



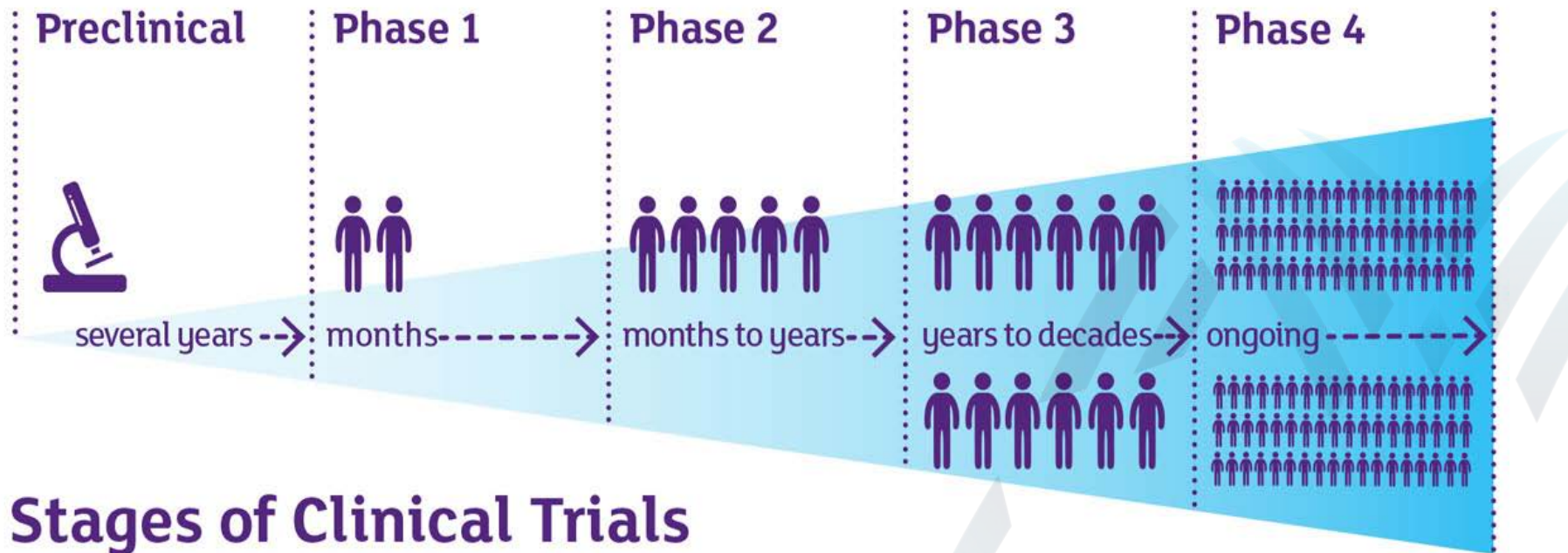
MICHALOPOULOU
& ASSOCIATES

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



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.



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](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:

