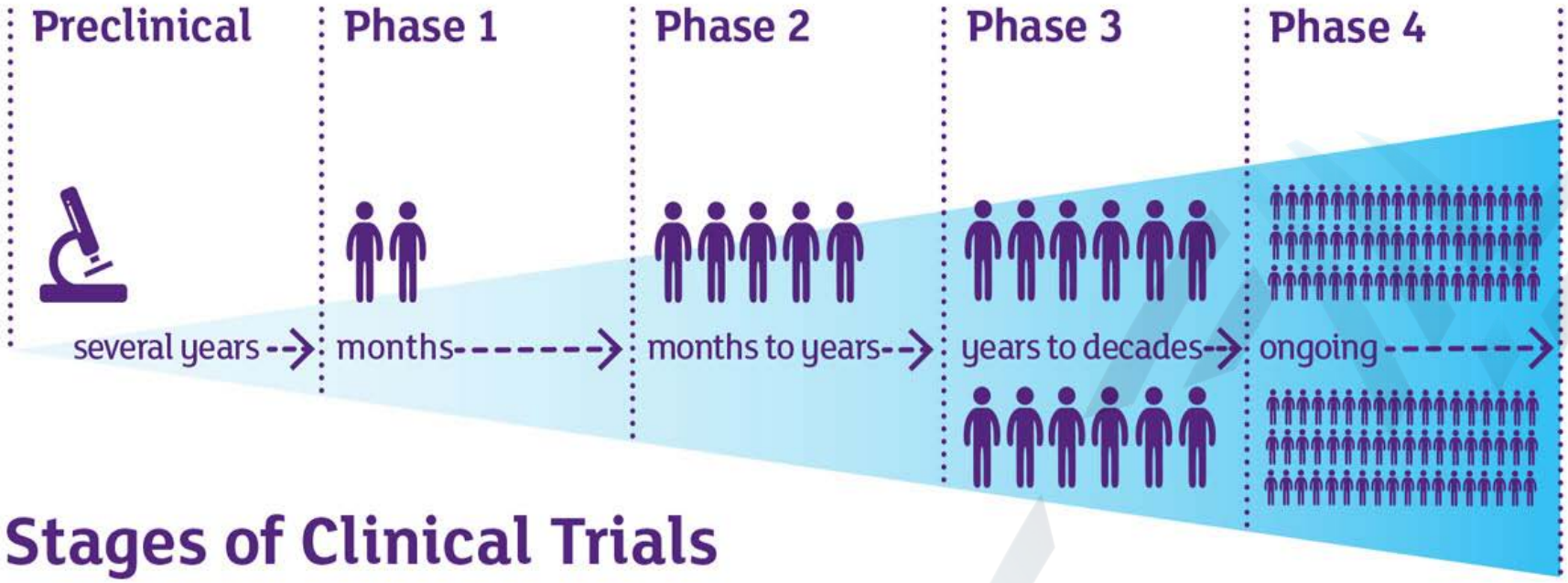
MICHALOPOULOU
& ASSOCIATES

Law under the microscope

CROs' position on Clinical Trials – Contemporary Reflections

March 8th, 2018



Stages of Clinical Trials

Clinical Trial Conduct-Supervision:

In-house vs Outsourced

Contract Research Organization (**CRO**)= an organization that provides support to the pharmaceutical, biotechnology and medical device industries in the form of research services outsourced on a contract basis.

In particular a person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

https://thecompleteherbalguide.com/join-study-trial/

Reasons for Outsourcing Clinical Trials

- ✓ Increasing technology expertise of CROs
- ✓ Increased Complexity of Regulatory Submissions
- ✓ Lessening of the burden on outsourcer, so they can focus on core competencies
- ✓ Growing Pressures to bring Drugs to the market more quickly

Unnecessary clinical trial procedures cost the pharmaceutical industry and sponsors around $5 billion a year. One way of cutting down on unnecessary procedures is clinical trial outsourcing, as, if planned and chosen correctly, it can save a company time, effort and money.

http://www.pharmatimes.com/news/unnecessary_trial_procedures_cost_up_to_us$5_billion_a_year_977029

