Challenges of Multicenter Studies in Europe, EURECNET, Bratislava, 13 April 2012

Hartmut Krafft, PhD
CTFG-Chair
VHP-Coordinator
Head, Section clinical trials
Paul-Ehrlich-Institut
Paul-Ehrlich-Str. 51-59
63225 Langen
Germany

Fax: +49 +(0)6103 771277
Phone: +49 +(0)6103 771811
E-Mail: CT@pei.de
http://www.pei.de

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Situation of clinical trials in Europe before CTD

Situation of clinical trials after the implementation of the Clinical Trials Directive in 2004

- 15/27 Member States working with the same english versions of documents like
  - Investigational Medicinal Product Dossier (IMPD)
  - Protocol
  - Investigators Brochure
  - SmPCs

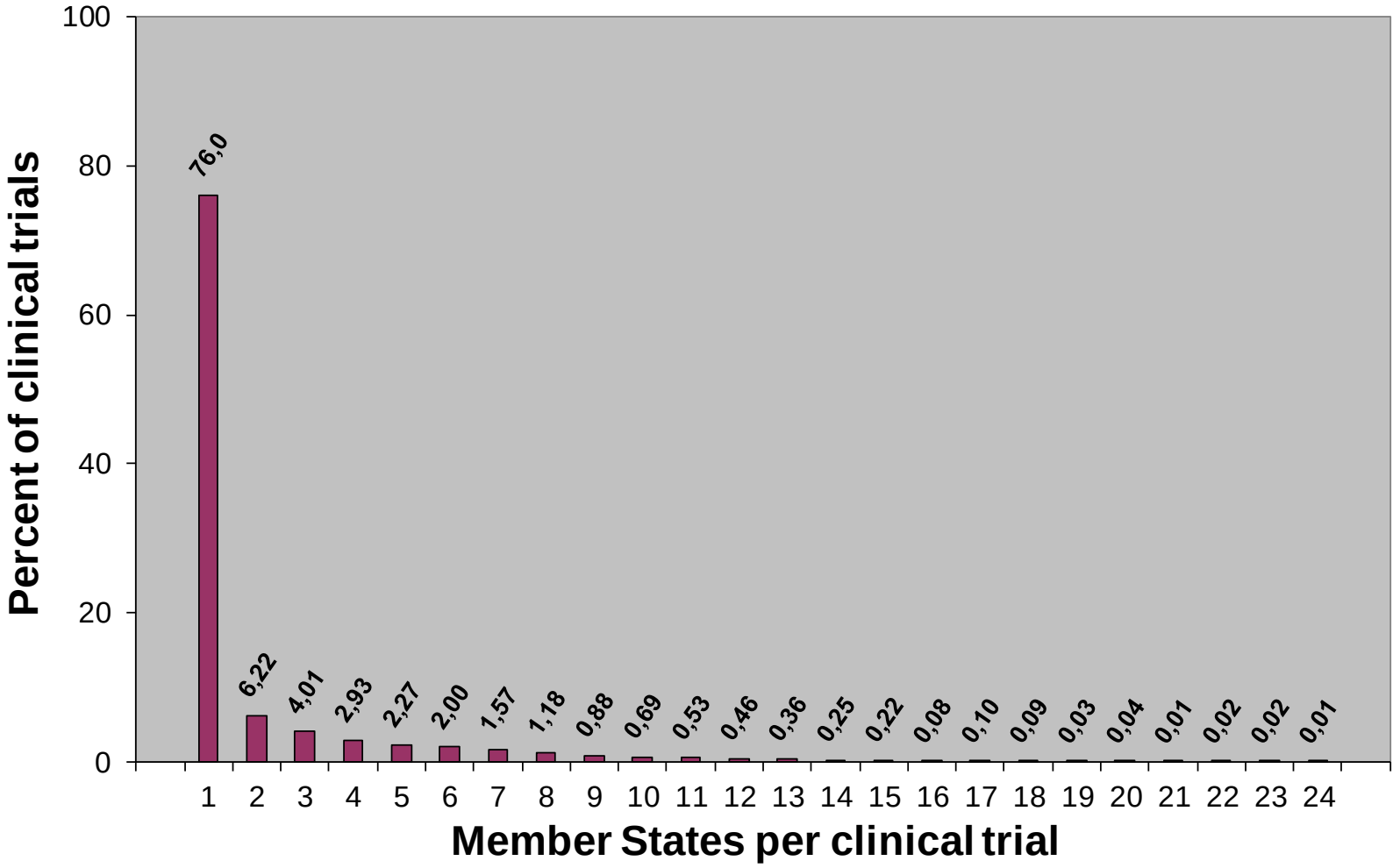
- but

Situation of clinical trials after the implementation of the Clinical Trials Directive in 2004

- not harmonised are
  - Assessments
  - Treatment options and standards
  - Some documents related to the clinical trial applications due to different interpretations of guidance documents
  - Application times at the national Competent Authorities

Distribution of Clinical Trials in Europe

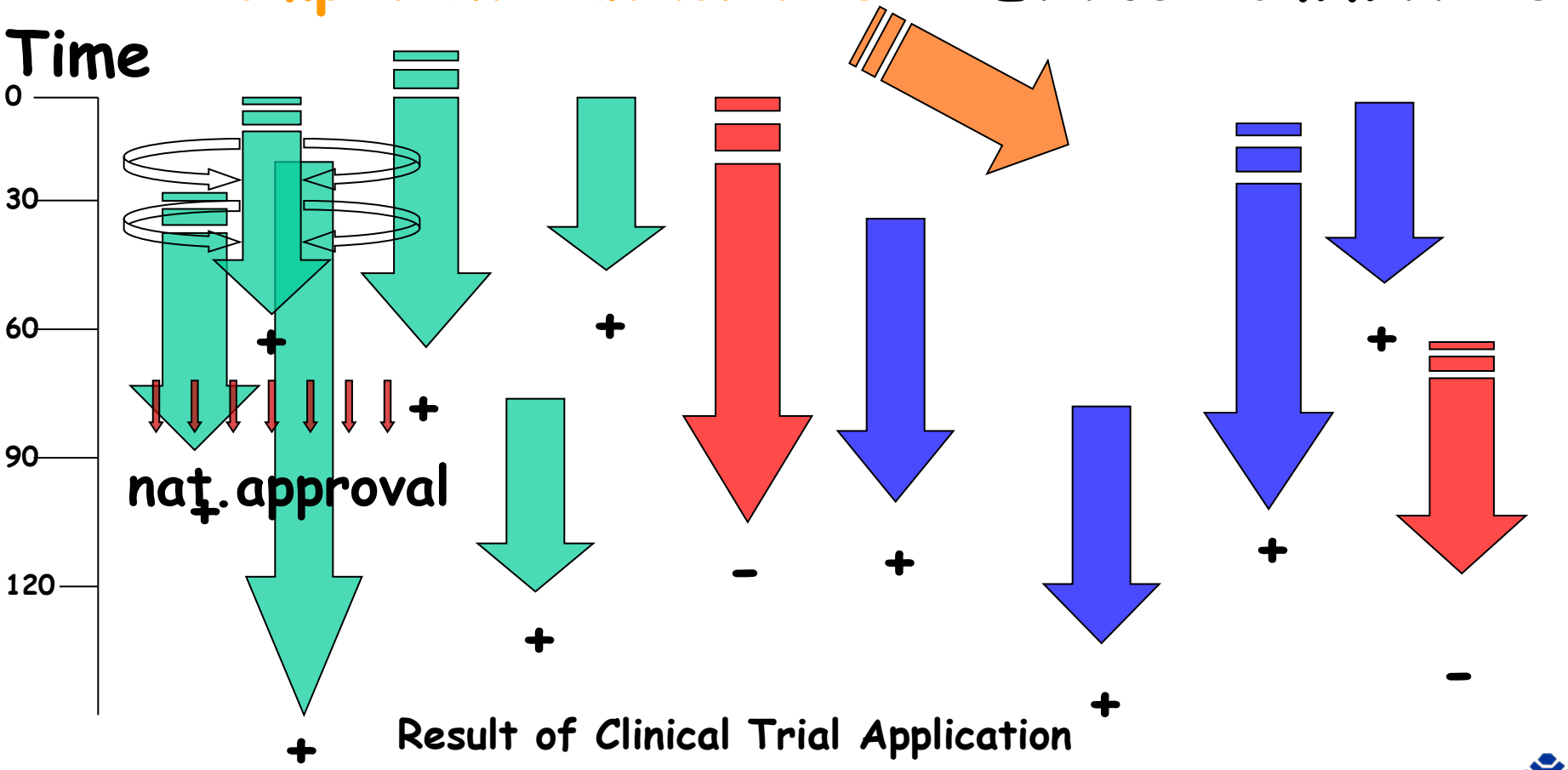
in one Member State vs multinational in percent



