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# to improve clinical trial exchange

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# Overall Project Objectives

- Development of a comprehensive model of Clinical trial (CT) research in order to identify suitable tools to automate the entire process, through:
  - Modelling the interaction between CT sub-processes
  - Identifying roles and information needs of the stakeholders directly participating to the process
  - Identifying the information need of stakeholders “outside” the process

Paper objectives  
• Providing ICT support for interoperability between organisations, platforms, applications

Within the various actions taken by international and national organisations to support the diffusion of CT information and the implementation of global public available registries, analyse:

- the various solutions of CT data representations adopted by National Health Authorities, information providers and standardisation organisations

# Methods

- Identification of data schemas developed by representative stakeholders:
  - Data schema comparison
  - Development of a “reference schema” able to include the metadata to be analysed
- Analysis of meta-data used to register CT protocols taking into account:
  - data set schemas proposed by
    - Regulatory Agencies
    - Organisations working on CT standardisation
  - and used in:
    - main CT protocol registries.
- Comparison of data elements, their description and values.
- Mapping the data elements with stakeholders' information needs.

# Clinical trial definition

[ICH E6 Guideline for good Medical Practice, CDISC Glossary]

## Related to CT Process

- “any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or pharmacodynamic effects of an investigational product(s) [...] with the object of ascertaining its safety and/or efficacy”

## Related to the CT protocol:

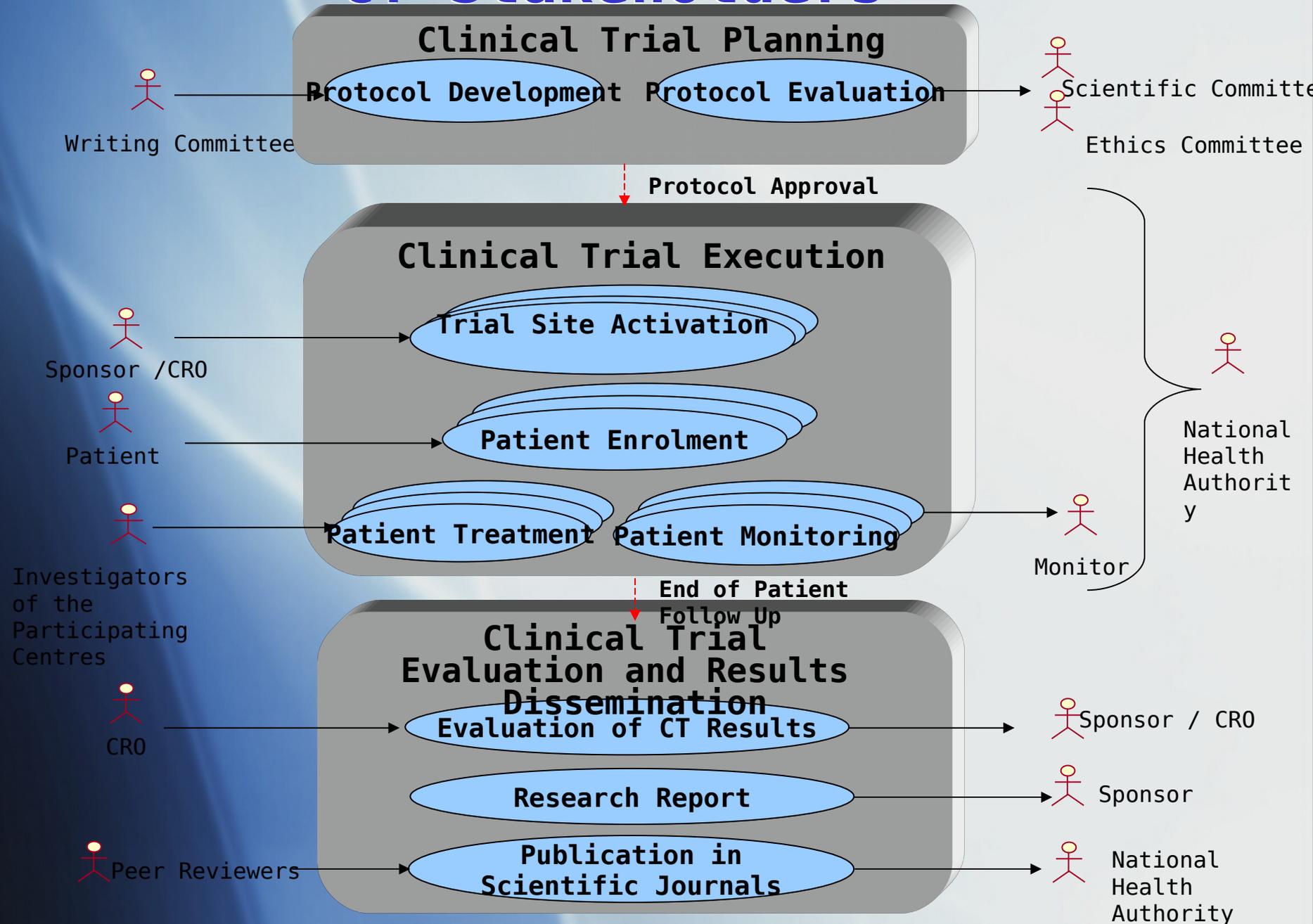
- “a document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial” [...] and usually also gives the background and rationale of the trial”

