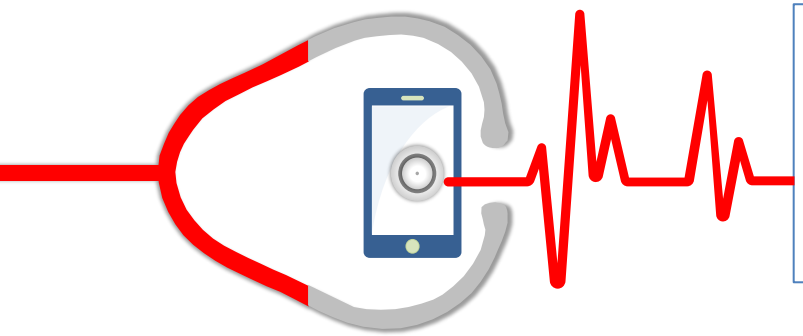
AVANTYO
INSTITUTE OF CLINICAL RESEARCH

INNOVATION IN EDUCATION

*"Stay Ahead of the Game:*
*Transformation in Clinical Trials*
*in the Age of Artificial Intelligence."*

# ANNUAL CLINICAL TRIALS SYMPOSIUM

November 8th, 2024



# Decentralized Clinical Trials: Overcoming Challenges and Embracing Opportunities in Supporting Investigators and Patients

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Dr. Florescu Moraid got her Medical Doctor Diploma in 1998 from „Carol Davila" University of Medicine and Pharmacy Bucharest, Romania and was accredited as Laboratory Medicine Specialist in 2005 and as Senior Laboratory Medicine Specialist in 2011, by the Romanian College of Physicians.
She got her Master of Science Diploma in 2006 , accomplished Postgraduated School of Clinical Trials Management, Gdansk in 2012 and the Postgraduated Leadership Development Programme at University of Sussex, United Kingdom in 2014.
Dr. Florescu Moraid was responsible for clinical trials operations at Synevo Central Lab, the clinical research wing of Swedish Medicover Group as Regional Director for Romania, Moldova, Bulgaria and Serbia between 2005-2018. She has been organizing National Clinical Trials Symposium for more than15 years.
Since the beginning of 2019, she is Co-founder of Avantyo - Institute of Clinical Research and CEO of Camina Medical Experts, developing tailored CT services for pharma sponsors, CROs and mid-size biotech companies.

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# Actual context of clinical research

- Covid 19 pandemic, with major impact on our patients lives, it is recognized more than ever the need for clinical research. The medical research community embraced DCT as a way to continue research when in person traditional methods were made impossible

- Many clinical trials already include decentralized elements. For example, laboratory tests are often conducted by **clinical laboratory facilities** at locations remote from traditional clinical trial sites.

- Advances in using electronic communications and information technology to interact with trial participants in different locations (i.e., telehealth) allow for fewer in-person visits to traditional clinical trial sites. **Digital health technologies** (**DHTs**), for example, have expanded the types of trial-related data that can be obtained remotely from trial participants.

- Decentralized clinical trials (DCTs) offer a more patient-centric approach, reflecting a transformational philosophy for the conduct of clinical trials in which fewer clinic visits are required and patient and caregiver burden is reduced.

- In many cases of ongoing hybrid trials, patients have been receiving medication at home as an emergency solution.

