ДАРНИЦЯ

Challenges in clinical trials during COVID-19 pandemics

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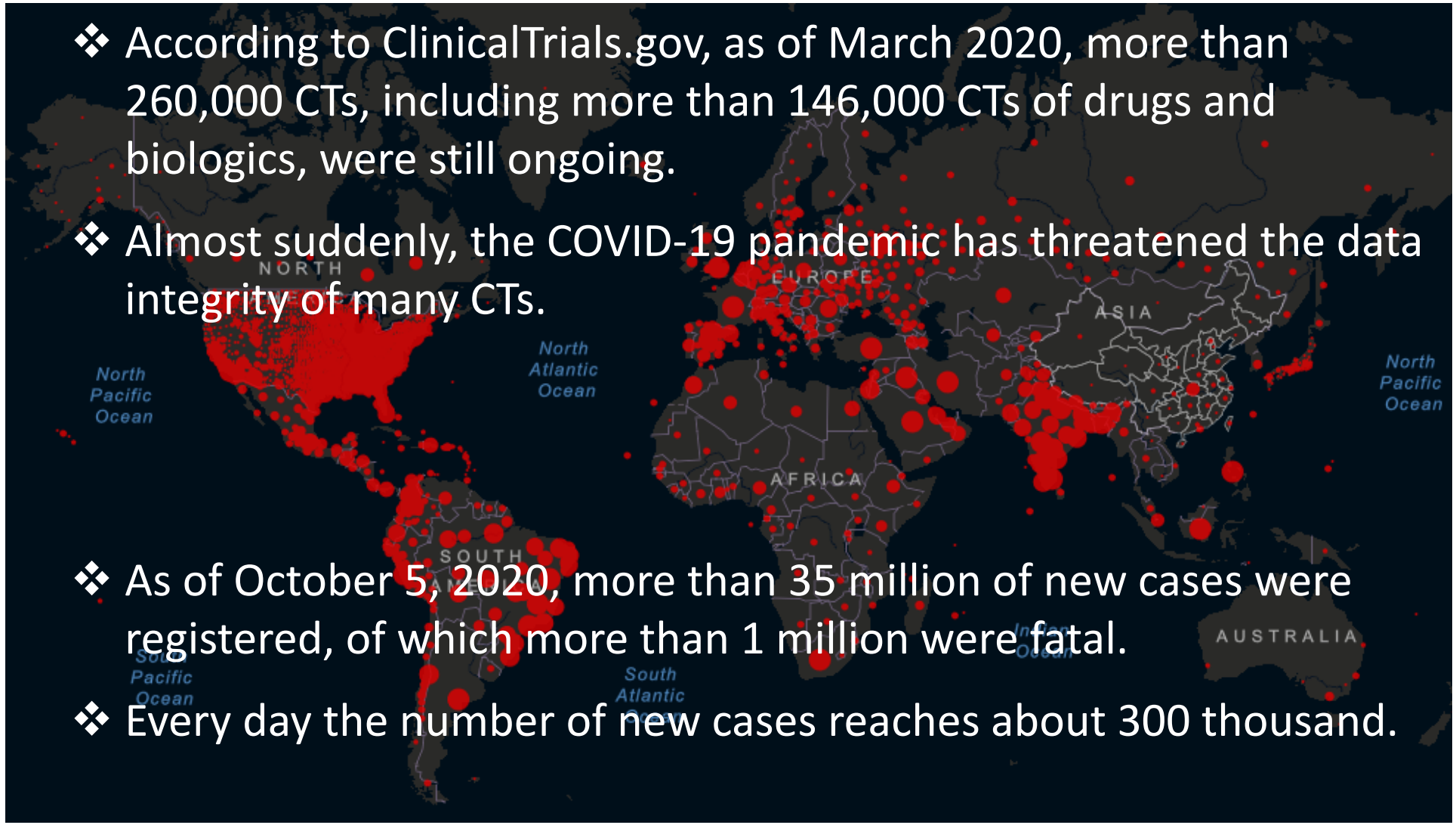
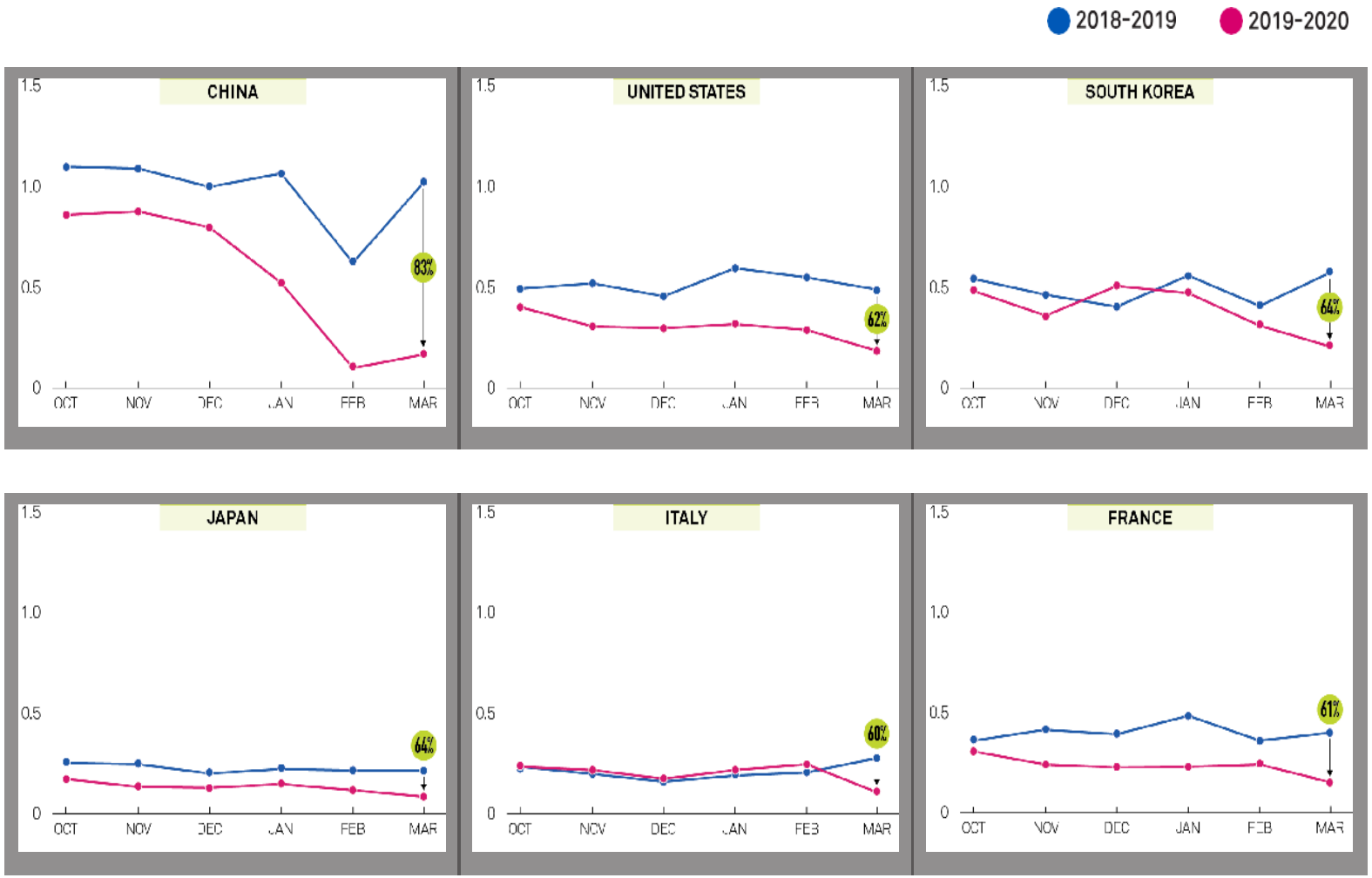
Global impact of COVID-19 on CTs