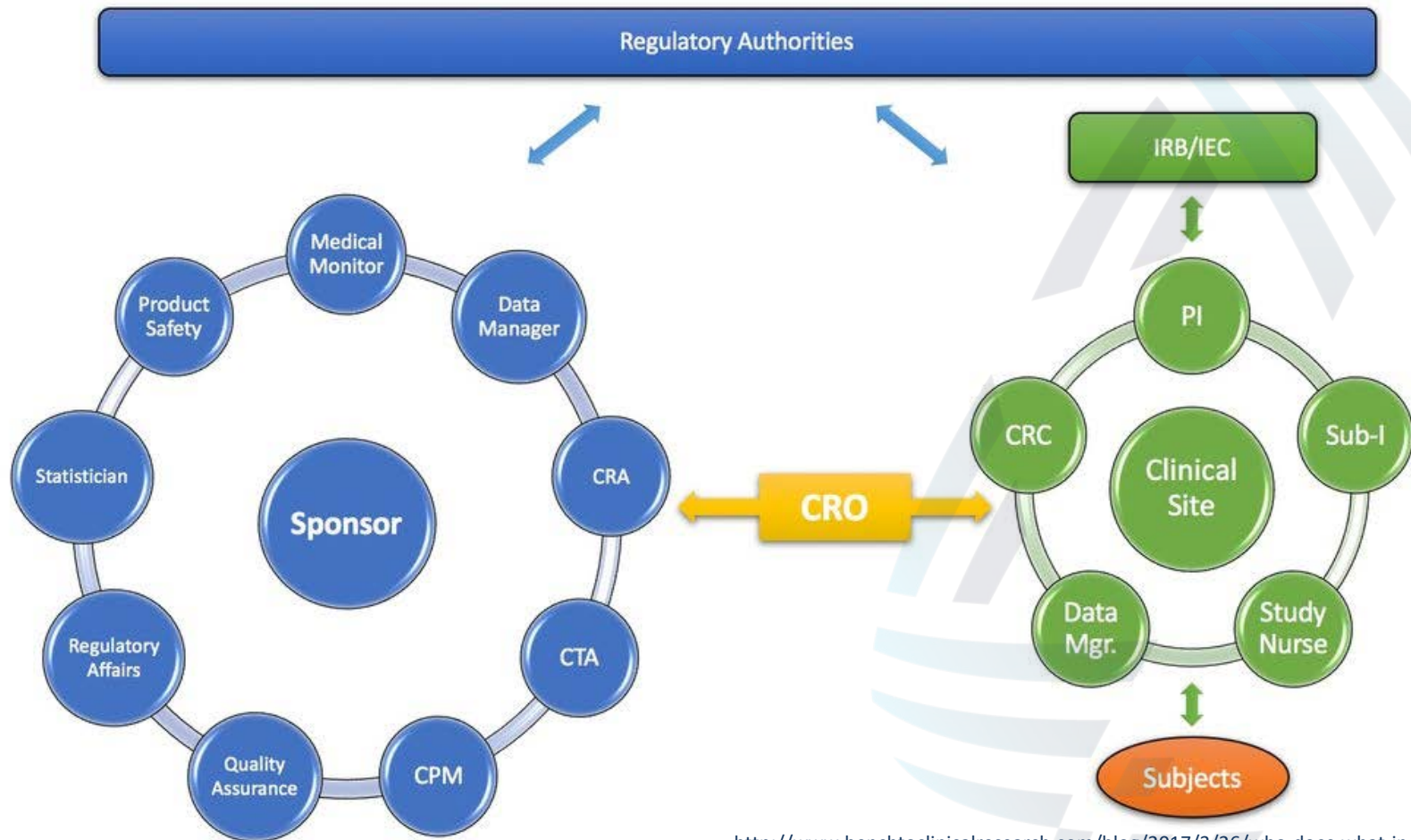
- *Project management*
- *Database design & build*
- *Data entry & validation*
- *Clinical trial data management*
- *Medicine and disease coding*
- *Quality and metric reporting*
- *Statistical analysis plans and reports*
- *Validation programming*
- *Safety and efficacy summaries*
- *Final study report*

