissues, with clinical data)***

Electronic patient records

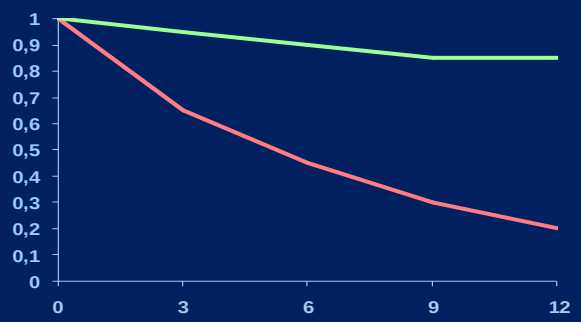
Quality of evidence…

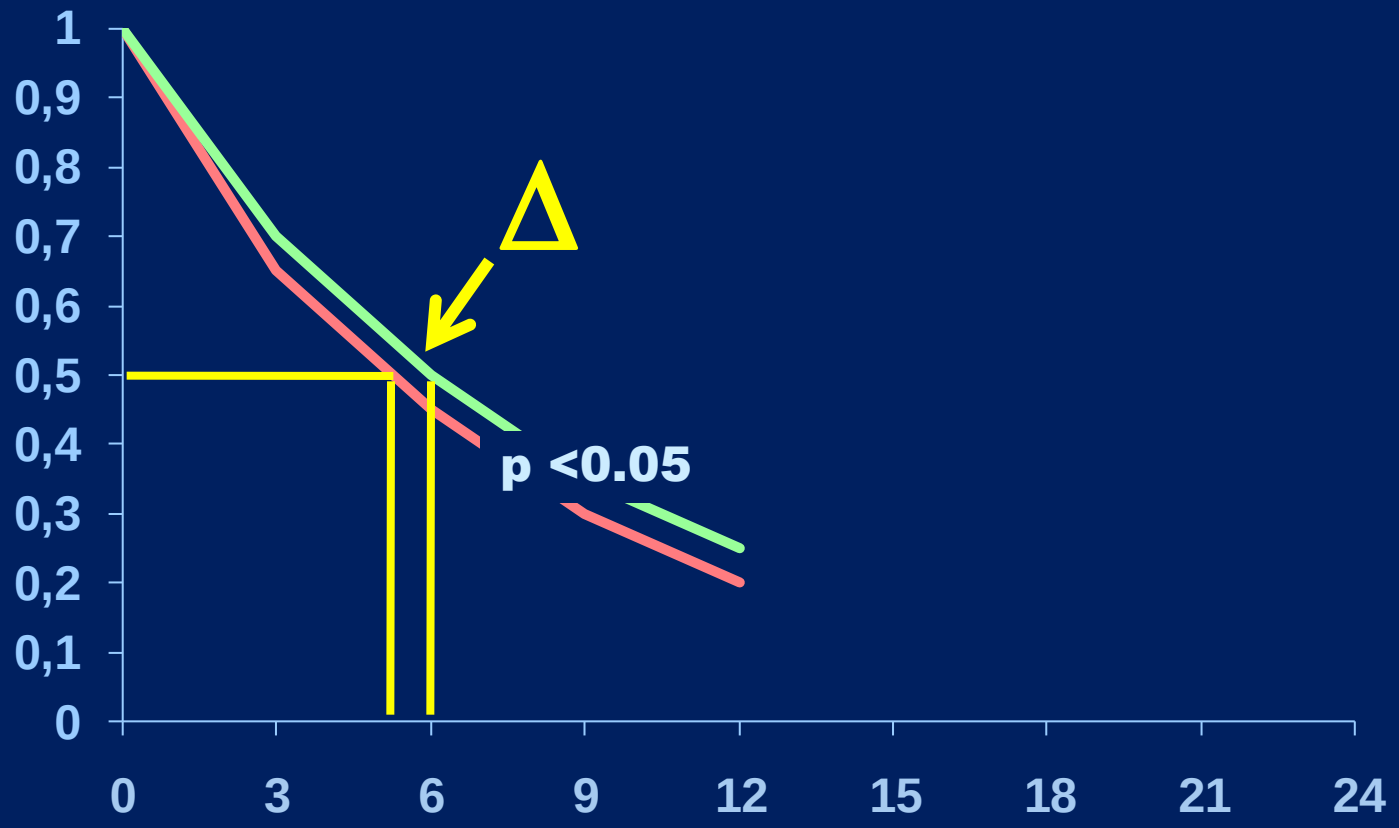