**Mandatory document to obtain the approval for the start of the clinical research by a scientific and ethics committees**



plan to be rigidly followed by the CT participating  
pharmacological reference point to obtain reliable results  
organisational and management framework

# CT Stakeholders



# Current CT framework and issues

- Internationally accepted Guidelines for Good Clinical Practice
- National/European Agencies establish regulatory requirements:
  - In Europe: EMEA + National Health Authorities
  - In US: FDA
- Issues:
  - Different policy for CT information diffusion
  - No comprehensive, international, public CT registry
  - Poor quality on key information
  - Publication bias
  - Negative results of basic clinical trials are often not published
  - Only a small percentage is published in ~ 3 years after drug approval
  - About half of the studies presented at



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# registration

## Food and Drug Administration Modernization Act (FDAMA)

- Mandatory submission for investigational new drug applications
- Public availability of CTs for serious or life threatening diseases

## World Health Organisation (WHO) - Registry Platform:

All interventional CTs should be registered  
 All registered data should be publicly disclosed

## International Committee of Medical Journal Editors

September 2004 Statement --> "Register or not publish"  
 May 2005 Statement --> urging "full registration"

## Ottawa statement

- Obtaining a internationally unique protocol identification number
- Registering the original protocol with subsequent amendments

## Pharmaceutical research and manufactures of America (PhRMA)

Opposition to the Registry the trial results  
 Opposite position on disclosure of clinical trial information

Proposals of minimum  
 protocol data set

# Our Analysis concerns:

## **International regulatory authorities:**

- *International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use - Guideline for Good Medical Practice (ICH E6)*
- *World Health Organisation (WHO) Registry Platform*
- *European clinical trials database (EUCTRACT)*

## **Organisation promoting standards:**

- *Clinical Data Interchange Standards Consortium (CDISC)*

## **Publicly available protocol databases:**

- *ClinicalTrials.gov (US National Institute of Health)*
- *Clinical trials PDQ (US National Cancer Institute)*
- *Current Controlled Trials Website (UK biomedical pub companies)*

# CT Information Providers and Publishers

## **International regulatory authorities:**

- *International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)*
  - promotes international harmonisation with representatives of EU, Japan, US and establishes common guidelines
- *World Health Organisation (WHO)*
  - Established of a Registry Platform secretariat
  - Proposes 20 items to be registered in a “Primary Register”
- *European clinical trials database (EUCTRACT)*
  - Registers all CTs in the Community
  - Provides a unique EUCTRACt protocol number

