

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 5 (13 August 2020)

- Changes compared to version 4 (22 June 2020): integration requirements (re)start clinical trials into one document, document on the website of CCMO is redundant
- Changes compared to version 3 (20 May 2020): (re)start clinical trials, monitoring
- Changes compared to version 2 (28 April 2020): Phase I trials
- Changes compared to version 1 (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.

(Re) start of clinical trials

At regular intervals the current COVID-19 situation is evaluated by the Dutch Government and , under conditions, relaxing measures are announced. These relaxing measures are only possible as long as the spread of the virus decreases, following less hospitalisations and/or (COVID related) deaths. In case of an eventual increase of the spread of the virus an earlier relaxing measure for more room might be revoked.

Based on the latest relaxing measures and the restart of regular care in health care institutions, for clinical research units (CRU) and health care institutions it becomes possible to gradually restart trials that were put on hold or start new trials provided [requirements](#) are complied with as they are formulated by the CCMO and the IGJ (with input of relevant stakeholders)

NOTE: These national requirements 'border' the extra possibilities/loosening of restriction as still applicable on the European level.

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.

As indicated before, the regular care in health care institutions in The Netherlands is (slowly) restarting. Based on the latest national relaxation announced (by the Dutch Government) of measures and the restart of regular care, the IGJ and the CCMO (with input of relevant stakeholders), formulated requirements to (re)start clinical trials, not being clinical trials in CRUs (see also paragraph **(Re)start of clinical trials**).

With respect to (partly) 'stepwise' restart of monitoring, it should be clear that this can only be implemented after careful consideration by, agreement from and under control of the health care institution. Moreover, the official policies of the institution and the measures of the Government applicable at that time regarding the control of the COVID-19 situation should be complied with. In accordance with the European Guideline and the documents published previously by the CCMO and the IGJ, a (re) assessment needs to be made of which data are considered critical in this phase of the COVID-19 situation. In addition, it should be evaluated to what extend on-site monitoring can (and needs to) be conducted. This should be a proportional process and all considerations should be risk-based (benefit-risk) and adequately documented. The impact on the rights, the safety and the wellbeing of trial participants, but also the safety of other patients and staff should prevail.

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 \(DPA\) o privacy and video calls](#) (in Dutch only)).

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 pseudonymised ('redacted') and in addition, 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 calls

version 2, May 2020

	Discord	FaceTime	Hangouts Google	Hangouts Meets Google	Houseparty	Jitsi*	Messenger Facebook	Signal	Skype	Talk Nextcloud	Teams Microsoft	Whatsapp	WebEx	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)						■							2	3
participation to conversation without creating an account			■	■		■			4	4	4		■	4
use in browser	■		■	■	5	■	■		6	■	■	7	8	■
use on different platforms (cross-platform)	■		■	■	9	■	■	■	■	■	■	■	■	■
Which data is collected by the app?														
address book		■	■	■	■		■		■		10	■		
location data		■	■	■	■		■		■		■	■		■
conversation data	■		■	■	■		■		■		■	■	■	■
data on conversations (metadata)	■	■	■	■	■		■		■		■	■	■	■
linking data to data of other products or profiles			■	■			■		■		■	■	■	
For which goals is data processed by the app?														
use of the app	■	■	■	■	■	■	■	■	■	■	■	■	■	■
improvement of the app	■	■	■	■	■		■		■		■	■	■	■
show (personalised) adds					■		■						■	
How does the data flow go?														
processing agreement possible				■		12				12	■	13	■	14
providing data to third parties (if so, which data and to whom)	15	16	17	17	18		19		20		21	22	23	24
location processing controller	VS	VS	IRL	IRL	VS	12	IRL	VS	IRL	12	IRL	IRL	VS	VS
data stay in the Netherlands						25		■		■				
data stay in the EU				■		25		■		■	■		■	26
Is communication secure?														
end-to-end encryption (even the provider of the app cannot access the content of the communication)***		■				■	27	■	28	■		■	29	
encryption of data during traffic to avoid access by third parties (note: the app provider might, but this does not necessarily imply this occurs)	■	■	■	■		30	■	■	■	■	■	■	■	■
minimised use of metadata		■				■		■		■				
encryption is switched on by default	■	■	■	■		■		■	■	■	■	■	■	■
source code can be checked (open source)						■		■		■				
Financial aspects of the app														
charged subscription or charged version	31	32		■					33	34	■		■	35
(personalised) adds			■		■		■		■			■		
donations								■						
other						36						37		
Where to find information?														
privacy statement (click on the icon to enter/access the web page)	□	□	□	□	□	□	□	□	□	38	□	□	□	□
privacy statement in Dutch	■	■	■	■	■		■		■	38	■	■	■	

1 Video only
 2 Via [WebEx Meeting Server](#)
 3 With a Business-, Education- or Enterprise-account. Note: meta data of users and meetings are controlled via the public cloud of Zoom, [see](#)
 4 Upon invitation
 5 Google Chrome
 6 Skype for Web in Microsoft Edge or Google Chrome
 7 But not for video or audio
 8 With the WebEx-app. The app is available for all common browsers
 9 Android, iOS, Google Chrome
 10 Mobile/exchange
 11 With other products of Facebook
 12 n.a. (self-hosted)
 13 Standard contract

14 For some sectors
 15 Meta data and IP-data for business purposes, but no sale of data
 16 To subsidiary companies and intermediaries of Apple
 17 Within Google
 18 To government agencies/authorities upon their request and to related companies
 19 Within Facebook and to external partners
 20 To governmental agencies/ authorities upon their request
 21 Within Microsoft
 22 To Facebook and to third parties, but not (yet) for advertisement purposes within Facebook
 23 Within Cisco and daughter companies, business partners or suppliers
 24 To supporting partners, but no sale of data
 25 Provided self-hosted
 26 For Pro-, Business-, Enterprise- or Education-accounts it is possible to select an area, [see](#)

27 Not for (video)calls/conversation; for chat sessions this feature has to be started using Secret Mode
 28 Only in private calls ([see: website](#))
 29 Note: some functionalities will be lost, [see](#)
 30 In group conversations
 31 Discord Nitro
 32 This is a standard/preinstalled app on new Apple-products
 33 Skype for businesses
 34 The enterprise-edition is charged for
 35 There are several subscriptions, but also a free version
 36 Project is fully supported by the company 8x8
 37 It is part of Facebook
 38 This depends on who offers a Nextcloud-service

* You can use Jitsi non-committal on meet.jit.si, but the software can also be used for self-hosting and management. Note: when a meeting is started on a public Jitsi-server, like meet.jit.si, then choose an automatic generated name and create a password. Otherwise choose a not easy to guess name for your meeting and a password.

** Note: if you use Zoom. Security and privacy aspects of Zoom are still in development [see](#)

*** Note: in group conversations there is either no end-to-end encryption, or only with a limited number of participants.