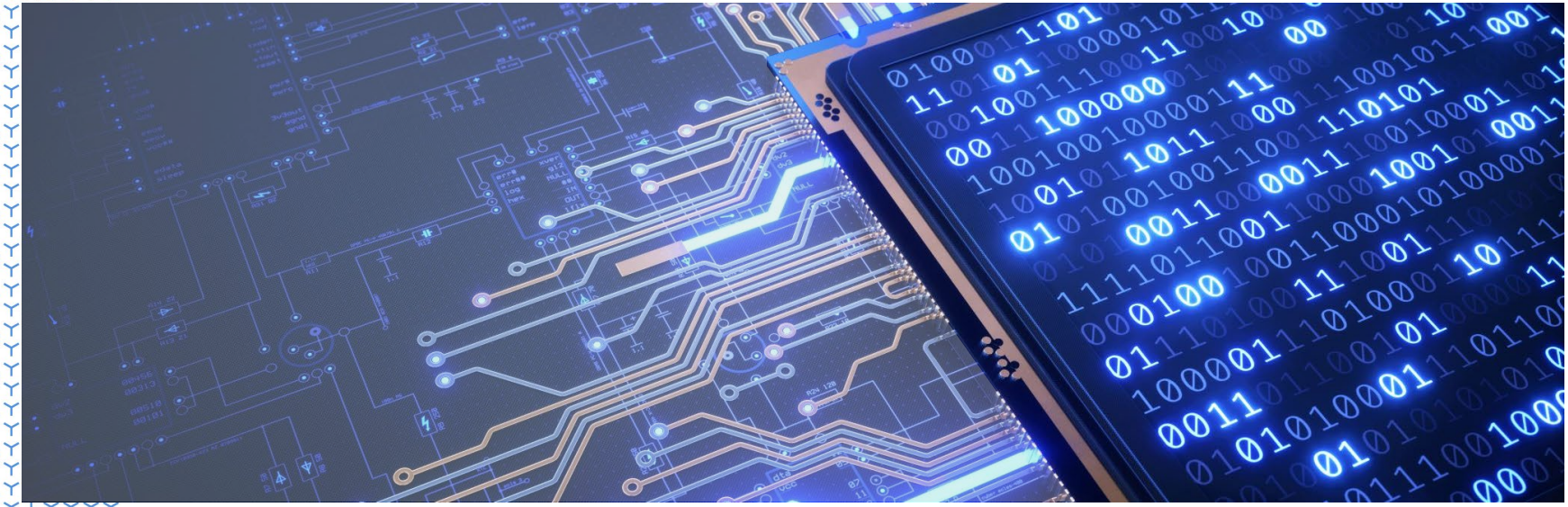

Where are we with Decentralized Clinical Trials (DCTs)

A Sponsor's review of the current regulatory landscape and potential barriers to scale

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Presented at CCEAR, 15th November 2022

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Agenda

An overview of today’s presentation

- Our Experience with DCTs
  - Regulatory Engagements
  - Participation in Industry Initiatives
- Global DCT Guidance
- Covid-19 & Temporary Guidances
- Lesson’s Learned

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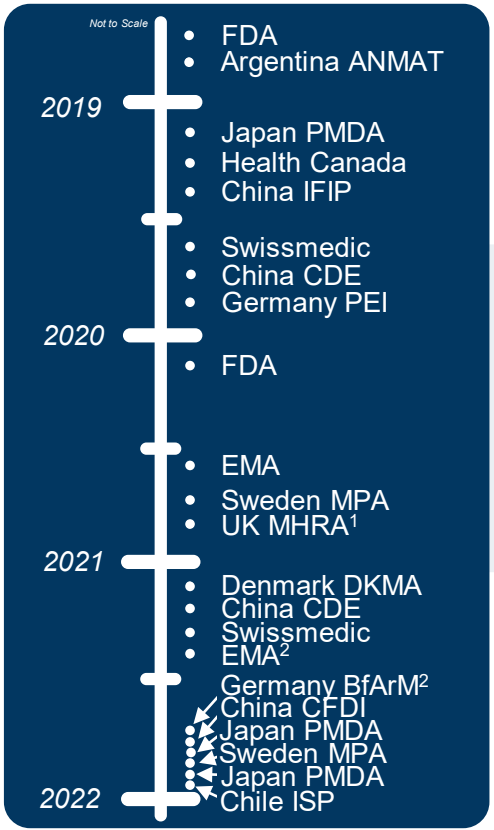
Our Experience with DCTs

Regulatory Engagements

Health Authority Interactions and Key Learnings



- Novartis has presented the DCT model to several HA's globally, through general discussions and protocol specific meetings

Key feedback:

- The benefits of DCTs with its enabling technologies are broadly endorsed, and the need for global adoption is recognized
- Compliance with ICH GCP guidelines for digital approaches is critical
- Data quality and integrity must be ensured for all digital approaches
- Investigator oversight and patient safety must remain the key focus of DCTs

- Proactively inform HA's of DCT elements when submitting Clinical Trial Applications

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Joint meetings held with TransCelerate[1] & IMI Trials@Home[2] consortiums

Participation in Industry Initiatives

Trials@Home Homepage

EFPIA's Home Page

PhRMA's Home Page

CTTI's Home Page

Danish Medicines Agency's Home Page

Swedish Medicines Agency's Home Page

TransCelerate's Homepage

BIO's Home Page

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Global DCT Guidance

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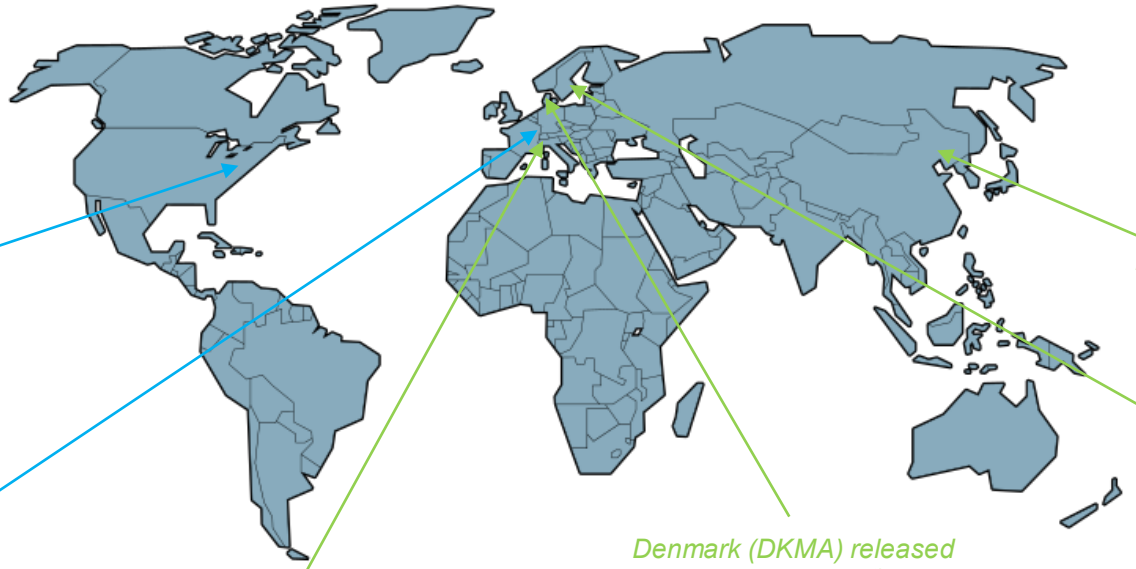
HA DCT Guidances Globally

Currently little available across the Globe

Canada (Health Canada) opened a public consultation on their Clinical Trial Modernization Initiative on 20th May 2021, now closed, which highlights the value of DCTs but does not provide specific guidance on implementation.

Japan (PMDA) is developing eConsent, Direct-to-Patient IMP and Home Nursing guidances to support DCT Trials, expected end of Q1 2023 .



US (FDA) DCT Guidance, now expected by end of 2022

European Guidance, via HMA's CTCG, now expected Q4 2022

China's Centre for Drug Evaluation (within NMPA) released "Technical Guideline for the Implementation of Patient-Focused Clinical Trials" August 2022

Switzerland (Swissmedic & Swissethics) released position paper on 9th Sept 2021 (V1) & 1st Nov 2021 (V1.1)

Denmark (DKMA) released DCT guidance on 4th May 2021 (V1) & Sept 2021 (V2), with (DVMK) releasing theirs on 1st Feb 2022 (V1)

Sweden (MPA) released a Q&A on DCTs on 18th June 2021 (V1), updated 17th Jan 2022

Guidance Available
Guidance Coming
Relevant Information

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ACCEPTANCE OF DCT ELEMENTS ACROSS EUROPE

Output of a mapping performed by the Trials@Home consortium

May 2021

TRIALS @HOME

Yes · No · Partial · To be clarified · Unknown

	Poland	Germany	UK	Spain	Finland	Denmark	Netherlands	Sweden	Italy	Hungary	Czech Republic	Norway	Slovakia	Latvia	Greece	Romania	Lithuania	Estonia	Belgium	France	Bulgaria
Digital recruitment Yes (all channels), NO (not allowed), P = google not allowed, T = google & Twitter not allowed	●	●	●	● (P)	● (P)	● (P)	●	● (P)	●	● (T)	● (T)	● (P)	● (T)	●	●	●	● (P)	● (T)	●	●	● (P)
Direct-to-Patient medication delivery (from sponsor or vendor depot)	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Telehealth	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
E-Consent	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
E-Signature	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Home nurse visits (via vendor)	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