- According to ClinicalTrials.gov, as of March 2020, more than 260,000 CTs, including more than 146,000 CTs of drugs and biologics, were still ongoing.
- Almost suddenly, the COVID-19 pandemic has threatened the data integrity of many CTs.
- As of October 5, 2020, more than 35 million of new cases were registered, of which more than 1 million were fatal.
- Every day the number of new cases reaches about 300 thousand.

Abbreviations: COVID-19 = coronavirus disease 2019; CTs = clinical trials.

Global impact of COVID-19 on CTs



- In China, as of 02.2020, the number of new patients enrolled in the study decreased by 83%
- In the US in the first half of March 2020, a decline is 62%
- Similar trends in other countries

Message: COVID-19 severely impacted CTs reducing enrollments of study participants.

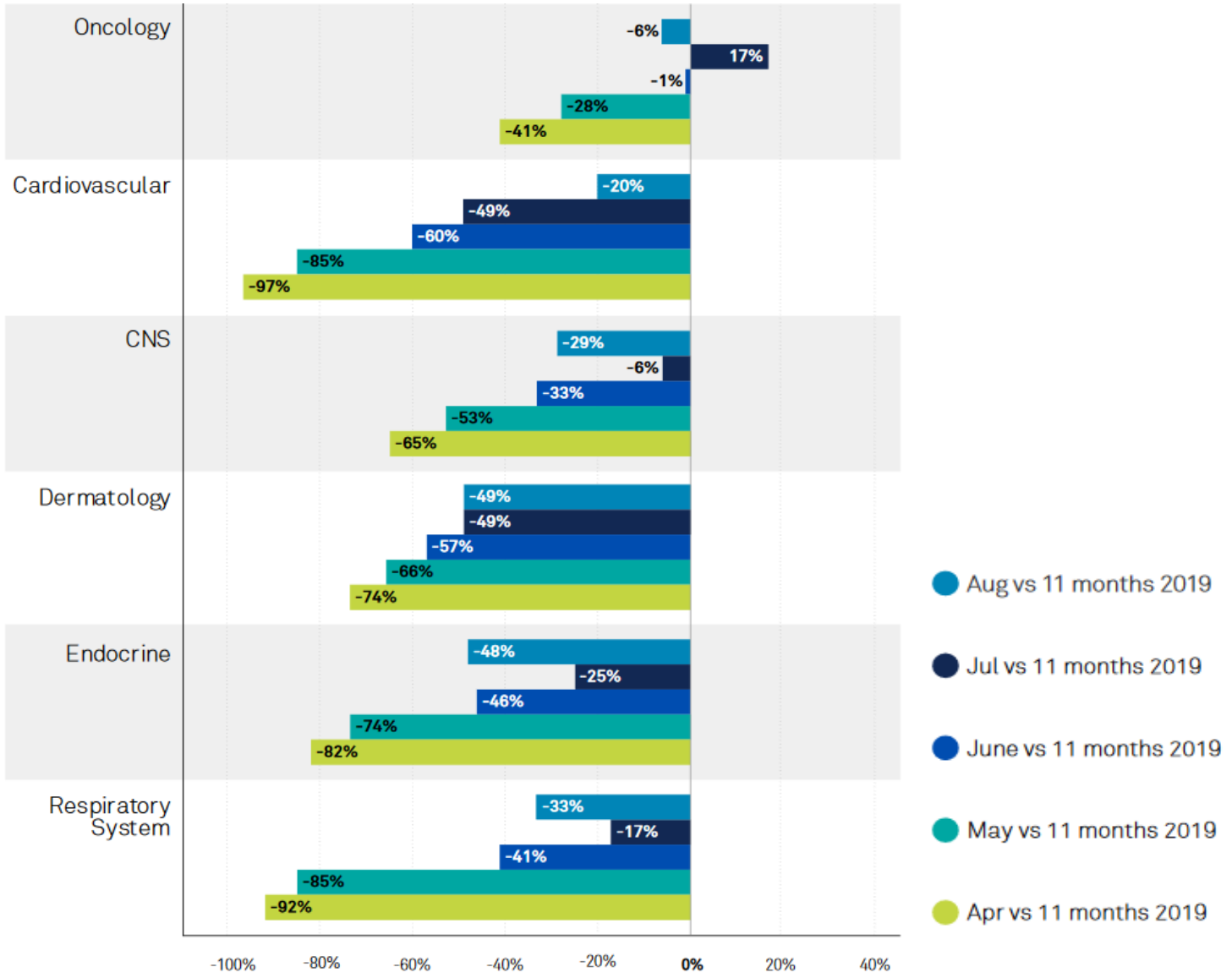
Abbreviations: CTs = clinical trials, COVID-19 = coronavirus disease 19.

Source: https://www.medidata.com/wp-content/uploads/2020/03/COVID19-Clinical-Trials_20200324-1.pdf

Global impact of COVID-19 on CTs

Change in new patients entering study-sites by therapeutic area

- Cancer CTs have been least affected by the pandemics compared to CTs in other TA
- As of 08.2020, the number of patients entered non-oncological CTs is 31% less than for the pre-pandemic level in 2019.



