Clinical studies start-up

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Summary

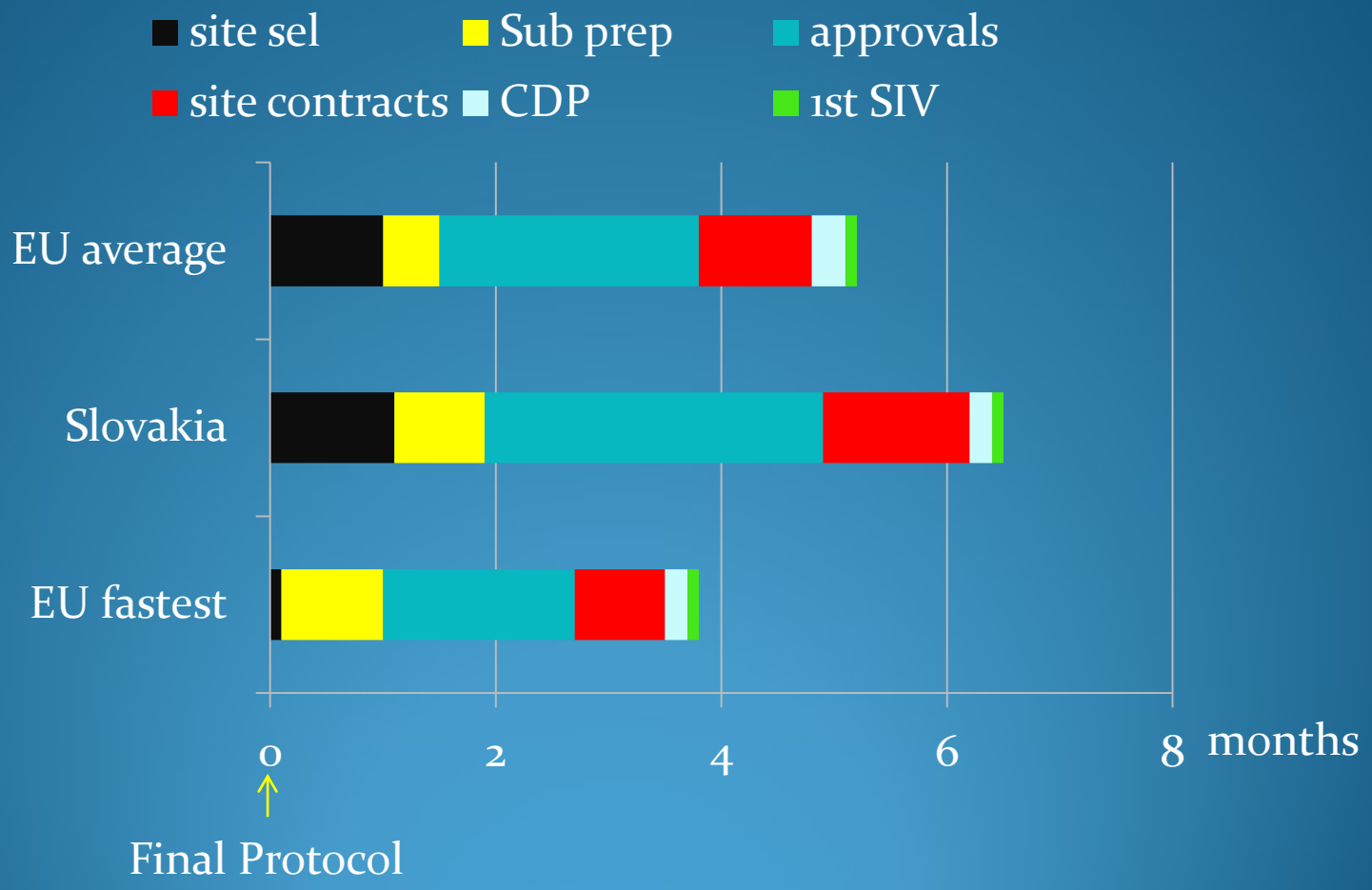
- Overview
- Feasibility and site selection
- EC and CA submissions and approvals
- Site contract negotiaion
- Site documents collection for drug release at site

Overview

Clinical studies have to be completed in the shorter possible time to contain costs and collect data for the development of a new drug in a timely manner

Fast site start up gives the sites more times to enroll patients in Clinical studies, thus contribute to the timely conclusion of the study

Study Start-up timelines



Feasibility and site selection

EU fastest: 1 week

Slovakia: 1 month → Slovakia slower

Biased data since priority is given to the fastest Country (usually Belgium)

It is very important to identify the best sites since the begenning because it would influence positively:

- EC submission preparation and EC queries
- Site contract negotiation and the collection of CDP docs for drug release
- Patient recruitment and retention

A good feasibility is the start to identify the best trial confirmed later with on site Visits

- Good sites are those that:
  - have a good patient population on the study indication,
  - Clinical Study expertise and GCP knowledge
  - Do not have currently ongoing compteting studies
  - Available staff to follow-up on all study stages

Site selection - problems

Unfortunately the best sites have also many studies but it is possible to check independently for competing studies on websites like:

www.clinicaltrials.gov

www.CiteLine.com

www.clinicaltrialsregister.eu.