## Our analysis 2)

### Organisation promoting standards.

*Clinical data interchange standards consortium (CDISC)*

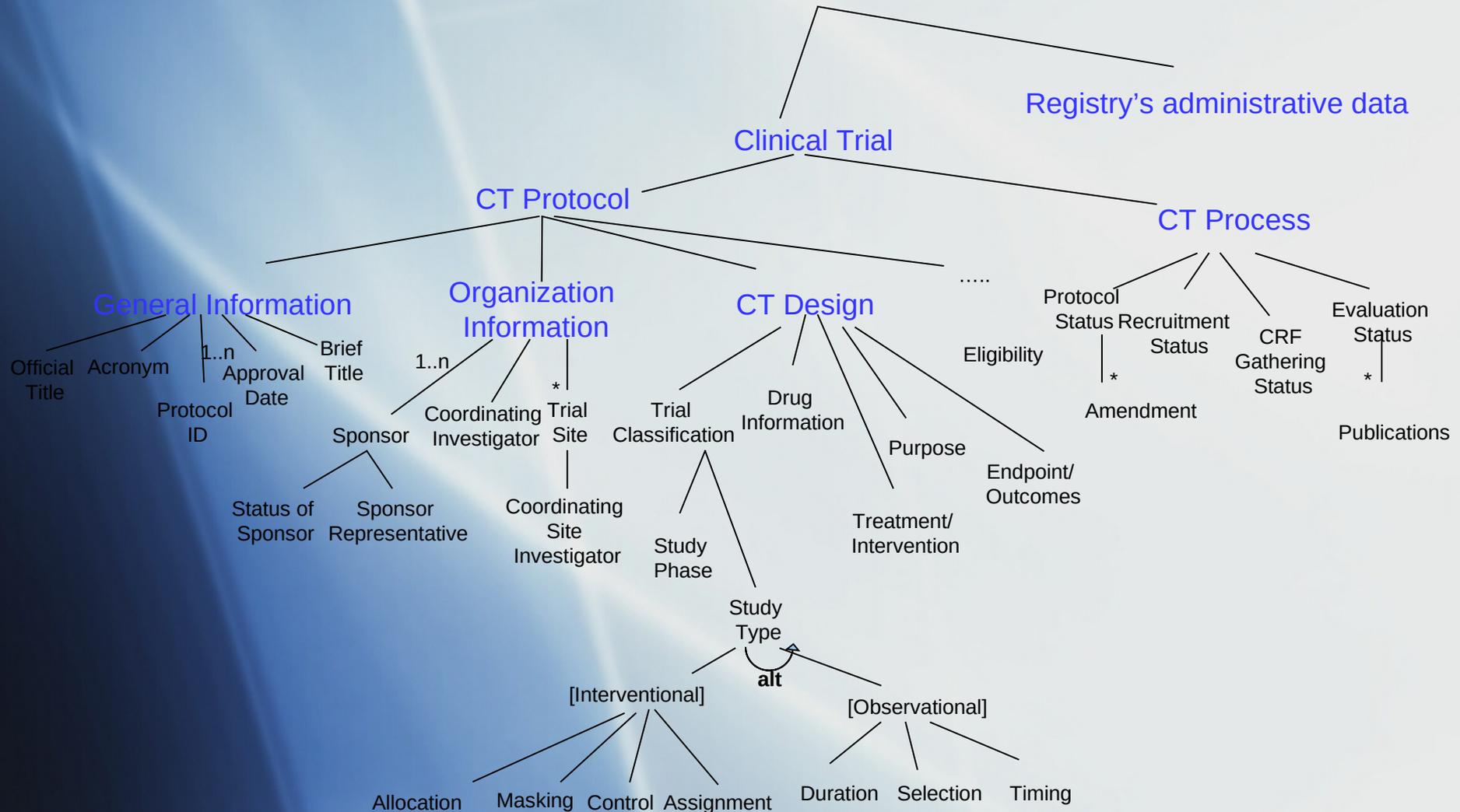
- leads the development of standards to improve electronic acquisition, exchange, submission and archiving of CT data and metadata