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Covid-19 & Temporary Guidances

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Covid-19 Temporary Guidances

Allowances made by the Authorities during the pandemic

- During COVID the value of the DCT model became clear
  - Technologies such as telemedicine, remote consent, direct to patient IMP shipment, home nursing, use of local labs became common place & enabled trials to continue
- *Internally over..
  - 59,000 Remote monitoring visits
  - 3,200 DtP IMP shipments were made
  - 3,200 remote Site Initiation Visits
  - Few Home Nursing visits conducted
  - Telemedicine Platform usage not tracked

Trials@Home EU Temporary Guidance Comparison

Table 2 Guidance published by the EMA and national competent authorities for different trial activities

Clinical trial phase	Recruitment and enrollment	Patient engagement	Intervention and follow-up						Operation and coordination				
Country (NCA)	Obtaining informed (re-)consent	Participant information and education	Clinic visits	Home health visits	Telemedicine visits	Self-monitoring	IMP (re-) supply	IMP adherence monitoring	Clinical trial monitoring	Documentation management	Regulatory management	Safety management	Total (12)
European Union (EMA)													11
Austria (BASG)													6
Belgium (FAMHP)													9
Bulgaria (BDA)													7
Croatia (MoH)													9
Czech Republic (SÚKL)													11
Denmark (DMA)													10
Estonia (SAM)													10
Finland (FIMEA)													4
France (ANSM)													7
Germany (BfArM)													6
Greece (EOF)													7
Hungary (OGYÉI)													10
Ireland (HPRA)													9
Italy (AIFA)													11
Latvia (ZVA)													8
Lithuania (VVKT)													9
Netherlands (CCMO)													8
Poland (URLP)													3
Portugal (INFARMED)													9
Romania (ANM)													6
Slovakia (ŠÚKL)													10
Slovenia (JAZMP)													2
Spain (AEMPS)													9
Sweden (MPA)													5
Total (25)	16	14	15	11	18	1	22	4	23	23	25	24	

The trial activities were aggregated from all the guidances that were identified.
Gray, guidance identified; white, no guidance identified.
AEMPS, Spanish Agency of Medicines and Medical Devices; AIFA, Italian Medicines Agency; ANM, National Agency for Medicines and Medical Devices of Romania; ANSM, French National Agency for Medicines and Health Products Safety; BASG, Austrian Federal Office for Safety in Health Care; BDA, Bulgarian Drug Agency; BfArM, Federal Institute for Drugs and Medical Devices; CCMO, Central Committee on Research Involving Human Subjects; DMA, Danish Medicines Agency; EMA, European Medicines Agency; EOF, National Organization for Medicines; FAMHP, Federal Agency for Medicines and Health Products; FIMEA, Finnish Medicines Agency; HPRA, Health Products Regulatory Authority; IFARMED, National Authority of Medicines and Health Products; IMP, investigational medicinal product; JAZMP, Agency for Medicinal Products and Medical Devices; MA, Medicines Authority; MoH, Ministry of Health; MPA, Swedish Medical Products Agency; MS, Pharmacy and Medication Department; NA, not applicable; NCA, national competent authority; No., number; OGYÉI, National Institute of Pharmacy and Nutrition; SAM, State Agency of Medicines; SÚKL, State Institute for Drug Control; URPL, Office for Registration of Medicinal Products, Medical Devices and Biocidal Products; VVKT, State Medicines Control Agency; ZVA, State Agency of Medicines of the Republic of Latvia.

Note: Grey boxes indicate a guidance was identified

*Figures correct as of Q2 2021, when tracking stopped

Barriers to scale...
Opportunities to expand...
Mitigating challenges...

Consolidated Lesson's Learned & Feedback

The benefits of DCTs with its enabling technologies are broadly endorsed and the need for global adoption is recognized, however,...

- Health Authorities advise 1) "Baby Steps", 2) Early advice meetings, 3) Describing DCT elements in CTA Cover Letters
- Compliance with ICH GCP guidelines for digital approaches is critical, but not well defined
- Demonstration of Investigator oversight of Patients, local Heath Care Providers (HCP) & offsite health care providers is required

- Data quality & Investigator Control of data must be ensured for all digital approaches
- Comparability between onsite and remotely assessed endpoints is critical
- Some HA's require/prefer initial visits to be conducted on site
- Risk assessments requested for DCT elements being implemented

- **Whilst COVID-19 has increased the awareness of DCT and demonstrated some feasibility, it hasn't "flipped the switch" regarding Health Authority acceptance**
- **Not all countries are in the same place: understanding, experience and stage of guideline development**
- **Complexity is driven by many factors, in addition, not everything is under the responsibility of HAs**