Also, Pharma companies have they preferred sites for other reasons which often turn out to be slow, not responding, and also poor enrollers.

Competent Authorities (CA)

EU fastest: 1-1,5 month

Slovakia: 2,4-3 months → Slovakia slower

All EU CA are now alligned with the (2001/20/EC directive) and there are only small difference on submission docs requirements across Countries.

The above discrepancy is mainly due to internal CA organisation.

In any case, slower CAs often do not really influence overall start up timelines

To further synchronize and align CA process in EU, on 2004 the Voluntary Harmonization Procedures (VHP) has been implemented but so far has shown a limited success because it damp down the performances of fastest CAs, not all the EU Countries participate due to the discrepancy on their respectives start-up Sequency, it does not really shorten timelines overall and it is risky in case of docs Revisions.

Ethic Committees (ECs)

EU fastest: 1-1,5 month

Slovakia: 2,4-3 months → Slovakia slower

EU average: 2 months

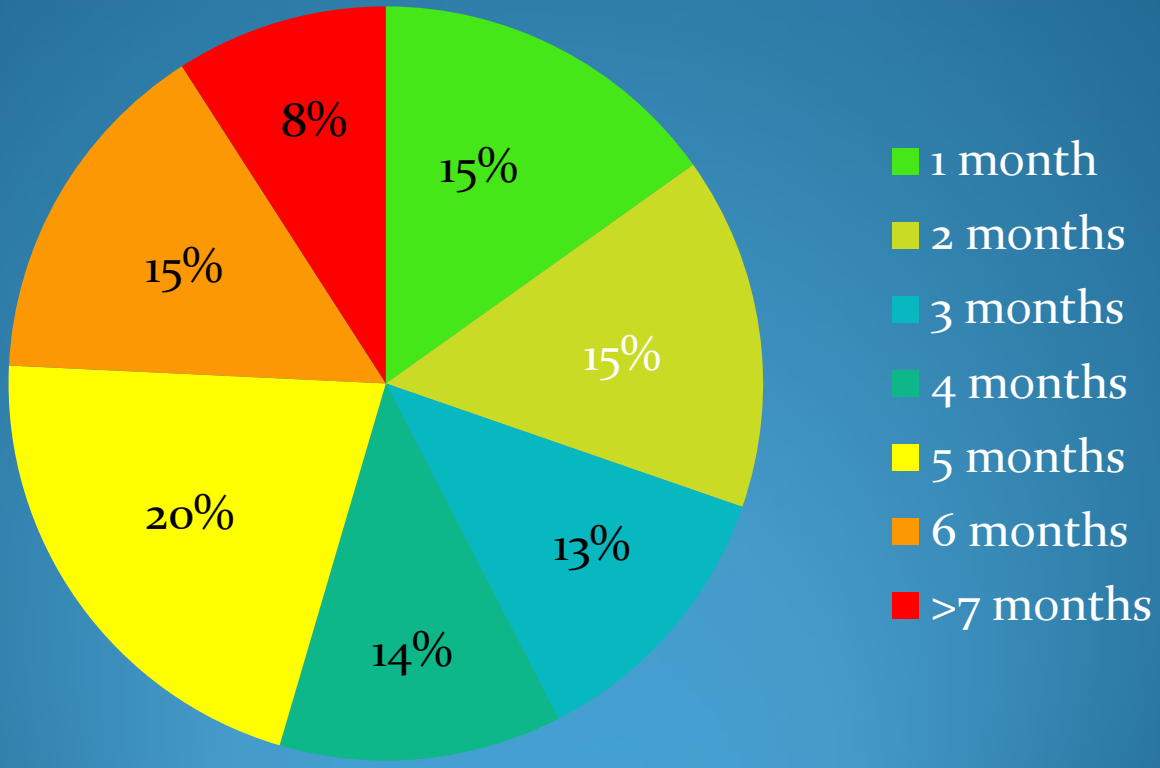
Overall, Countries with only a central EC (in this case UK is the fastest) have a quicker approval process while Countries with also singularly independent Local ECs (Slovakia) are longer.

This is due to 2 factors:

- different organisation from EC to EC ,
- Different evauation of the submitted documention creating different demands and queries.

Site contract negotiation I

Data from 2 clinical studies with more than 10 EU Countries each.
The timelines are taken from the EC approval to the contract execution date for each site and expressed in percentage on months.



Site contract negotiation II

High variability of efficiency from site to site, site contract negotiation and execution (site contract signed by all parties) is the major cause of site activation delays.

It can be partially compensated by early knowledge of all site requirements but little can be done if the site administration is slow on contract revision (close FU with the site is relatively succesful) and does not work at all if there are legal disputes between parties.

The only way to really shorten it, is to drastically reduce negotiation cycles.

Site documents collection for drug release

This is again heavily dependent on site but usualy does not create problems because done at the same time of contract negotiation, which, being usually quite long, gives ample time to collect all the others ducuments

Conclusions

Where ever variation of a process is possible, there are potential delays and we seen them on:

- Local EC approval vs central EC approval process
- Site contract negotiation

So the system to overcome the problem is to limit variability:

- On Local ECs, harmonizing the procedures across all of them
- On site contract negotion, set common lanuguage to be apply to all sites.