### Publicly available 'protocol' databases:

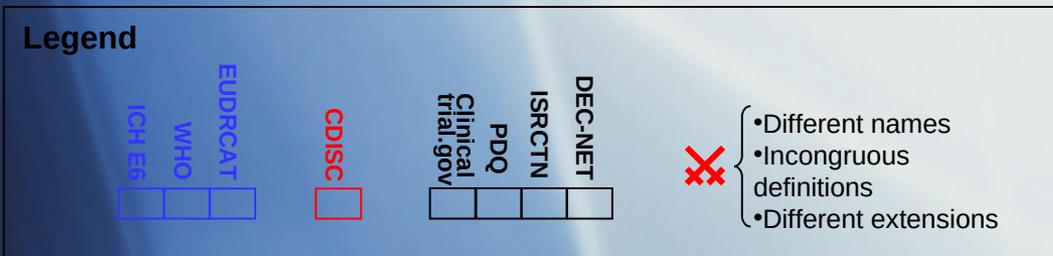
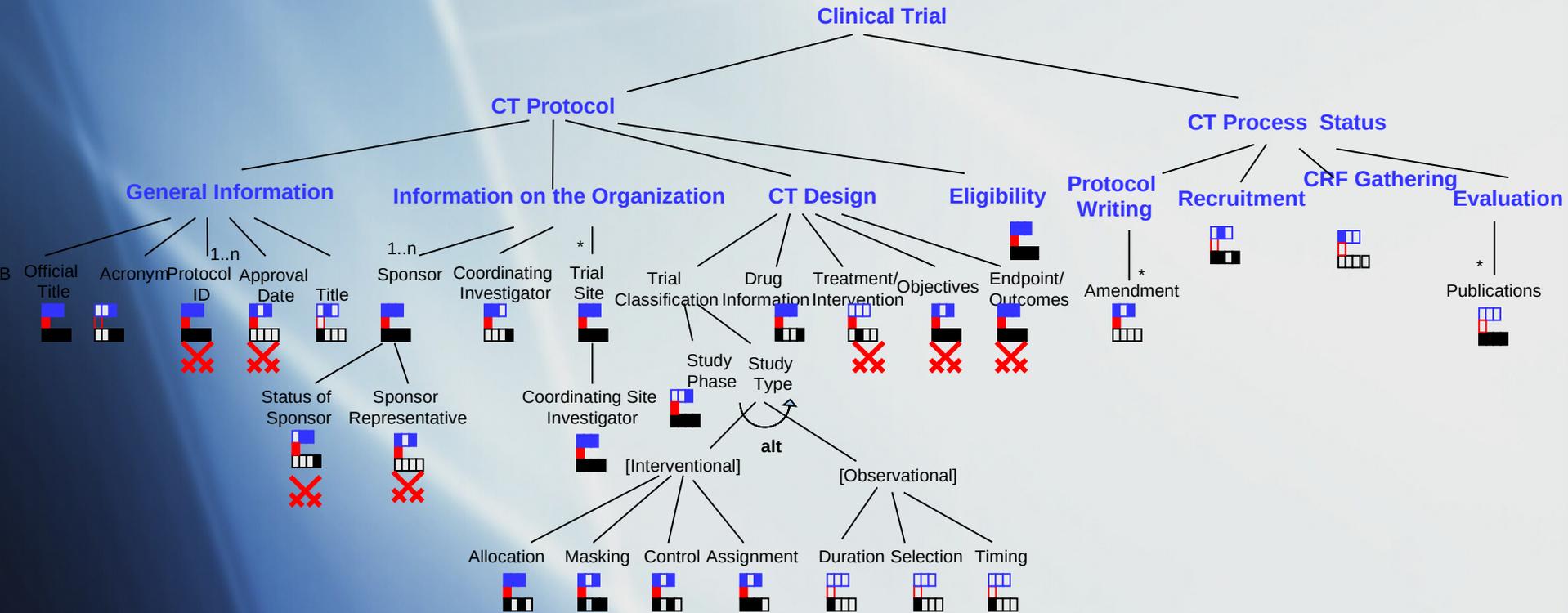
- ClinicalTrials.gov (US National Institute of Health)
  - established by FDAMA 113 Act, provides public access to US commercial, non commercial and international CTs
- Clinical trials PDQ (US National Cancer Institute)
  - includes most CTs sponsored by NCI
  - gives patients' and health professionals' views of the CTs
  - exchanges data with clinicalTrials.gov
- Current Controlled Trials (UK biomedical publishing companies)