# DCT by definition*

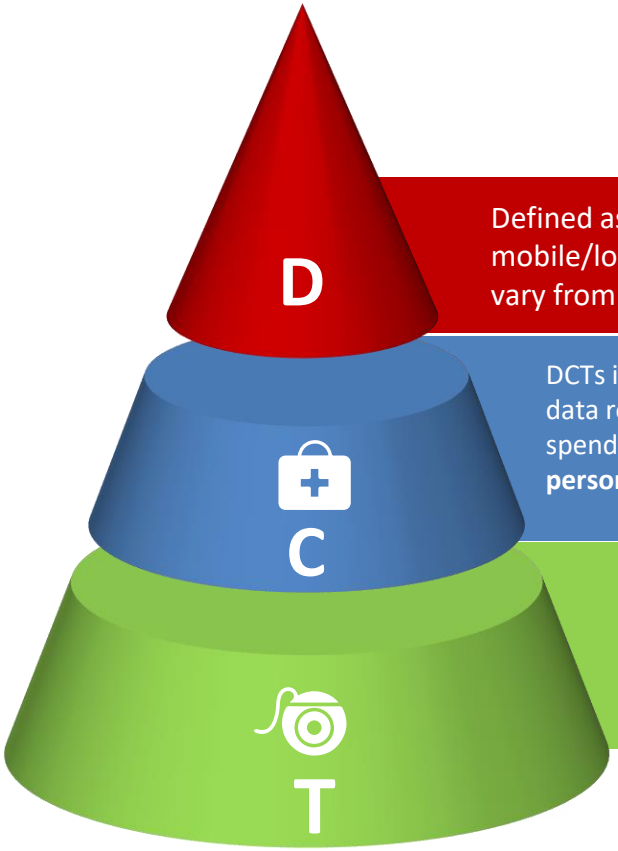
A **decentralized clinical trial** (**DCT**) refers to a clinical trial that includes decentralized elements where trial-related activities elements occur at locations other than traditional clinical trial sites

Decentralized elements allow trial-related activities to occur remotely at locations convenient for trial participants.

Decentralized elements can include, among other things, **telehealth** visits with trial personnel, **in-home visits** with remote trial personnel, or visits with local health care providers (HCPs).

* “Conducting CT with decentralized elements-Guidance for Industry, Investigators and other Interested parties”-FDA, Sep 2024