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**

**Better
Compliance**



=

**Better
Data**



=

**Better
Results**



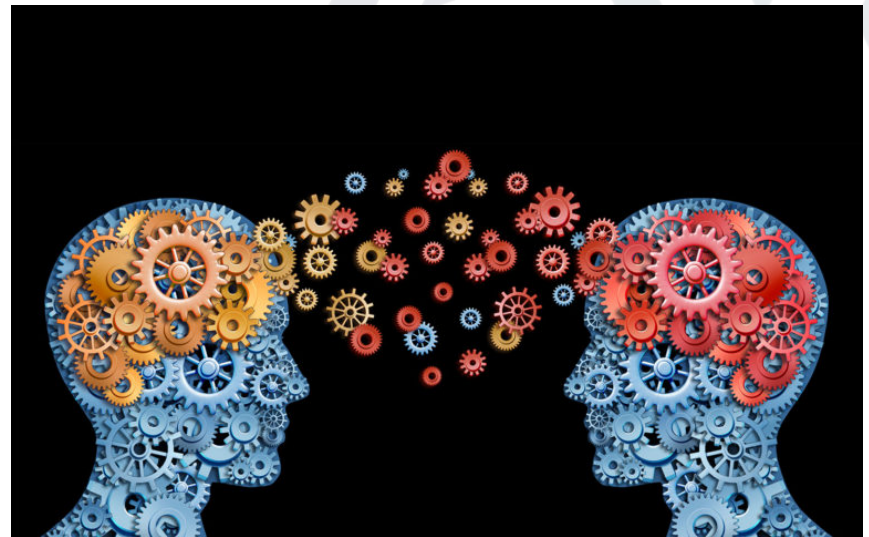
EU 679/2016 Regulation-GDPR

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**

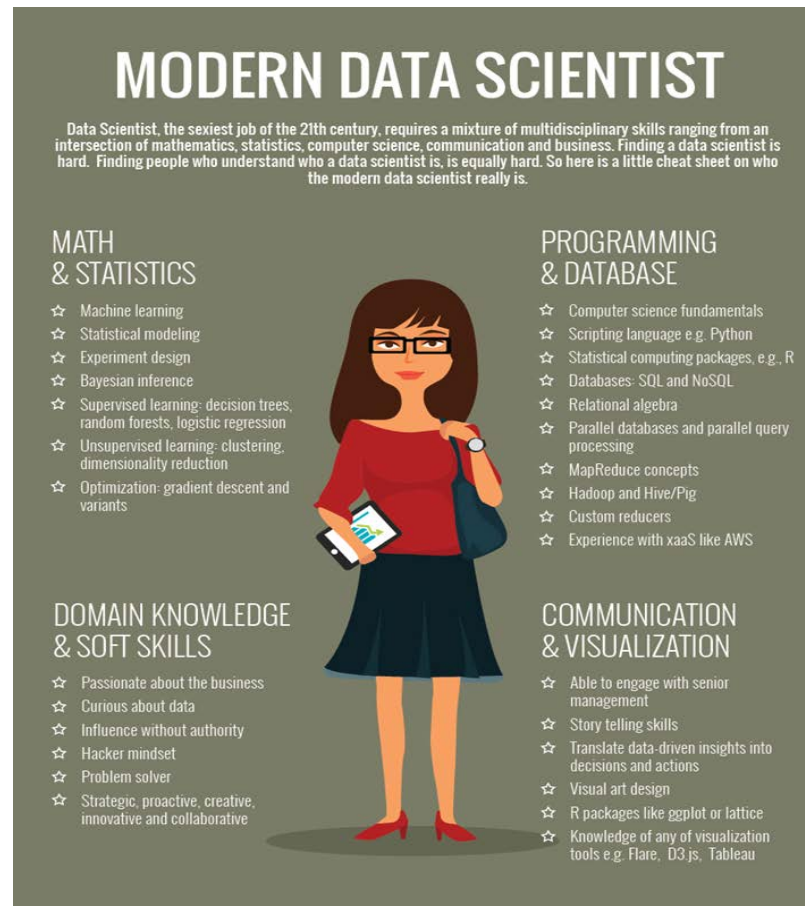
And Much More...

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?



MODERN DATA SCIENTIST

Data Scientist, the sexiest job of the 21st century, requires a mixture of multidisciplinary skills ranging from an intersection of mathematics, statistics, computer science, communication and business. Finding a data scientist is hard. Finding people who understand who a data scientist is, is equally hard. So here is a little cheat sheet on who the modern data scientist really is.

MATH & STATISTICS

- ☆ Machine learning
- ☆ Statistical modeling
- ☆ Experiment design
- ☆ Bayesian inference
- ☆ Supervised learning: decision trees, random forests, logistic regression
- ☆ Unsupervised learning: clustering, dimensionality reduction
- ☆ Optimization: gradient descent and variants

PROGRAMMING & DATABASE

- ☆ Computer science fundamentals
- ☆ Scripting language e.g. Python
- ☆ Statistical computing packages, e.g. R
- ☆ Databases: SQL and NoSQL
- ☆ Relational algebra
- ☆ Parallel databases and parallel query processing
- ☆ MapReduce concepts
- ☆ Hadoop and Hive/Pig
- ☆ Custom reducers
- ☆ Experience with xaaS like AWS

DOMAIN KNOWLEDGE & SOFT SKILLS

- ☆ Passionate about the business
- ☆ Curious about data
- ☆ Influence without authority
- ☆ Hacker mindset
- ☆ Problem solver
- ☆ Strategic, proactive, creative, innovative and collaborative

COMMUNICATION & VISUALIZATION

- ☆ Able to engage with senior management
- ☆ Story telling skills
- ☆ Translate data-driven insights into decisions and actions
- ☆ Visual art design
- ☆ R packages like ggplot or lattice
- ☆ Knowledge of any of visualization tools e.g. Flare, D3.js, Tableau

MarketingDistillery.com is a group of practitioners in the area of e-commerce marketing. Our fields of expertise include: marketing strategy and optimization; customer tracking and on-site analytics; predictive analytics and econometrics; data warehousing and big data systems; marketing channel insights in Paid Search, SEO, Social, CRM and brand.

Marketing
DISTILLERY
(c) Krzysztof Zawadzki