EU regulator





National regulator

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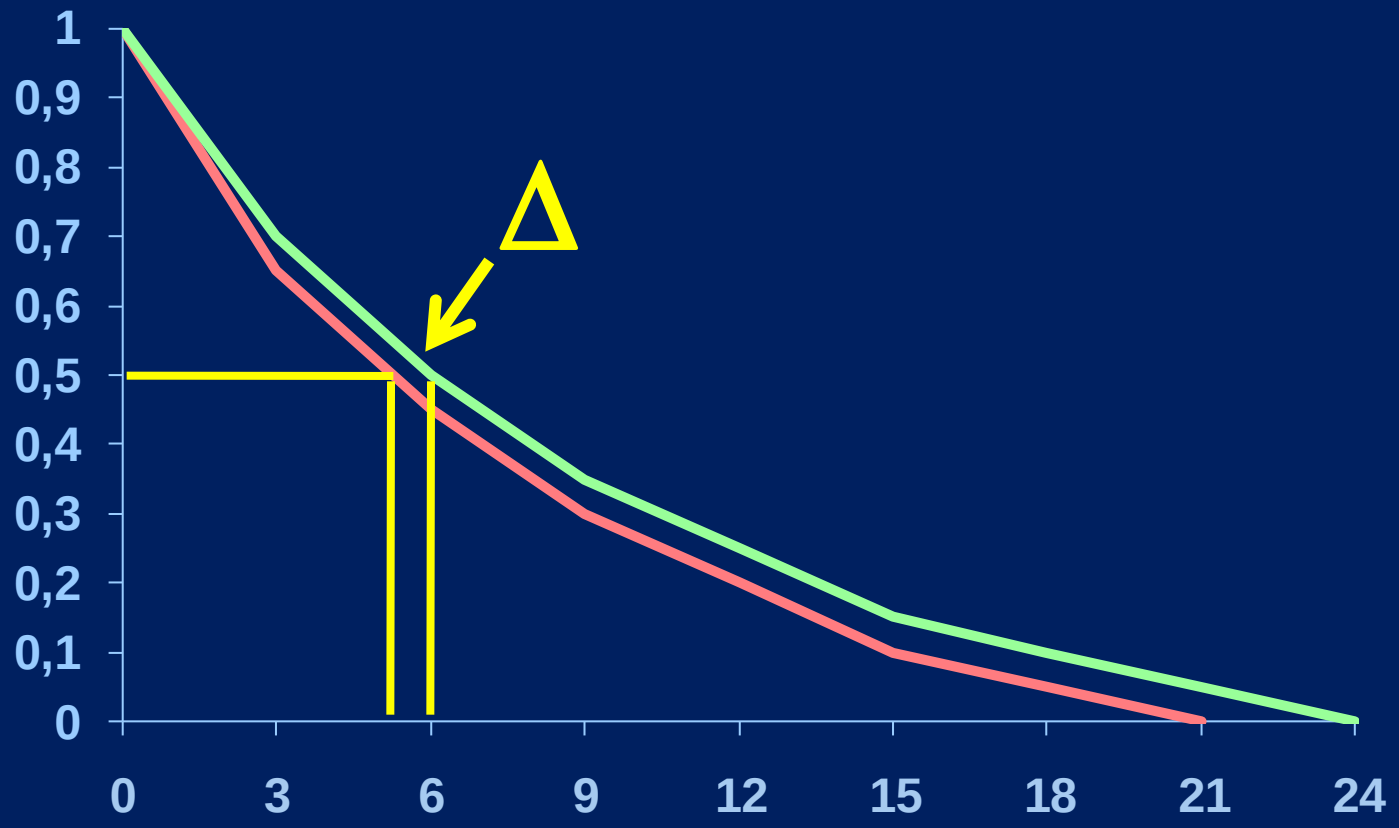
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