# Decentralized Clinical Trials



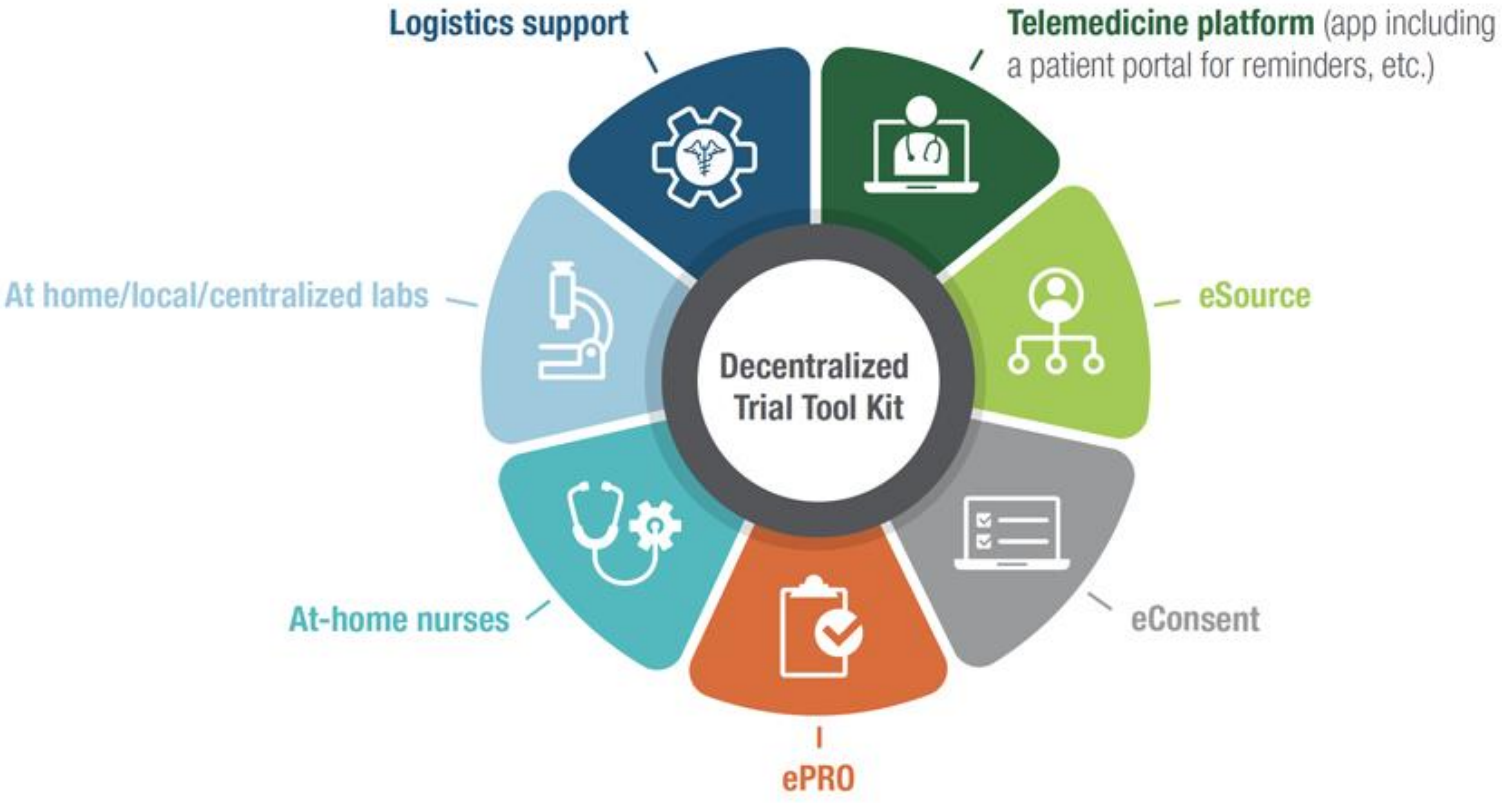

Defined as studies “executed through telemedicine and mobile/local healthcare providers(HCPs), using procedures that vary from the traditional clinical trial model.”

DCTs incorporate **technology,** so patients and clinical trial staff can share data remotely, effectively **reducing the amount of time** patients have to spend at the trial site and on the other hand, reducing the **number of in-person visits** sponsor monitors must make to sites.

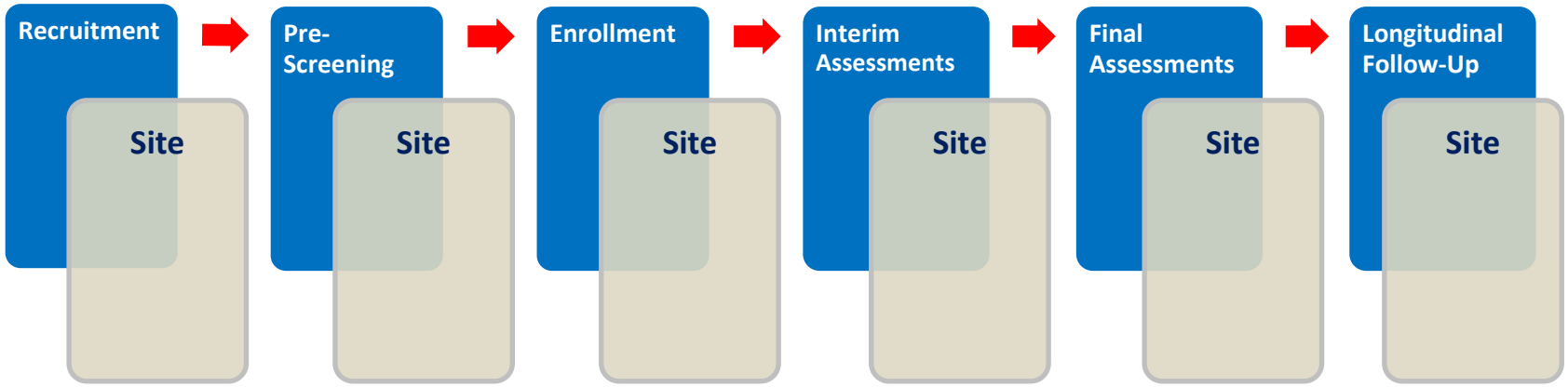
As a consequence, sponsor monitors can view essential documents online, and patients can visit local community health centers and pharmacies instead of only the research site.

https://ctti-clinicaltrials.org/recommendations-and-resource/
https://www.forbes.com/sites/forbestechcouncil/2021/06/10/how-decentralized-clinical-trials-can-play-a-role-in-increasing-patient-recruitment-and-diversity/?sh=385c15d52ae9

