Coronavirus (COVID-19): impact on the conduct of clinical trials under the Medical Research Involving Human Subjects Act (WMO)

Note: If needed, the information given below may be adjusted. Please check our website and the information given by other parties (see hyperlinks below) regularly for updates. The information below is valid during the COVID-19 pandemic until the situation is normalised and this is stated on the website of the Health and Youth Care Inspectorate (IGJ).

Version 2 (28 April 2020)

Changes compared to version 2 (8 April 2020): Phase I trials, remote source data verification

The COVID-19 pandemic affects health care services and the society in general. The conduct of clinical trials and also trial participants in clinical trials might be affected as well. The situation evolves and pragmatic measures might be required to manage the situation regarding the conduct of clinical trials and to ensure the rights, safety and wellbeing of trial participants. These measures should be proportional and based on a risk analysis (benefit-risk assessment). The impact on the rights, the safety and wellbeing of trial participants should prevail.

On the websites of the Government and the National Institute for Public Health and the Environment (RIVM) general information can be found regarding measure taken due to the COVID-19 pandemic. In order to mitigate the negative impact on the conduct of clinical trials during the period of the COVID-19 pandemic, a European Guidance has been developed. Additionally, the Central Committee on Research Involving Human Subjects (CCMO) formulated several recommendations on her website.

In addition to the European Guidance, IGJ emphasises that Dutch legislation (such as the WMO and Medicines Act) might prevail on some issues over the European Guidance. Below you will find several relevant issues.

Phase I-units
Given the current COVID-19 circumstances, hospitals might not be able to comply with agreements with Phase I-units to use an emergency department or intensive care unit in case serious side effects of IMP occur.

The IGJ expects, except clinical trials related to COVID-19 or concerning a serious disease with no satisfactory treatment option:
- all first in human (FIH) trials to be (temporary) suspended, and recruitment for these trials halted;
- new Phase I trials are not initiated;
- ongoing Phase I trials with higher dosing then already known are halted. Only treatments that are of interest for the trial participant can be continued.

In case of urgent questions, you can contact the IGJ (gcp@igj.nl). The IGJ will adjudicate on a case-by-case basis whether deviation of the above might be justified.

Investigational medicinal products (IMP)
The Medicines Act cites specific requirements regarding distribution and handing over of IMP.
It might occur that IMP, as a result of the current COVID-19 measures, cannot be handed over per regular practice to the trial participant.

During the COVID-19 situation, the IGJ allows:
- IMP to be send by courier from the (hospital) pharmacy to the trial participant;

- IMP to be send from the hospital pharmacy to the public pharmacy. Please refer to additional information on the website of IGJ (in Dutch only);
- Verbal consent by trial participants to use personal information necessary for sending IMP. The obtained verbal consent should be documented and, if possible, be confirmed by the trial participant via e-mail; there is no requirement to obtain written consent retrospectively.

The IGJ emphasises that shipment of IMP by the sponsor to the trial participant is **not** allowed.

Signals have been noted that shortages of certain registered medicinal products might occur because those are prescribed in clinical trials for COVID-19 patients. This might affect regular treatment, ongoing clinical trials and clinical trials for COVID-19. More information regarding shortages of registered medicinal products can be found on the IGJ website (in Dutch only). Advice what to do in case this results in a (temporary) halt or premature suspension of a clinical trial can be found on the CCMO website (see the link above).

In case of urgent questions, you can contact the IGJ (gcp@igj.nl). The IGJ will adjudicate on a case-by-case basis whether deviation of regulation might be justified.

Informed Consent
Obtaining (re) consent of trial participants for clinical trials can be hampered by the physical condition of the trial participant and/or the COVID-19 measures.
In case a trial participant is unable to provide (re)consent in an emergency situation for a clinical trial, obtaining consent can be deferred under specific conditions. The applicable conditions are cited in the memorandum and flow chart "Deferred Consent" of the CCMO. To be able to use the possibility of deferred consent it is mandatory to obtain approval by an independent ethical committee (METC/IEC) in advance. On the website of the CCMO, information can be found regarding accelerated procedures (fast track) for review of research dossiers.