Benefits of using a CRO

In general, CROs allow drug developers to save on the long term expenses of establishing a comprehensive in-house infrastructure for preclinical and/or clinical testing. Overall, **CROs are able to shorten clinical testing times by as much as 30%.**

Research reveals that compared to low CRO usage projects, those with high CRO usage:

- Showed a median of **78 days, compared to 98 days,** from protocol readiness to First Patient, First Visit (FPFV).
- Reached study data availability from protocol readiness in **196 days, compared to 231 days.**
- Moved from protocol readiness to Last Patient, First Visit (LPFV) in **294 days, compared to 308 days.**
- Required an average of **42 days to move from Last Patient, Last Visit (LPLV) to database lock, compared to 56 days.**

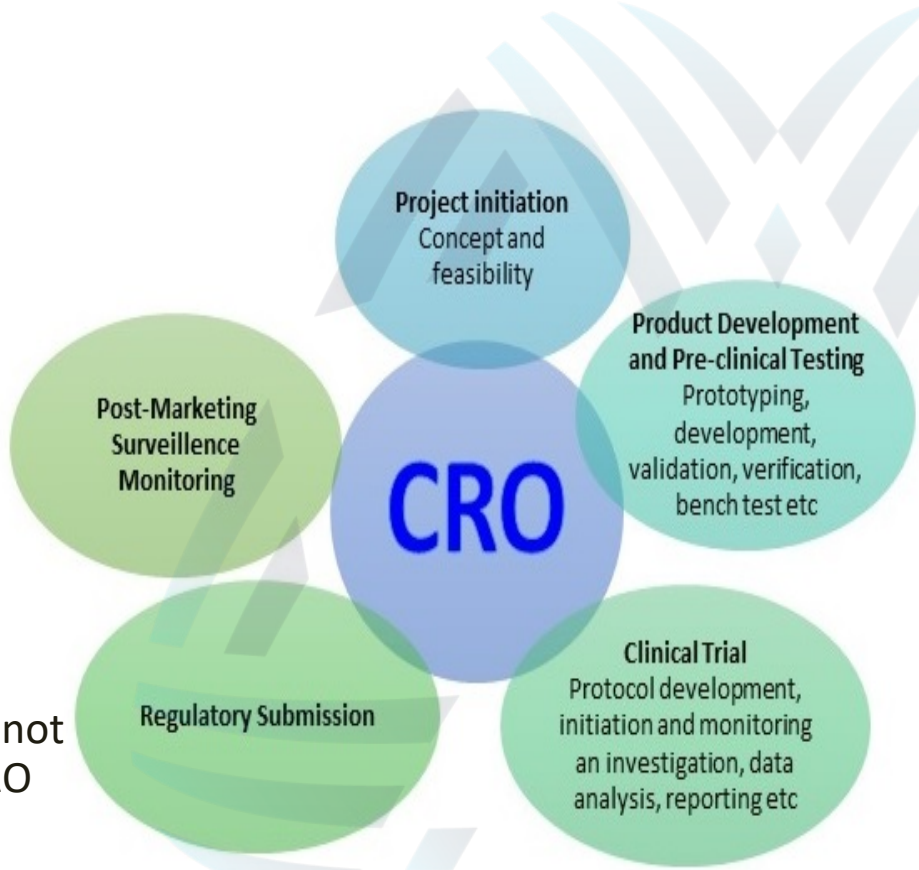
source: https://www.contractpharma.com/issues/view_features/clinical-research-outsourcing

CRO Services

A CRO may **undertake any or all** of the sponsor's trial-related duties and functions such as:

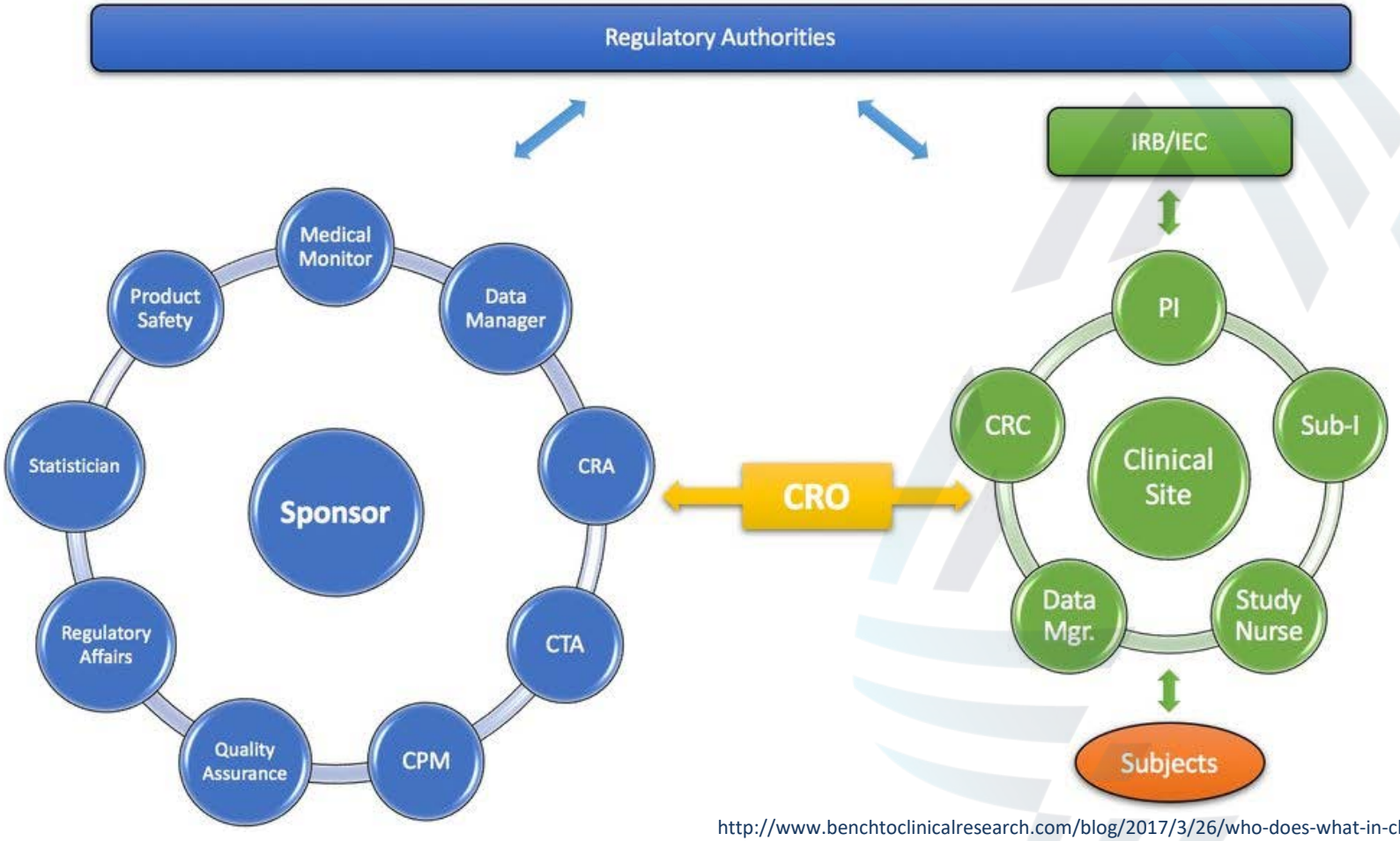
- *Project management*
- *Database design & build*
- *Data entry & validation*
- *Clinical trial data management*
- *Medicine and disease coding*
- *Quality and metric reporting*
- *Statistical analysis plans and reports*
- *Validation programming*
- *Safety and efficacy summaries*
- *Final study report*

Pls note: Any trial-related duties and functions not specifically transferred to and assumed by a CRO are retained by the Sponsor.



https://www.andamanmed.com/technical_resources/contract-research-organization

Relationship between SPONSOR-CRO



http://www.benchtoclinicalresearch.com/blog/2017/3/26/who-does-what-in-clinical-research