Message: CTs by TA are gradually restoring with non-oncology CTs have not reached the pre-pandemic levels of enrollment (-31%).

Abbreviations: CTs = clinical trials, TA = therapeutic area.

Source: COVID-19 and Clinical Trials: The Medidata Perspective, Release 9.0, SEP21, 2020

Lessons learned from the pandemic and what can be implemented for CTs

1. Pragmatic or “straightforward" research

Studies can be planned with longer and flexible time frames and simplified data collection requirements.

2. Use of technologies to reduce the number of in-person visits:

- remote obtaining of informed consent (incl. **e-consent**)
- virtual patient visits ("**telemedicine**")
- **electronic signatures** as a standard
- home delivery of drugs (incl. IMP)

Stephen M. Hahn,

FDA commissioner

3. Decentralized CTs

Pros: close to real-world evidence, improving the generalizability or external validity of data obtained during CTs without violating internal validity. **Cons**: logistical load, additional training activities, possible difficulties in the registration of AE, may not be applicable to parenteral IMP.

4. Real world evidence

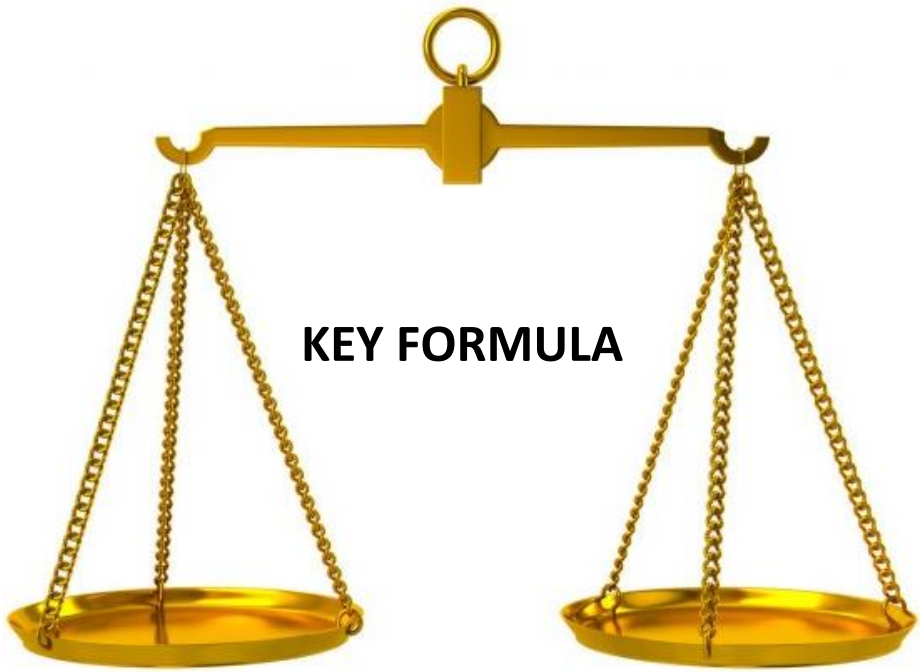
Example 1. Patient with melanoma entering CT requires only one thing – to fight the disease. This normally may correspond to the primary endpoint of the study, but other study assessments (PK, exploratory markers etc) may burden the patient (and study team) and make study protocol onerous.

Example 2 Patient with severe chronic pain should take study medicine and visit his investigator in strictly predetermined time intervals. It makes study protocol far from real world evidence with more flexible and symptom-driven management approaches.

Recommendations of Regulators

on CTs conduct during the COVID-19 pandemic

DATA INTEGRITY IN CLINICAL TRIALS



SAFETY, WELL-BEING AND RIGHTS OF SUBJECTS

Abbreviations: CTs = clinical trials.

Recommendations of Regulators

on CTs conduct during the COVID-19 pandemic

ДАРНИЦЯ

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Державний Експертний Центр МОЗ України

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HMA
Heads of Medicines Agencies

GUIDANCE ON THE MANAGEMENT OF CLINICAL TRIALS DURING THE COVID-19 (CORONAVIRUS) PANDEMIC

Version 3

28/04/2020

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 May 2020
EMA/INS/GCP/162006/2020

Guidance on remote GCP inspections during the COVID-19 pandemic

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 26 June 2020
2 EMA/158330/2020 Rev. 1
3 Committee for Human Medicinal Products (CHMP)

4 Points to consider on implications of Coronavirus disease
5 (COVID-19) on methodological aspects of ongoing clinical
6 trials

Державний Експертний Центр МОЗ України

Пошук

До уваги заявників та дослідників!