Status 19.5.2010

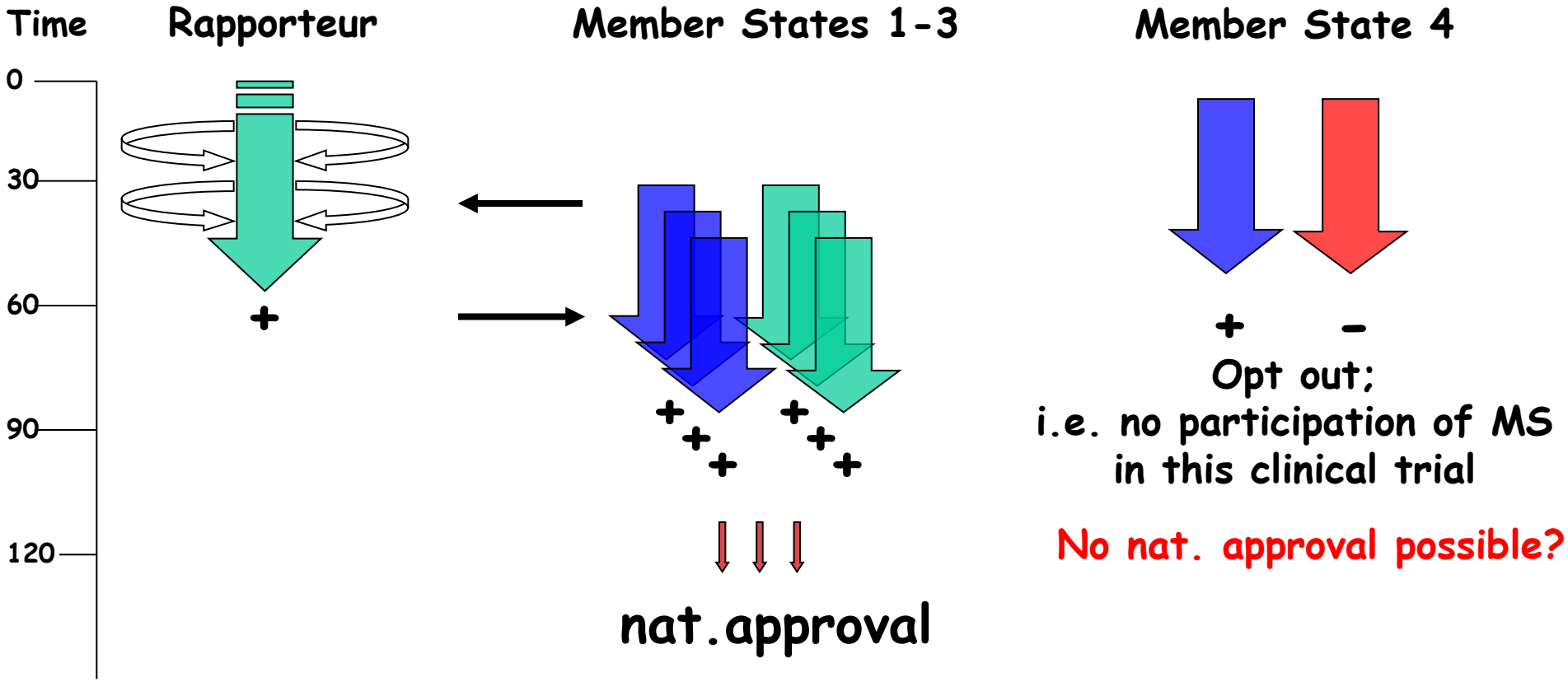
The Voluntary Harmonisation Procedure offers a solution to address these points within the existing European legal framework