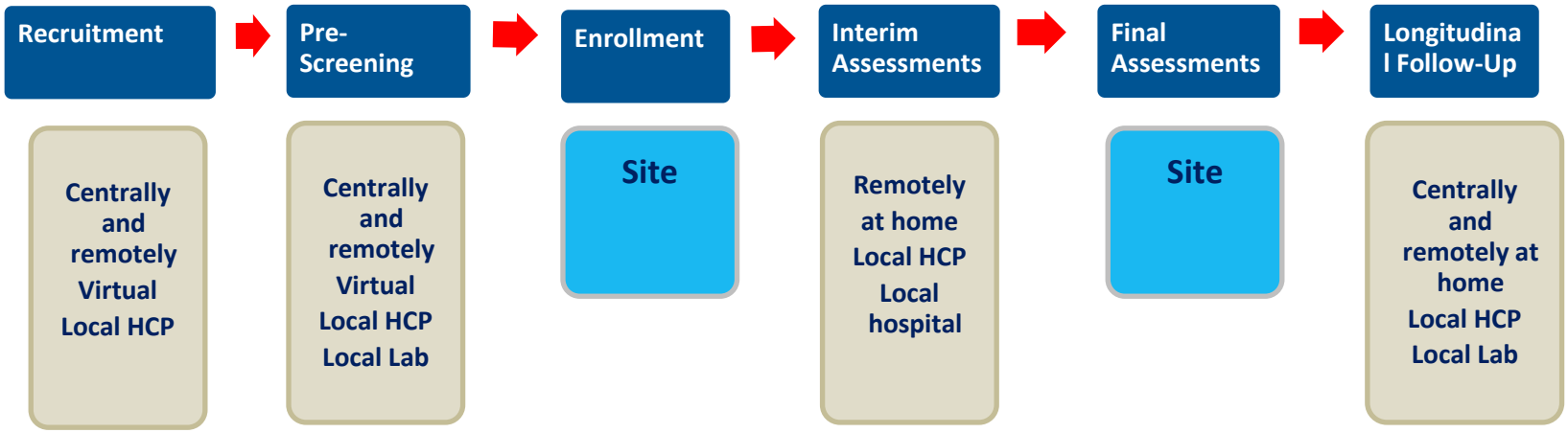
# DCT services



# The current model of CT




# The future model of CT



# Classic vs DCT

| Phase/Function | Traditional Methods | Decentralized tech and Tools |
|---|---|---|
| Recruitment | site based and physician-to-physician referrals, preSCR via TV, radio, recruitment agencies | Targeted digital recruitment, preSCR via SM |
| Enrollment and onboarding | F2f consent<br>SCR and site-based assessments & in person training | Accompanied electronic consent (e-consent)<br>Access to live chat with clinical study team<br>Virtual training |
| IP distribution and administration | Study staff dispensing, collection and performance<br>Drug accountability at site | IP shipped directly to patient<br>Drug accountability remotely |
| Data collection | Take home paper diaries<br>F2f data collection at sites | Electronic paper reported outcomes(e PRO)<br>Remote monitoring via wearables, medical devices) |
| Assessments | F2f at site<br>Electronic clinical outcome (eCOA) assessment by HCP at site | eCOA via telehealth mobile/home visits<br>Centralized experts |

# Patient centered activities

## Future State: All activities are centered around the patient

**Hospitals and PIs**
Investigators continue their current responsibilities and oversee larger numbers of remote patients whose trial activities occur in the community, at home and virtually.

**Participant access**
More patients access and participate in trials, including diverse and difficult to recruit populations, that are conducted (fully or partially) in more convenient locations that reduce time and travel commitments.

**Participant experience**
Patients are able to integrate trial activities into their daily lives with minimal disruption and reduced burden.

**At home**
HCPs complete trial related activities within the patients home.

**Virtual**
Patients and/or their caregivers complete trial activities without an HCP physically present, independently or with an HCP / site staff via telemedicine.

**Community / local health clinic**
HCPs complete trial activities in retail health clinics, community practices, outpatient facilities, etc. that are located proximate to patients homes and work.