28.09.2020 4518 Подобається 19 Поширити

Оновлені рекомендації щодо проведення клінічних випробувань лікарських засобів в умовах подовженого карантину в Україні

Рекомендації розроблені на підставі чинних нормативних вимог в Україні щодо проведення клінічних випробувань лікарських засобів (далі – КВ) в умовах карантину для запобігання поширенню гострої респіраторної хвороби COVID-19 та з урахуванням рекомендацій Європейської Агенції з лікарських засобів (ЕМА, Версія 3 від 28.04.2020).

1. **Вступ**

Дії спонсора, дослідників та інших осіб, залучених до проведення КВ повинні бути відповідними до прийнятих владою вимог на національному та місцевому рівнях та ґрунтуватися на критеріях оцінки користь/ризик для досліджуваних, дослідників та якості даних, отриманих при проведенні КВ.

З огляду на потреби дотримання соціальної дистанції, якщо досліджуваний не може прибути до місця проведення випробування (далі – МПВ), можуть бути здійснені інші заходи, такі як патронаж на дому, якщо це можливо, чи комунікація по телефону або за допомогою відеозв'язку (телемедицини), що можуть знадобитися для виявлення небажаних явищ та забезпечення постійної медичної

Contains Nonbinding Recommendations

FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on September 21, 2020

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions on clinical trial conduct during the COVID-19 pandemic, please email Clinicaltrialconduct-COVID19@fda.hhs.gov.

Contains Nonbinding Recommendations

Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency

Guidance for Industry

June 2020

Recommendations of Regulators

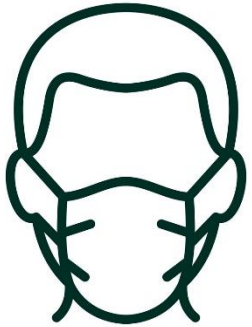
on CTs conduct during the COVID-19 pandemic

Key recommendations concern:

1. Risk-based CTs assessment
2. Changes to informed consent (incl. remote)
3. Remote subject visits and assessments (“telemedicine”)
4. IMP distribution and delivery to subjects
5. Remote monitoring (centralized and off-site monitoring, remote SDV)
6. Maintaining GCP-principles
7. CT design flexibility but risk of biases must be considered

Abbreviations: CTs = clinical trials; GCP = good clinical practice; IMP = investigational medicinal product; SDV = source data verification.

The COVID-19 pandemics affected all aspects of CTs



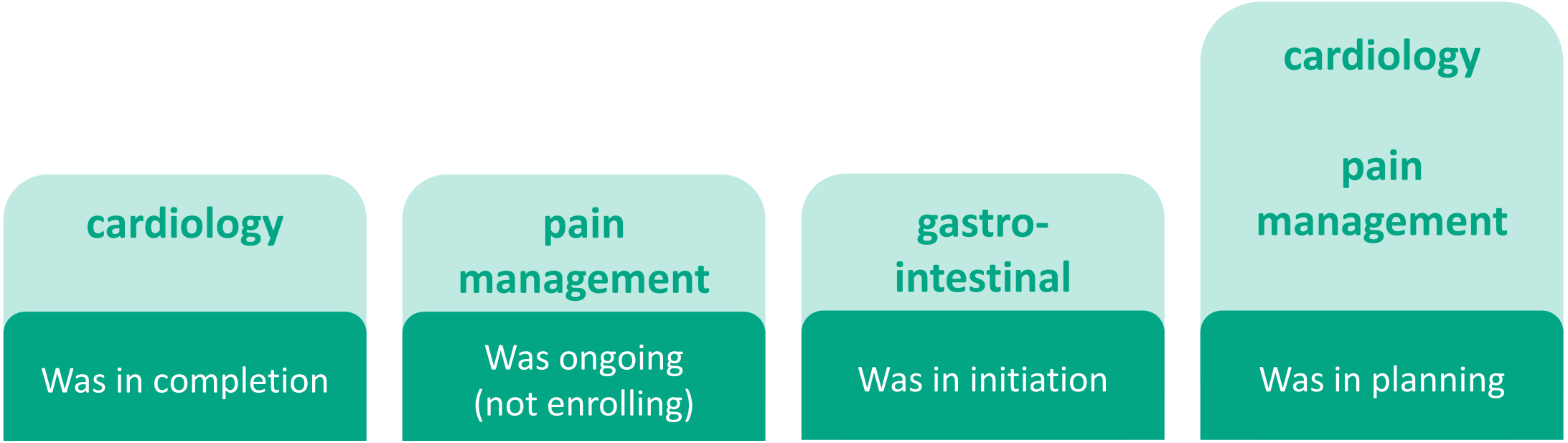
- Brought the need for strict anti-epidemic measures
- Disrupted transport communications
- Influenced the psycho-emotional state of researchers and subjects