Present situation for the approval of a EU Voluntary Harmonisation Procedure (VHP) for a multinational Clinical Trials



Coordinated Assessment Procedure (CAP) for a multinational Clinical Trials?

Competent Authorities and Ethics Committees



Key features of the Voluntary Harmonisation Procedure

- Only electronic documents sent to one address (one stop shop)
- Only general documents required, which are part of any clinical trial application (Protocol, Investigators brochure, Investigational Med. Product Dossier)
- Reliable timelines for Sponsor and Member States
- Harmonised scientific discussion resulting in harmonised applications in the Member States
  - no Member States specific modifications necessary
  - consolidated lists of grounds for non-acceptance, if needed

Features of a New Regulation

- **Single (electronic) portal**
  - Harmonisation of requirements*
- **Assessment Committee & Assessment Coordination**
  - A Coordinated Assessment Procedure (CAP)*
- **Risk Adaptation**
  - adapt requirements (regulatory, monitoring, pharmacovigilance, insurances, etc.) for clinical trials to the related risks*
- **Decisions**

*** http://www.biopeople.dk/fileadmin/filer/Jette/Final_Report_-_EFGCP_EORTC_Consensus_Workshop_4_July_2011.pdf**

Submission of the clinical trial application

- **Single portal for NCAs and ECs**
  - really for 75% clinical trials in 1 Member State (3000 CT p.a.)?
  - Portal for Clinical Trial Applications and substantial amendments
  - Not only distributing or forwarding documents >>> 27 copies
  - Containing all documents
    - also the country specific info. like informed consent
    - information on trial centers
  - Access of all MS to all information (as in EudraCT) not only concerned Member States
  - Validation by VHP-C and Ref-NCA
- **Repository for NCA and EC for shared documents**
  - e.g. Assessment reports; Status (reports) for each procedure
  - anybody can not do ~1000 multinational CT p.a. by mails etc.