**Biopharma**
continues current responsibilities and leverages new trial delivery channels to tailor trial designs based on patient needs and preferences.

**CRO**
No near term changes to CRO activities; anticipated shift to DCT adapted monitoring strategy in the future.

# Recommendations for implementing DCTs

1. DCT Design and Conduct

2. Remote CT Visits and CT- related activities

3. Digital health technologies

4. Roles and responsibilities of sponsor and investigators

5. Investigational product in a DCT

* “Conducting CT with decentralized elements-Guidance for Industry, Investigators and other Interested parties”-FDA, Sep 2024

# DCT Design and Conduct

- CTs should be designed to limit variability in the data collected by including specific instructions in the protocol for performing trial related activities which occurs at locations other than traditional sites

- DCTs that permit tests to be performed independently by participants at home (e.g., spirometry) may introduce **variability** compared to tests performed under supervision at traditional clinical trial sites. Training or video supervision (i.e., during a telehealth visit) may reduce such variability.

- The protocol should specify which visits will be conducted at traditional clinical trial sites, which visits will be conducted remotely

# Remote CT Visits and CT- related activities

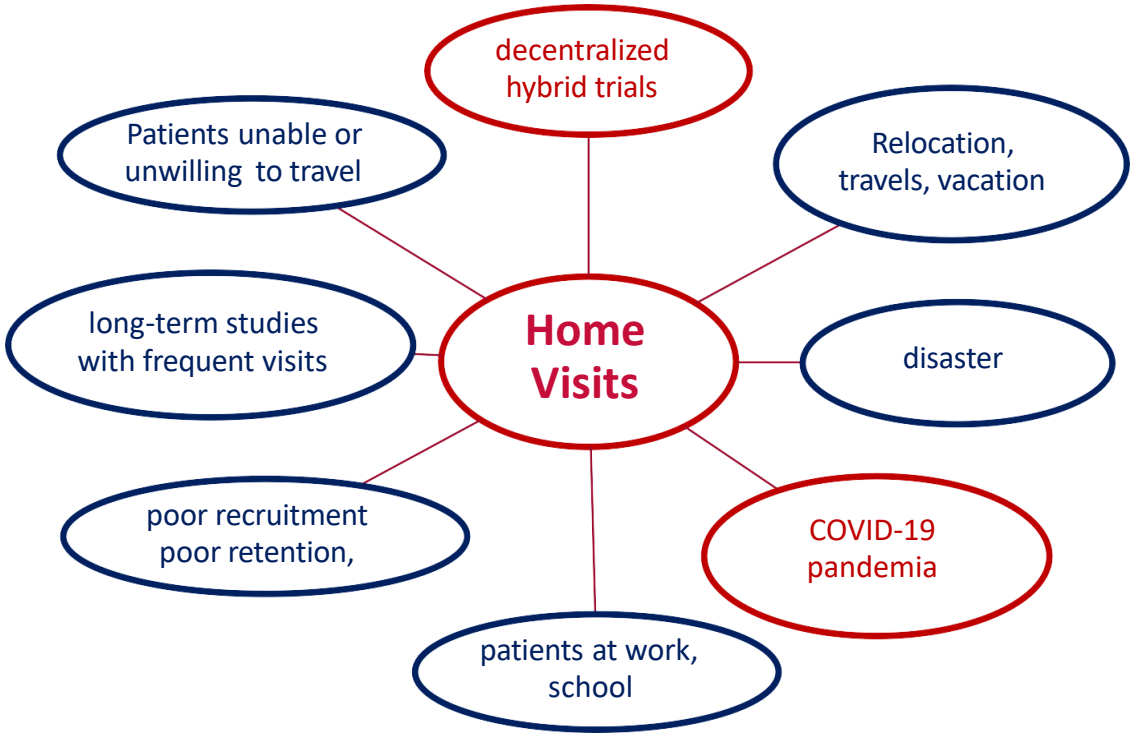
- Remote clinical trial visits may include telehealth visits, participant visits to local HCPs, or in-person visits by trial personnel or local HCPs to participants' homes.
- The following should be considered when planning remote clinical trial visits :