1. Planning and preparation
2. Logistics (including IMP distribution to subjects)
3. Ability to recruit patients in CTs
4. Ensuring the safety of subjects and investigators
5. Conducting visits and evaluations
6. Quality assurance and monitoring
7. Data management and analysis

Abbreviations: CTs = clinical trials; IMP = investigational medicinal product.

Darnitsa's experience of CTs during the pandemics

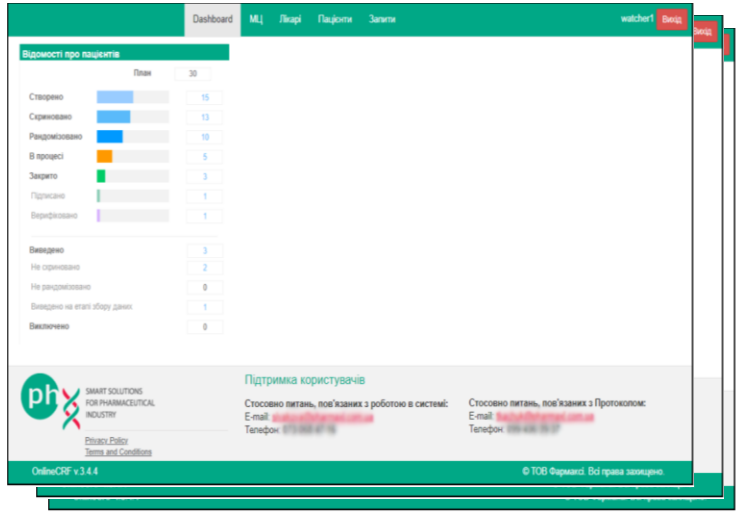
Darnitsa's CT dashboard during the rise of COVID-19 era



Darnitsa's CT team is able to meet pandemics-related novelties in trial conduct and follow applicable recommendations.

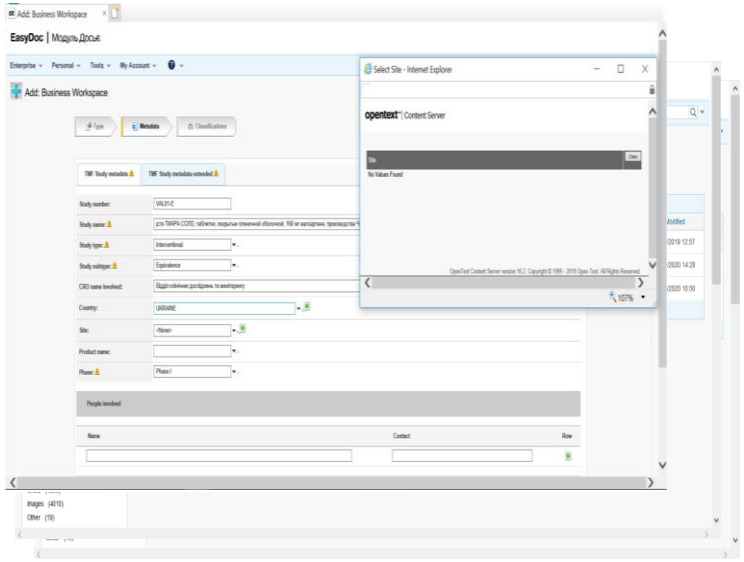
Abbreviations: CT = clinical trial.