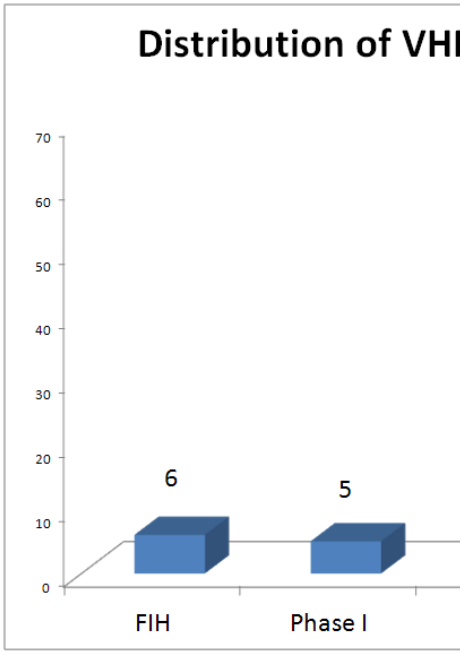
Evaluation Process

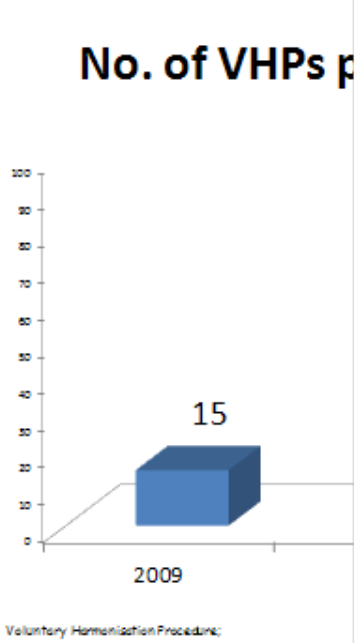
- **The Assessment Committee:**
  - Representation of each MSs NCA and EC
  - Meeting every month / dealing with 80 CTA?
  - Tremendous Costs
  - Legal basis for CTFG to serve as Assessm. Com.
- **Assessment Coordination**
  - No proposal of Rapp. by Sponsor (independence)
  - Coordination per procedure needs harmonisation again, better one coordinating body
  - Who answers questions/by mail/phone

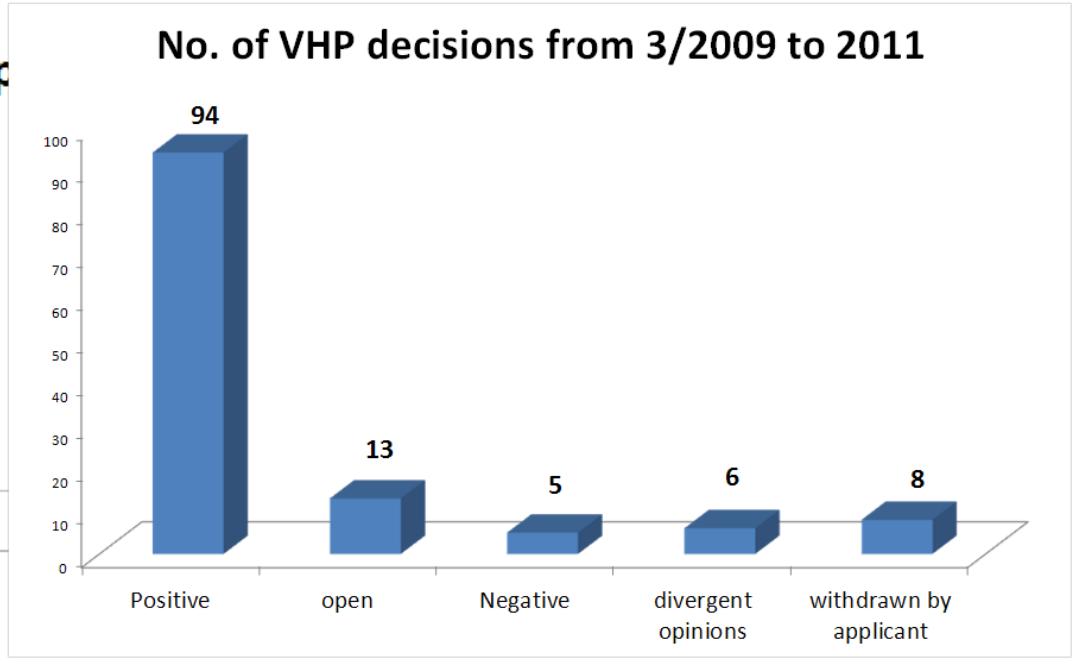
Decisions

- Majority votes / opting out / serious health concerns are contradictions
- After a joint positive assessment by the Member States approval should be issued by each Member States in short timelimes
- In a second wave the Member States must have the same rights as in the first (GNA and timelines, etc)
  - Support by the Ref-NCA
  - Access to the repository