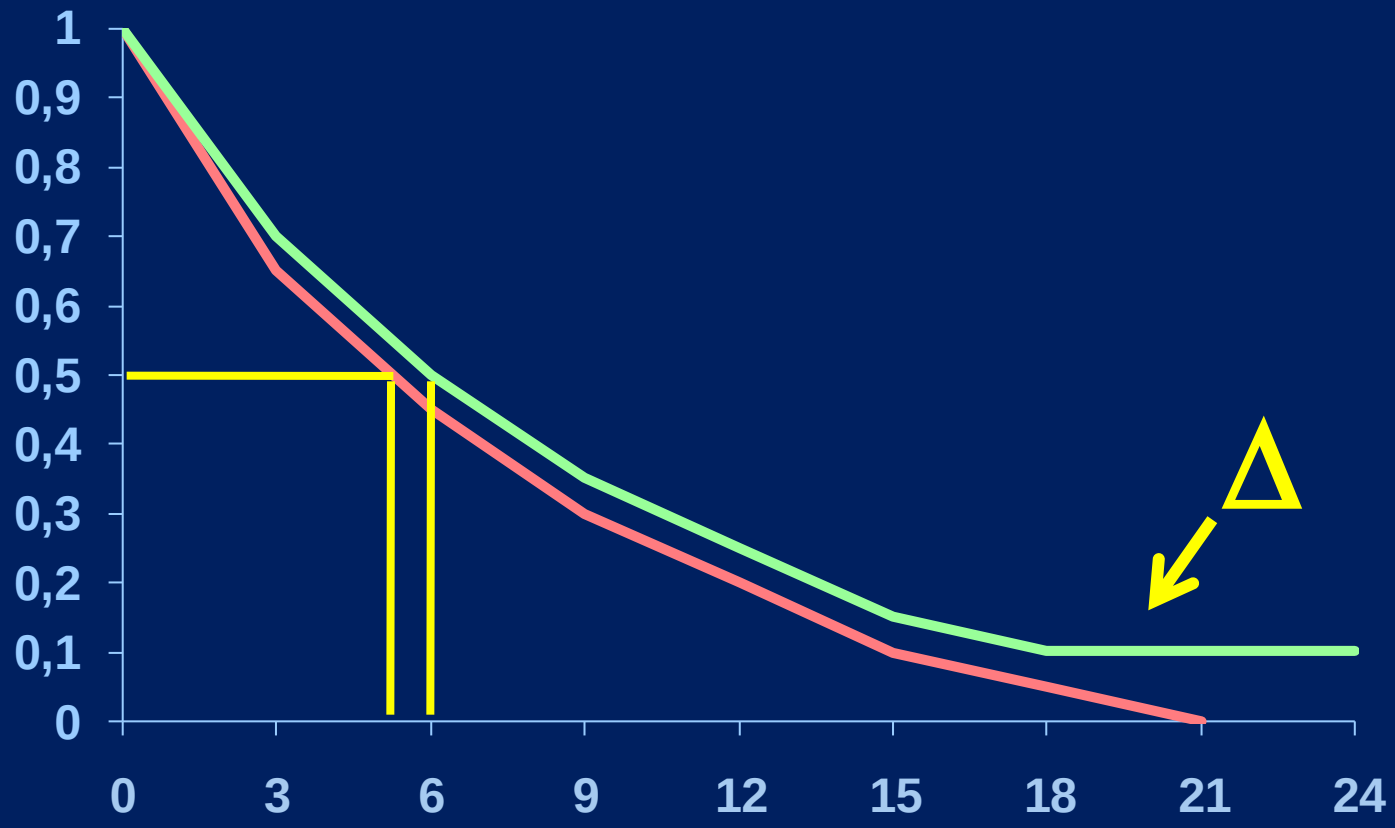
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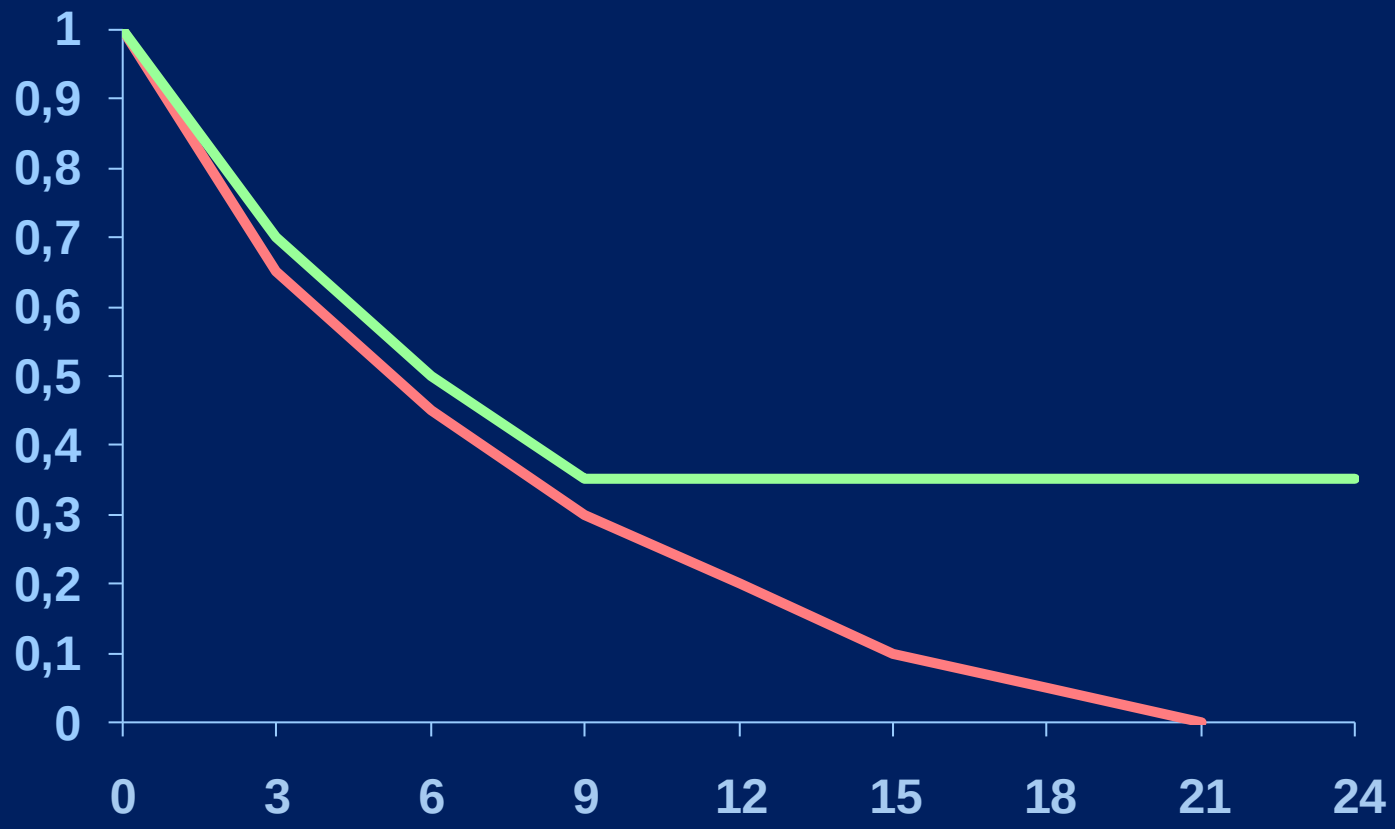