Note: the memorandum and flow chart are only available in Dutch.

Monitoring
The IGJ emphasis that European and national legislation cite on-site monitoring and central monitoring. Given the COVID-19 situation, on-site monitoring will not or hardly be possible.

Remote source data verification (SDV)
During the COVID-19 situation, the IGJ allows, like most other European countries, remote SDV provided that they follow strict requirements and for a selection of clinical trials only. The IGJ does **not** allow remote SDV in general. The clinical trial should be, in accordance with the European Guidance, COVID-19 related, concerning a serious disease with no satisfactory treatment option, or in a phase where the current situation might result in a delay of registration of the medicinal product.
Remote SDV is only allowed based on the outcome of the evaluation of a risk assessment per clinical trial, including the motivation of the critical data that needs to be verified. The health and safety of the trial participant prevails.

Direct remote access to the electronic health record (EHR) is temporary (during the COVID-19 situation) and allowed only when adhering to requirements to verify critical data relevant for clinical trials by monitors/CRA's. It is recommended that this takes place at the office in accordance with the following requirements and/or restrictions:

- Using a specific, access controlled space (1 person, logged etc.);
- Using a logged PC/laptop (Who, What, When);
- Upfront a screenshot/short video impression (**not** while having access to the EMD!) regarding the setting/arrangement (office and/or home situation);
- In no way recordings (video, screenshot, screen-capture) will be made; moreover the functionality to do so should be disabled;

- Adequate documentation; the agreed method and requirements are put down in writing and confirmed.

The IGJ strongly recommends, if feasible (technical, safe, burden for the research team etc.), to conduct remote SDV where the hospital/research centre is in charge. This means that the monitor/CRA is able to review the EMD and other relevant source documents by means of reading along/on the screen of the person at the hospital/research centre. The platform to be used should be safe and workable for both parties involved (see also the recommendations of the Data Protection Authority (DPA) on privacy and video calls attached to this document below).
If the method mentioned above is not feasible due to the burden for a hospital/research centre, direct remote access to the EMD by the monitor/CRA can be an alternative method. Access to the EMD should be assigned on name and function (already assigned accounts should not be used).

In addition, in general:

- The monitor/CRA should be able to access EMDs of trial participants only and, only those parts that are strictly necessary to verify the critical data. Which data is to be considered critical and which (data) as a consequence needs to be accessed, should be reasoned and documented in a complete/correct manner. Access to more than the critical data should be requested with due motive. Unauthorised access to more than the documented critical data is considered a data protection breach and should be reported to the DPA as such.
- Per clinical trial it should be documented which monitor/CRA has been granted access to the EMDs and which ones. The number of monitors/CRA's should be limited to a bare minimum.
- The trial participants should be informed, by means of an updated PIF, regarding the remote access to the EMD in order to, if required, refuse consent thereof or withdraw consent at all. See also Informed Consent above.

- The IGJ does **not** allow data verification conducted by means of copies from the medical dossier. These copies could be insufficiently anonymised and moreover, it could contain information that is not strictly necessary to evaluate the data described in the protocol. Furthermore, issuing of such copies, and where necessary de-identifying those, are considered a disproportional extra burden for hospitals/research centres. In addition, the trial participant consents to review his medical dossier, not to copy parts thereof and send those via and to third parties. This method is potentially violating the rights of the trial participant.
- The IGJ does **not** allow reading aloud (by site staff) source data via telephone contact. This is considered an inadequate method with a potential for a high margin of error, no factual verification of source data and moreover a significant extra burden for investigators and their team.

In case of urgent questions, especially concerning this document, you can contact the IGJ (gcp@igj.nl). The IGJ will adjudicate, on a case-by-case basis, whether deviation of the current opinion (following strict conditions) might be justified.