Learn from the 3 years experience of CTFG





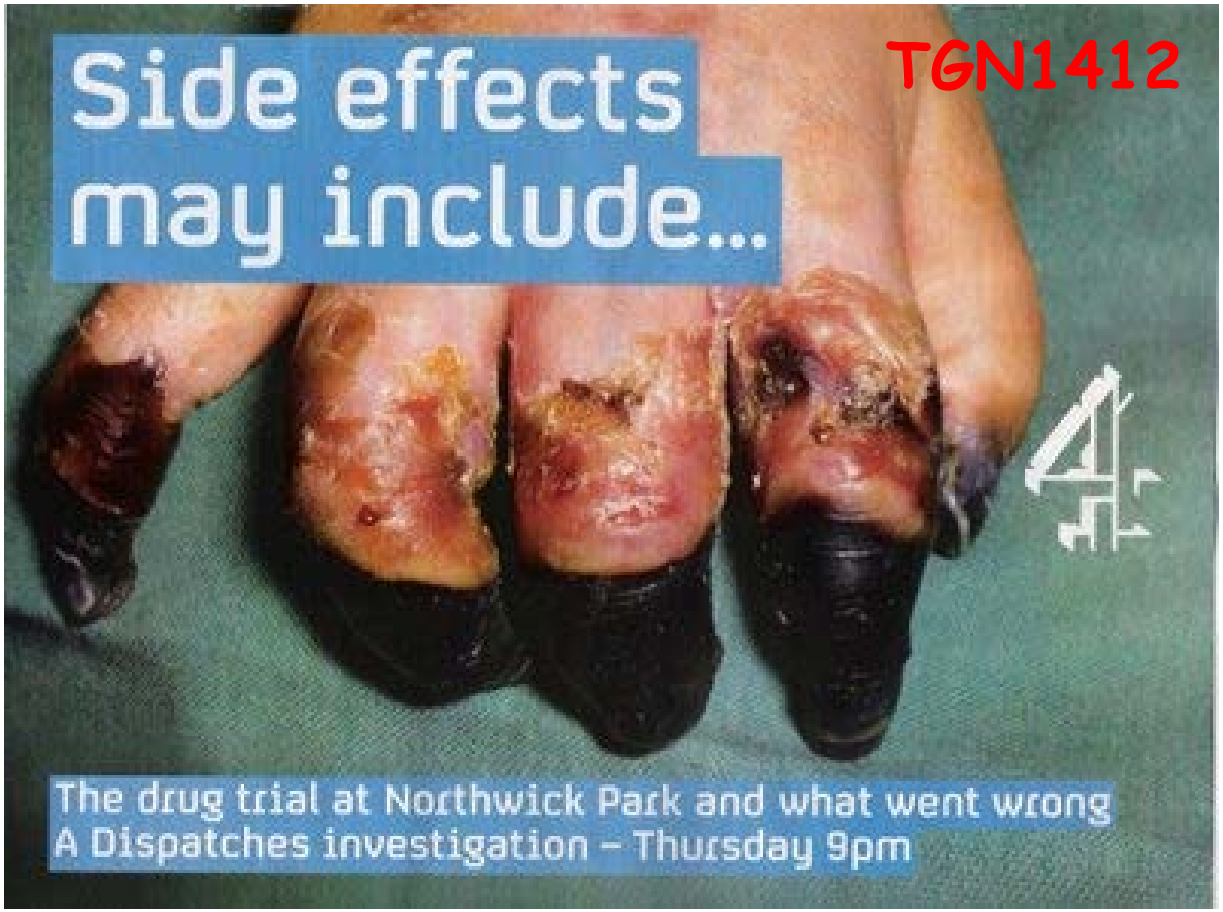


More than 170 VHPs

Lessons from 3 years VHP

- Saving resources by avoiding unnecessary assessment
- Effective IT is crucial
- No separation of administrative and scientific steps possible without losing quality and time
- Active scientific management is needed to meet timelines and find solutions case by case
- Flexibility in the decisions has to be possible (conditions, commitments, for new questions ask the concerned MS)
- Fees are justified for the procedure as a lot of resources at the sponsor is saved (consolidated list of GNA, one application, no paper, etc)

Don't forget: Saving time and simplification is not the most important issue



Avoiding this and worse is the issue!