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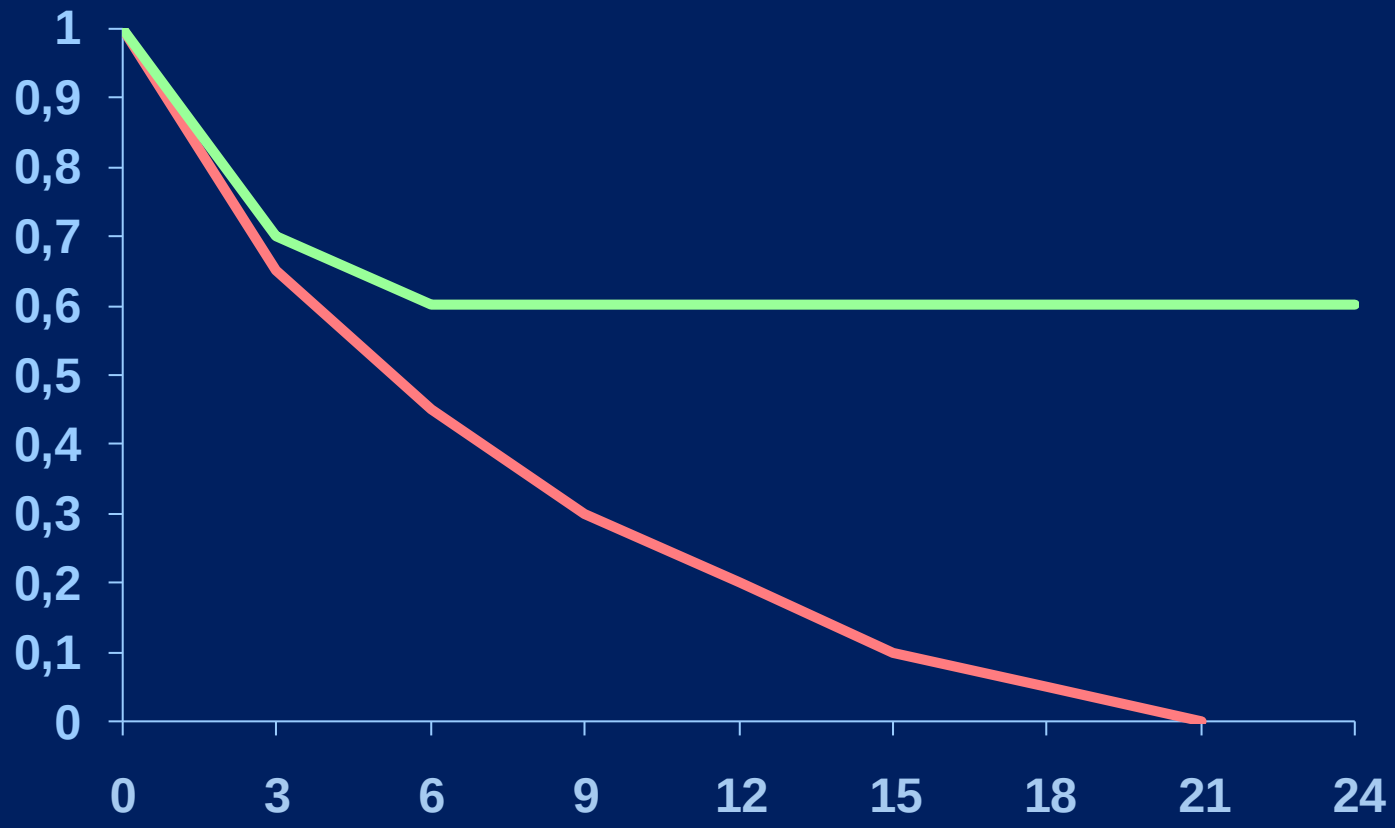
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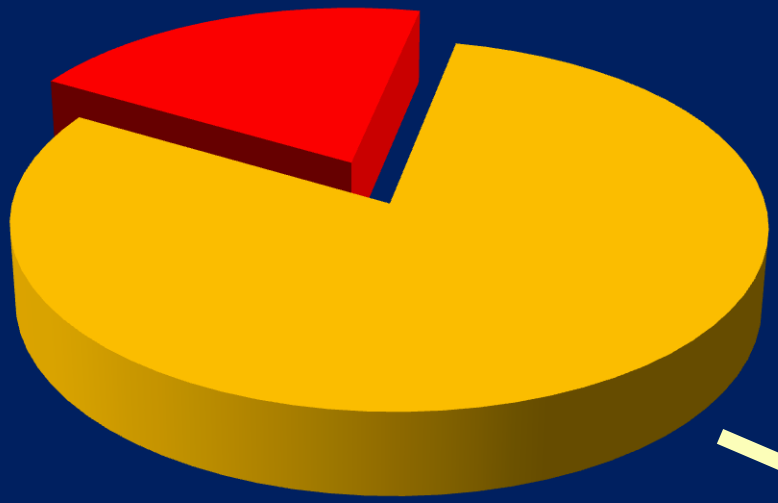