Decision Aid Privacy Video Call Apps

Version 15 April 2020

	Discord	FaceTime	Hangouts Google	Hangouts Meets Google	Houseparty	Jitsi	Messenger Facebook	Signal	Skype	Talk Nextcloud	Teams Microsoft	Whatsapp	Zoom*
What does the app offer?													
(group)chat (text)	■	■	■	■		■	■	■	■	■	■	■	■
1-on-1 conversation (audio and/or video)	■	■	■	■	1	■	■	■	■	■	■	■	■
group conversation (audio and/or video)	■	■	■	■	■	■	■		■	■	■	■	■
self-start and management (self-hosted)						■				■			
participation to conversation without creating an account			■	■		■			2	2	2		2
use in browser	■		■	■	3	■	■		4	■	■	5	■
use on different platforms (cross-platform)	■		■	■	6	■	■	■	■	■	■	■	■
Which data is collected by the app?													
address book		■	■	■	■		■		■		7	■	
location data		■	■	■	■		■		■		■	■	■
conversation data	■		■	■	■		■		■		■		■
data on conversations (metadata)	■	■	■	■	■		■		■		■	■	■
linking data to data of other products or profiles			■	■			■		■		■	8	
For which goals is data processed by the app?													
use of the app	■	■	■	■	■	■	■	■	■	■	■	■	■
improvement of the app	■	■	■	■	■		■		■		■	■	■
show (personalised) adds					■		■						9
How does the data flow go?													
processing agreement possible				■		10				10	■	11	12
providing data to third parties (if so, which data and to whom)	13	14	15	15	16		17		18		19	20	21
location processing controller	VS	VS	IRL	IRL	VS	10	IRL	VS	IRL	10	IRL	IRL	VS
data stay in the Netherlands						■		■		■			
Data stay in the EU				■		■		■		■	■		
Is de communication secure?													
end-to-end encryption (even the provider of the app cannot access the content of the communication)**		■				■	22	■	23	■		■	
encryption of data during traffic to avoid access by third parties (note: the app provider might, but this does not necessarily imply this occurs)	■	■	■	■		24	■	■	■	■	■	■	■
minimised use of metadata		■				■		■		■			
encryption is switched on by default	■	■	■	■		■		■	■	■	■	■	■
source code can be checked (open source)						■		■		■			
Financial aspects of the app?													
charged/paid subscription or charged/paid version	25	26		■					27	28	■		29
(personalised) adds			■		■		■		■			■	30
donations								■					
other						31						32	
Where to find information?													
privacy statement (click on the icon to enter/access the web))	🖳	🖳	🖳	🖳	🖳	🖳	🖳	🖳	🖳	33	🖳	🖳	🖳
privacy statement in Dutch	■	■	■	■			■		■	33	■	■	

1 Video only
2 Upon invitation
3 Google Chrome
4 Skype for Web in Microsoft Edge or Google Chrome But not for video or audio
5 Android, iOS, Google Chrome
6 Mobil/exchange
7 With other products of Facebook
8 Please note: does apply when calling via website
9 Please note: only when calling via website
10 n.a. (self-hosted)
11 Standard contract
12 For some sectors
13 Metadata and IP-data for business purposes, but no sale of data
14 To subsidiary companies and intermediaries of Apple
15 Within Google
16 To government agencies/authorities upon their request and to related companies
17 Within Facebook and to external partners
18 To governmental agencies/ authorities when they ask
19 Within Microsoft
20 To Facebook and to third parties, but not (yet) for advertisement purposes within Facebook
21 To supporting partners, but no data sale
22 Not for (video) conversation; for chat it needs to be started separately using Secret Mode
23 Only in private call (see: website)
24 In group conversations
25 Discord Nitro
26 This is a standard/preinstalled app on new Apple-products
27 Skype for businesses
28 The enterprise-edition is charged for
29 There are several subscriptions, but also a free version
30 Please note: applicable when calling through the website
31 Project is fully supported by the company 8x8
32 It is part of Facebook
33 This depends on who offers a Nextcloud-service

* Be careful when using Zoom. This app is still under development.
** Note: in group conversations there is either no end-to-end encryption or only inn case of a limited number of participants.

Note: The de DPA has not been able to conduct extensive, technical research into the apps. The DPA relies on information provided by the companies themselves about how their video call apps process your data, e.g. in their privacy statement