# Information structuring schema of CT registries

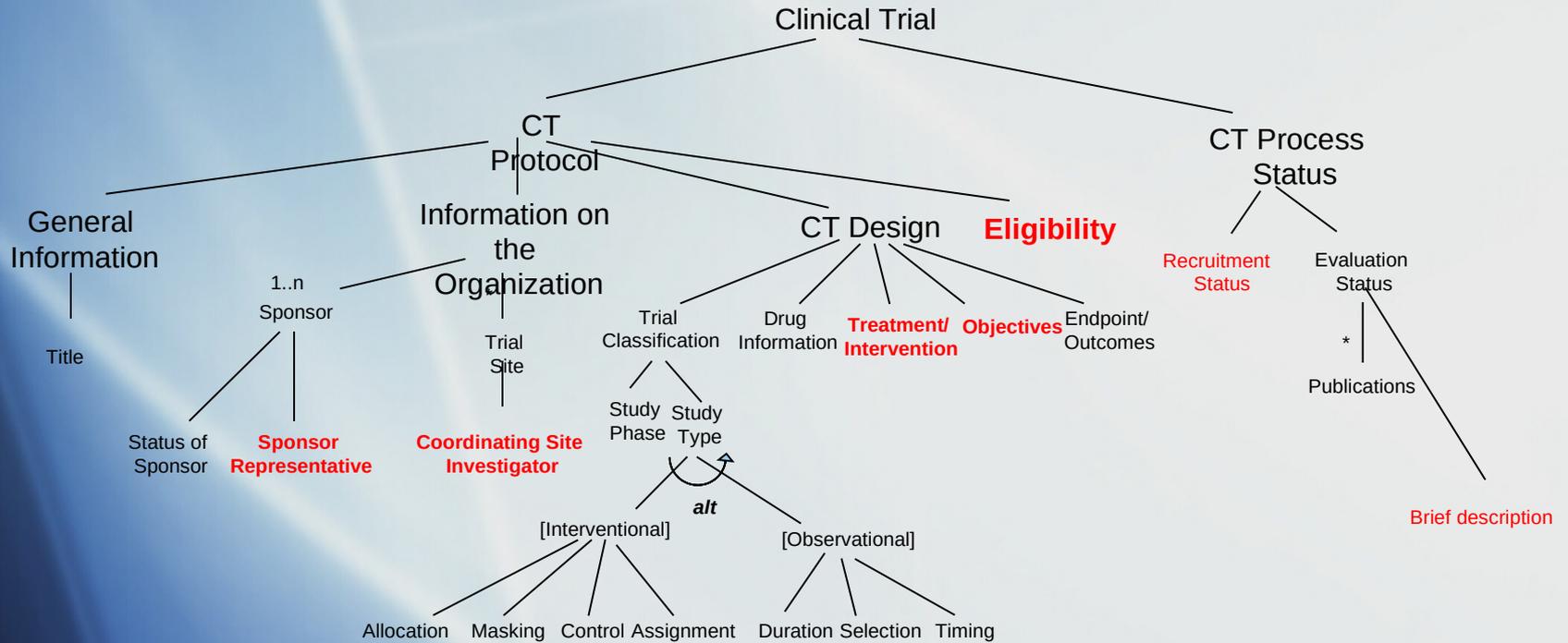
Clinical Trial Registry



# Results of Meta-Data Analysis



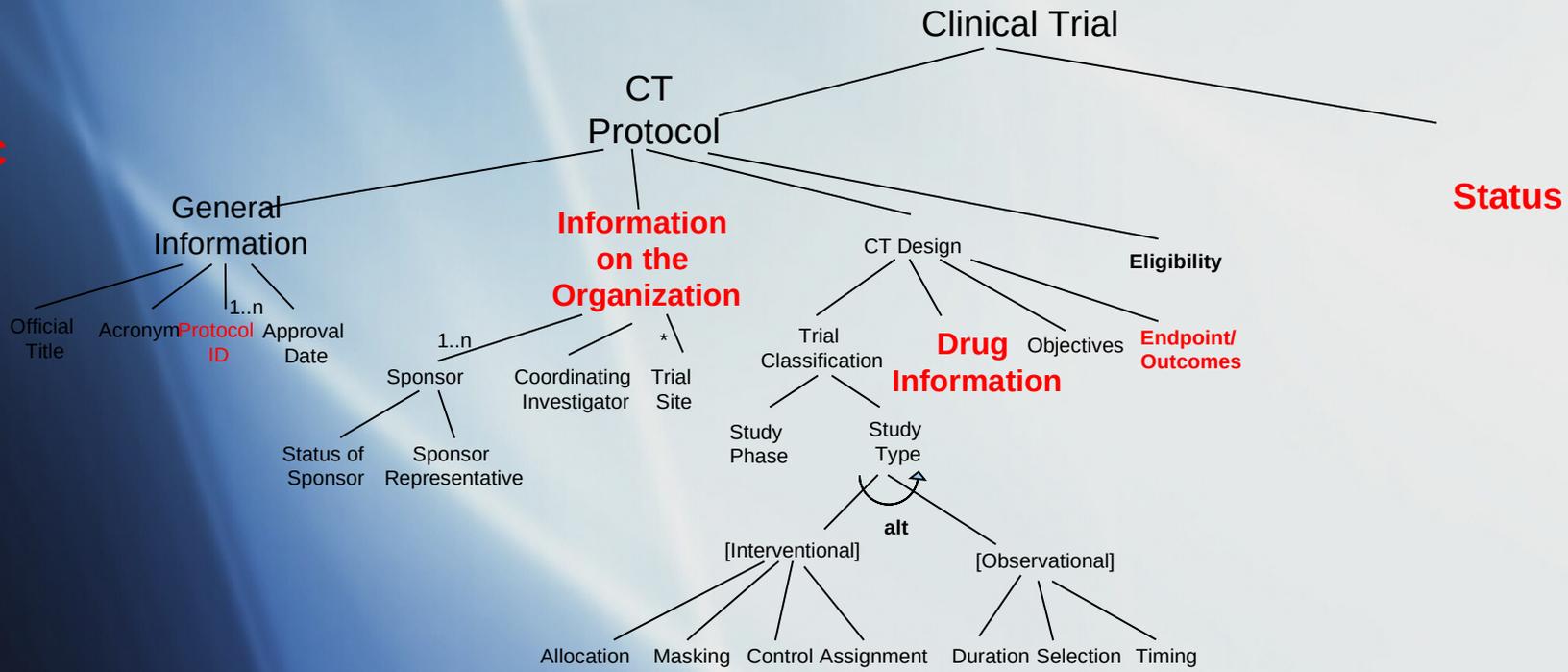
# Patient's View



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# View



# RESULTS and CONCLUSIONS

- Identification of the CT research:
  - The majority of information has to be selected from the entire document using a pre-defined template
  - A unique CT identification number is recommended, in the meantime secondary IDs have to be managed
- Different points of view of information sources:
  - The aim of the registry influences the information acquisition model
    - Regulatory authorities are concerned about investigational drugs, CT organisation and responsibilities
    - CDISC is concerned with CT protocol elements, not with the process
- CT Meta-data analysis:
  - Different databases tend to focus on elements (Ex: and care providers' information needs) on the organisation)
  - Incongruous definition (Ex: Purpose of the study)
  - Different terminologies (Ex: Endpoints and outcomes)

Need for a standard CT representation encompassing CT process

Use of interoperable representation models (XML)

A standard representation could provide tailored