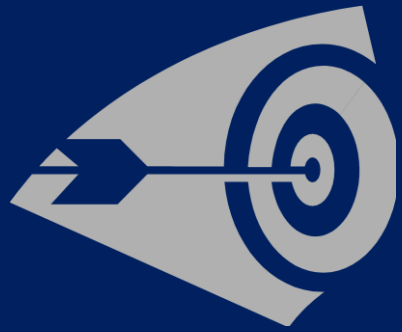
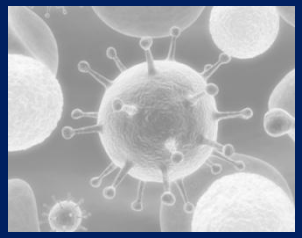
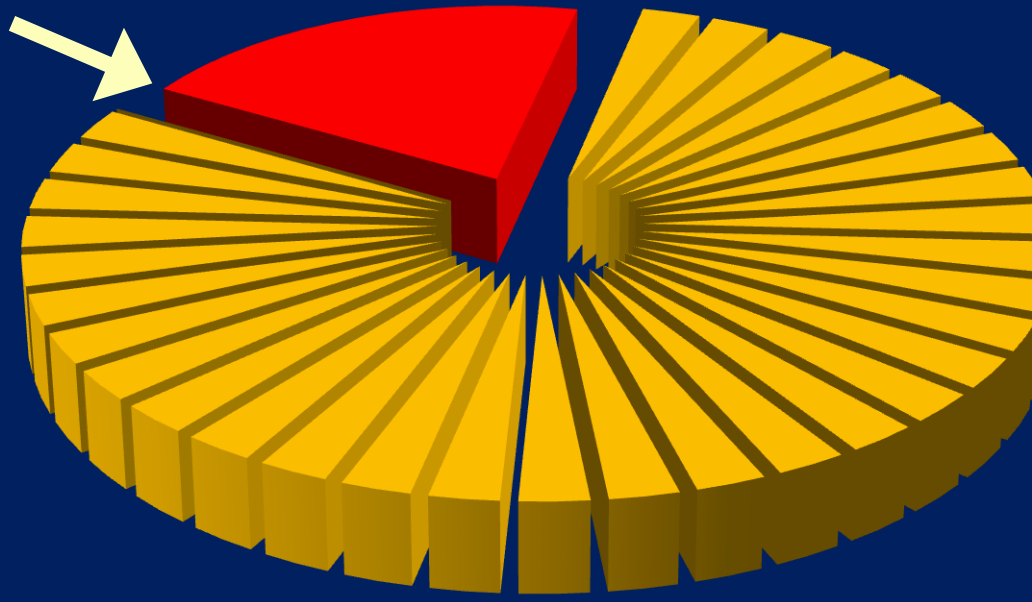
All cancers are rare…