1. for telehealth visits, the study protocol should specify when a telehealth visit with a trial participant is appropriate and when a participant should be seen in person
2. home visits and trial-related activities can be conducted by trial personnel(local doctors or nurses) who are sent to participants' homes or participants' preferred locations
3. trial-related activities that are unique to a research study require a detaild knowledge of a protocol, IB, IP and should be performed by qualified and trained personnel
4. study records should indicate if a visit was conducted via telehealth and should include the date of the visit and the name of the person who conducted the visit
5. trial protocol should specify how adverse events identified remotely will be evaluated and managed.

# Home care health services role

- Home visit is defined as the process of **providing the nursing care to patients at their doorsteps**.
- Home Health services take the clinical trial to the patient by conducting visits in the home.
- This reduces the number of visits to study sites and significantly lessens the burden on patients and their families.

# Patient-centric home care visits



# Service Providers may be depending on study requirements

## General practice and primary care

- First-contact, comprehensive, continuous, coordinated and personalised
- In some countries very expensive

## Physicians

- Highly motivated to participate in clinical research
- Additional income

## Nurses

- In some countries not allowed to perform specific activities (e.g. blood draws)

SERVICE PROVIDERS

# HOME CARE SERVICES
# business model

HEADQUARTER PROJECT MANAGER

COUNTRY COORDINATOR

NURSE/HCP

PATIENT

HOME CARE SERVICES ARE DEVELOPED BY OUR COUNTRY COORDINATORS THROUGH THEIR NATIONAL NETWORK OF NURSES

Our nurses/doctors are in permanent contact with investigative sites, being part of the study teams, but always follow the patients at home

# Roles and Responsibilities

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| Project Manager | Country Coordinator | Home care provider |
|---|---|---|
| • Coordinate and oversee in-home or alternate location study visits<br>• Act as liaison between sponsor, investigator sites and home care service providers<br>• Communications with sponsor, CRO, central lab and other vendors<br>• Develop study-specific home care training manuals and documents<br>• Identify, qualify and train country coordinators and local service providers<br>• Day-to-day logistics<br>• Centralized contracting and billing<br>• Quality assurance, regulatory compliance, records retention | • Identification of adequate qualified home care Service Providers within the country<br>• Management and coordination, training and supervision of the home care Service Providers within the country<br>• Quality control of home care services<br>• Compliance with GCP/ICH guidelines and applicable local and national regulations<br>• In depth knowledge of local medical practices<br>• Understanding of cultural differences | • Study drug administration (infusion, injection, topical)<br>• Blood draws (safety labs, pharmacokinetics, genomics)<br>• Other biologic sampling (nasopharyngeal and oral mucosal swabs, urine)<br>• Clinical assessments (vital signs, ECGs, concomitant medications, adverse events)<br>• Patient training and education (e.g., self-administration)<br>• Study compliance checks (patient diary, drug storage)<br>• Patient questionnaires<br>• Visit documentation<br>• Records retention |