Use of technologies to reduce the number of in-person visits



What is possible in Ukrainian realities:

- ❖ eCRF (electronic data capture)
- ❖ eTMF (electronic trial documentation)
- ❖ ePRO (‘electronic subject diary’)



What is insufficient or lacking:

- E-signature in medical environment
- E-education, especially in elder population
- E-ICF (consent)
- E-submission of CTA
- Public Health digitalization

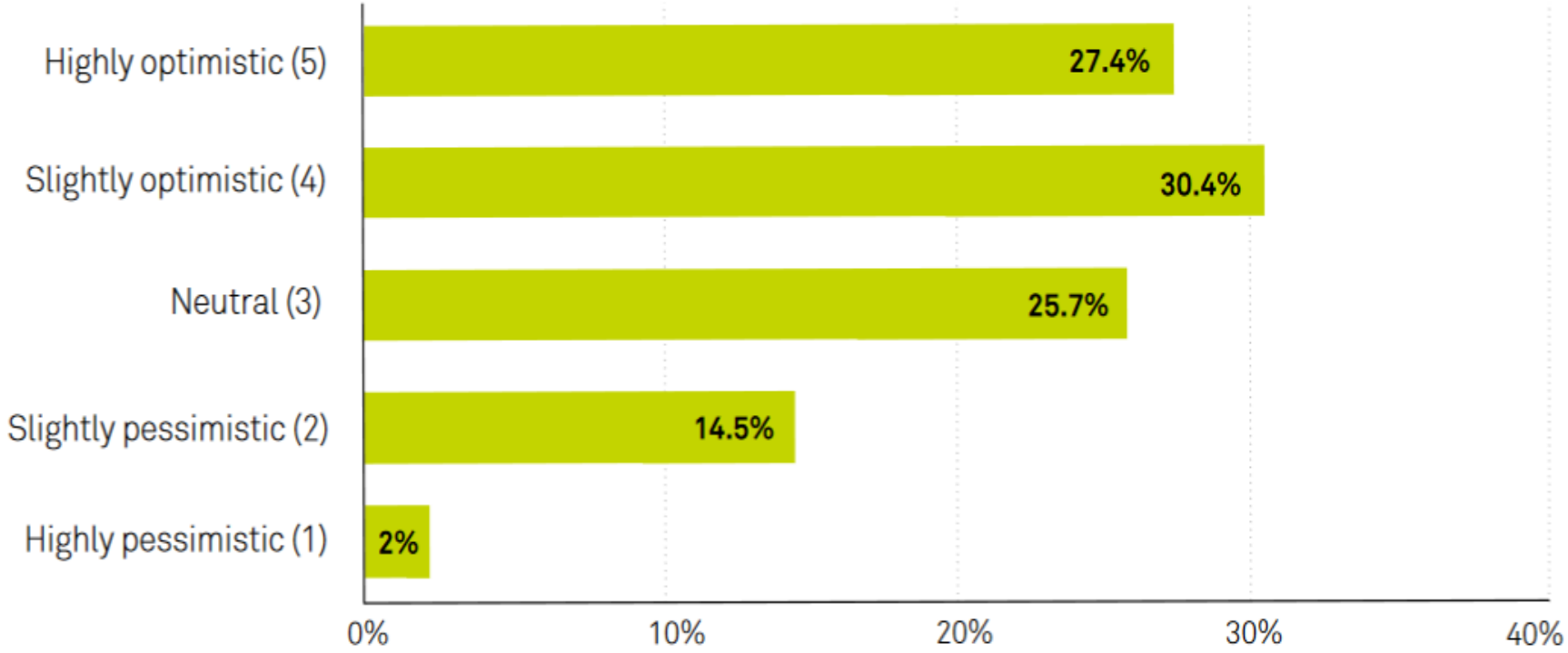
Darnitsa

- **eTMF which opens the possibility of e-submissions of CTAs**
- **eCRF services which is helpful for centralized and off-site monitoring**

Abbreviations: CTA = clinical trial application; eCRF = electronic case report form; eICF = electronic informed consent form; ePRO = electronic patient reported outcome; eTMF = electronic trial master file.

What is your opinion about the future of CTs (for the next 6 months)?

According to a site survey conducted by Medidata on 08.2020, n=734



The weighted average of the responses was 3.67, almost 60% of sites were optimistic, while only 16.5% were pessimistic.

Message: CTs' future is optimistic in general.

Abbreviations: CTs = clinical trials.

Source: COVID-19 and Clinical Trials: The Medidata Perspective, Release 9.0, SEP21, 2020

Thank you for attention!

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