RARE
CANCERS
EUROPE


ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology


EURORDIS
Rare Diseases Europe


EUROPEAN
CANCER
PATIENT
COALITION


EORTC
European Organisation for Research and Treatment of Cancer


Conticanet


EuroBoNeT


ECL
Association of European Cancer Leagues


cmlsupport
chronic myeloid leukaemia support group


IBTA
INTERNATIONAL
BRAIN TUMOUR
ALLIANCE


orphanet


FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI


CML AdvocatesNetwork


IEO
European Institute of Oncology


SIOPE
SIOP Europe


ESO
European
School
of
Oncology
Learning to care


EUROPEAN ONCOLOGY
NURSING SOCIETY


European
Society of
Pathology


NOVARTIS
ONCOLOGY


Pfizer
Oncology


sanofi aventis
Because health matters


RARE CANCERS EUROPE
Joining forces for action
Rare cancers – more common than most people think
clinical decision-making
methods to combine evidence
new study designs
surrogate end points
organization of studies
Eurocan+Platform for cross border cancer research launched
European Society for Medical Oncology
Sign the Call to Action Against Rare Cancers!


ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
ESMO
SEARCH
LOGIN
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European Society for Medical Oncology
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Influencing EU health policy and informing medical oncologists
Political initiatives impact medical professionals, oncology specialists and cancer patients in various areas, including issues either directly related to cancer or to health in general:
- Access to care and to information
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- Health technology assessment
- Best practices
- Sharing resources and capacities
- Shortage of professionals
- Recognition of professional qualification, etc.
In 2006 ESMO opened a Political Affairs office in Brussels to be close to the European decision centers, authorities, and institutions.
The ESMO Political Affairs office helps ESMO and its members in their mission and activities by providing specific support concerning political and European affairs.
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RARE CANCERS EUROPE

Joining forces for action

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

European Society for Medical Oncology

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