# Roles and responsibilities

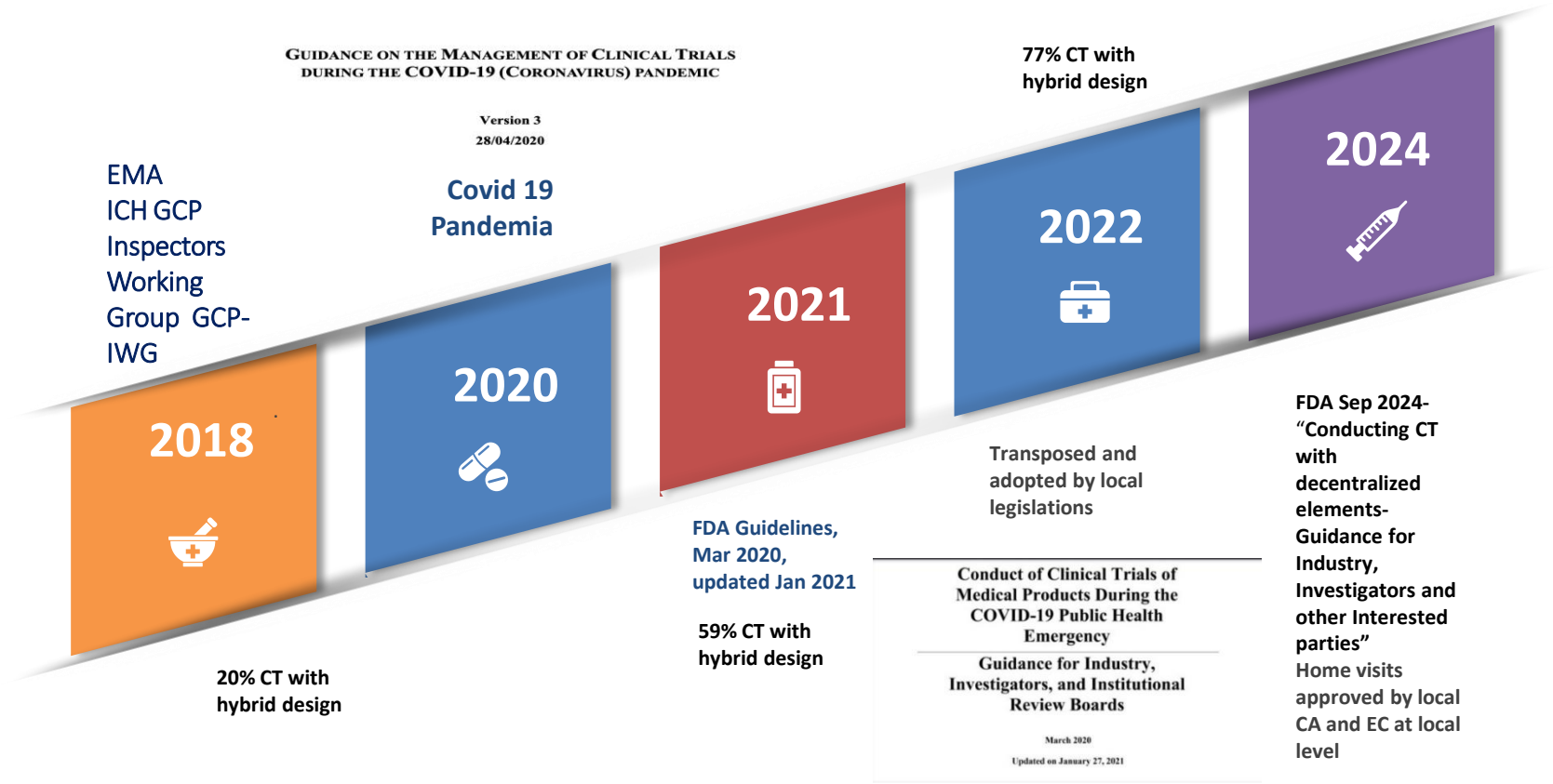
- **SPONSOR**: should ensure proper coordination of decentralized elements(e.g. remote trial personnel for home visits, shipment of IP to patients & should very well describe in the protocol how operational aspects of DCT will be implemented (i.e. scheduled and unsch. visits, safety monitoring and management of adverse events), should ensure with local legislation governing medical practice for IP administration, etc.
- **INVESTIGATOR**: responsible for conduct of DCT, must maintain accurate records, should review data from other trial personnel than investigative site which belong to his site, must ensure assessments are being completed consistent with the protocol. Videoconferencing may be useful to allow investigators to oversee trial personnel performing activities at patients' home. Investigators should enroll only as many trial participants as they can appropriately manage to ensure adequate supervision of DCT related activities
- Obtaining informed consent remotely (can include a remote home visit) may be considered as part of DCT. IRB oversight is required to ensure the process is adequate and appropriate.

# DCT– regulatory considerations

**Regulatory concerns:** The U.S. FDA has promoted the use of decentralized methods in trial design; but, in other countries, regulatory bodies are not always as accepting. DCT adoption rates in Europe have been slower - unclear guidance from government agencies. This doesn't mean hybrid trials can't be successfully conducted in regions outside of the U.S.