Legal and Regulatory Context

- INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE-**Guideline for Good Clinical Practice**-*Article 5.2*
- **REGULATION (EU) No 536/2014** OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
- **Ministerial Decision no. 59676/22.12.2016**-*Article 24 "*Requirements for the Functioning of Contract Research Organization (CRO) to participate in the conduct of clinical trials".
- **DIRECTIVE 2001/20/EC** OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL relating to the implementation of Good Clinical Practice in the conduct of Clinical Trials on medicinal products for human use
- **Regulation (EU) 2016/679 effective as of May 25th 2018** of the European Parliament and of the Council on the protection of natural persons with regard to the processing of personal data and on the free movement of such data **(GDPR)**

Ministerial Decision no. 59676/22.12.2016-*Article 24*
"Requirements for the Functioning of Contract Research Organization (CRO) to participate in the conduct of clinical trials".

- **Written assignment** of CROs' duties
- CROs should be **seated in Greece** and have a **Greek VAT number**
- To appoint a **Scientific Manager** who shall work **full time and exclusively**
- To ensure that all appropriate **safety and security measures** have been taken
- Third Party Assignment (i.e.Freelancers): **Objective Liability**
- Should submit before the National Organization for Medicines a **declaration of their activity→ National CRO Database**
- **Certification** is necessary (i.e. ISO 9001)
- To appoint a **Quality Assurance Manager**

Liability

- The CRO can also be **held liable in case of non compliance with existing legislation**
- Hence, a CRO should act **in accordance with all ethical principles and protect itself** from any unlawful action it may fall to its attention
- WAWRZYNEK v. STATPROBE, INC. (E.D.Pa. 10-25-2007) "***The Court sees no legal theory or compelling policy reason to allow the CRO to use the Sponsor and its wrongdoing as a shield***."

Best Practices-
Ethical guidelines

Ethical-Legal Guidelines:

- ✓ **Transparency**
- ✓ **Scientific Validity**
- ✓ **Collaborative partnership**
- ✓ **Confidentiality**
- ✓ **Privacy & Data Protection**
- ✓ **Good Clinical Practice Guidelines**

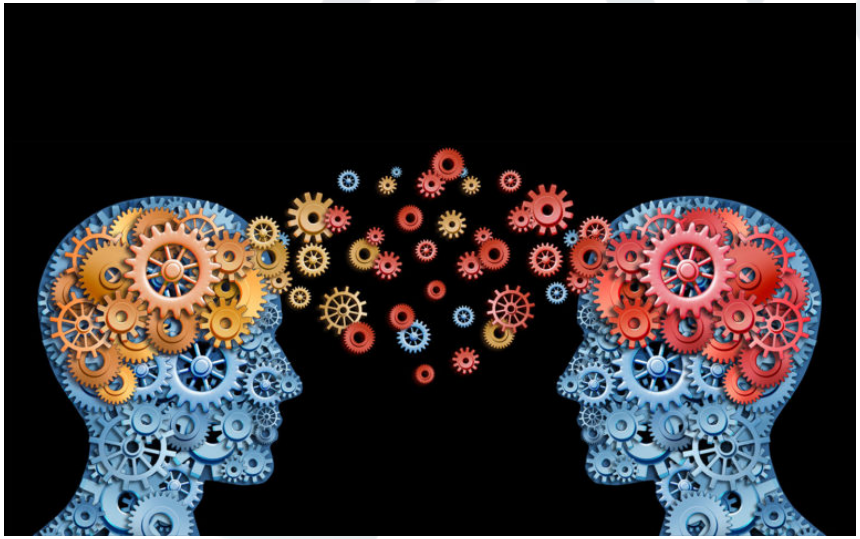
EU 679/2016 Regulation-GDPR

The GDPR sets new requirements for the CRO:

- Participants' consent should be updated: **informed, specific, explicit written consent, freely revocable is a must**
- Application of **technical and organisational measures** for the safety of participants' personal data
- Participants**' adequate information in regards to their rights**
- **Prior Written Sponsor's Consent**→ Freelancers
- Principle of **data minimization, proportionality, transparency, accountability**

And Much More…

Pls note: GDPR makes specific reference in regards to clinical research!



https://www.cbronline.com/verticals/the-boardroom/gdpr-controller-processor-heres-need-know

Future Challenges of the CRO?