It does require an in-depth understanding of each country's regulations and, in many cases, can be aided by direct conversations with regulatory bodies who are still low on the DCT learning curve. Specific country regulations will dictate how to design protocol and which elements are safe to decentralize.

# Home visits – regulatory considerations




*https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice/qa-good-clinical-practice-gcp*

https://www.advarra.com/blog/defining-decentralized-clinical-trials-and-understanding-their-nuances/

Question no.1
**Have you been involved in running DCT in your country?**

**Question no.2**
**What would you need the most from DCT services for your projects?**

https://www.menti.com/al6cqju63pts

https://www.menti.com/alxzpatd9ss8

Question no.3
What are the roadblocks found in your country in using home care services?

# How are physicians, researchers and patients responding to new CT models?

1. **Sponsors & CROs**-people who actually build the model so you can have the patients enrolled- for them it is about building the services and use all the lessons learned
2. **Patients**- it is about working with patients' groups/associations, collecting insights from them about how the study I designed and get all their input (i.e. mobile spirometry for children with COPD).
3. **Sites**- the majority of sites have to move to virtual business model, but they need to be educated, trained, they need to understand how the system works because they need to be seen as modern business model, to use a kind of hybrid virtual models, how profitable may be, BUT it is a giant change management exercise that still needs a lot of time, effort and education

# The future of clinical research is now present

REGULATORS
have issued new guidelines that further enables DCT services


SPONSORS
have embraced innovative ways of working

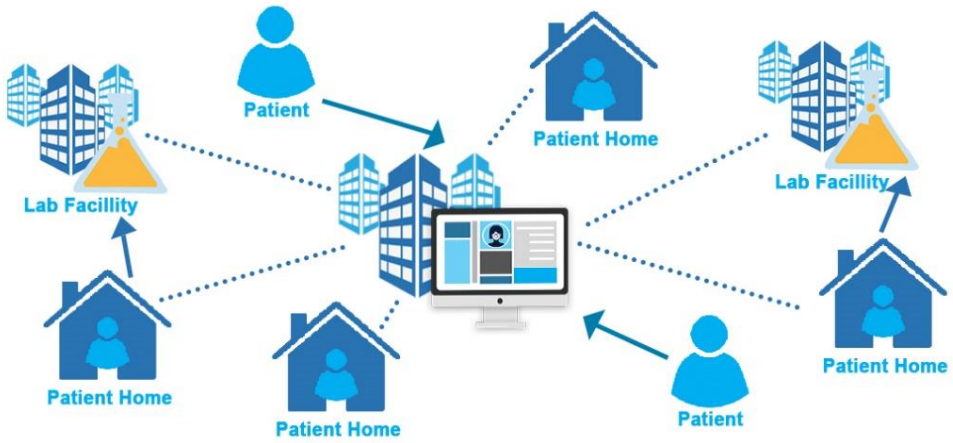
SITES
are using DCT services more frequently and proactively

PATIENTS
have adapted to new tools that facilitate participation and compliance

# RCTs-Hybrid Trials-DCTs

**RCTs**

- participants attend all in person visits at sites for all study activities
- challenges persist in patient recruitment




**DCTs**

- the majority trial activities are conducted remotely
- offers patients enhanced accessibility and convenience but it may diminish oversight and control

**Hybrid trials**

- both in person and remote/virtual components are combined in the trial design
- Incorporate DCT elements into study design
- it is essential to ensure that the scientific rigor of RCTs is maintained while incorporating real world data collection

# CONCLUSIONS

Bringing trial-related activities to participants' homes may **reduce** the need for travel and **improve** engagement, recruitment, and retention and satisfaction amongst potential participants who have challenges accessing traditional clinical trial sites.

**DCTs are not "one-size-fits-all"** and oftenly, a hybrid approach will be necessary.

DCT is not a new type of CT, it is much better said an approach / toolbox that changes how a study is conducted, it is a **shift** to modernize CTs. It is about the ability to be flexible.

DCT is not an easy work, it's complicated shift on how to do CTs; it is a change in perception or mentality from" **tell me why?"** to "**tell me how**?"

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