Declaration of the End of Trial Form (cf. Section 4.2.1 of the *Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial*[1])

NOTIFICATION OF THE END OF A CLINICAL TRIAL OF A MEDICINE FOR HUMAN USE TO THE COMPETENT AUTHORITY AND THE ETHICS COMMITTEE

For official use

Date of receipt :	Competent authority registration number : Ethics committee registration number:

To be filled in by the applicant

A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE :

B TRIAL IDENTIFICATION

B.1 EudraCT number :	**(2020-001417-21)**
B.2 Sponsor's protocol code number:	**(ITM202004)**
B.3 Full title of the trial : An open label single center randomized controlled trial to evaluate the effect of hydroxychloroquine on viral shedding in mild COVID-19	

C APPLICANT IDENTIFICATION (please tick the appropriate box)

C.1	**DECLARATION FOR THE COMPETENT AUTHORITY**	☒
C.1.1	Sponsor	☒
C.1.2	Legal representative of the sponsor	☐
C.1.3	Person or organisation authorised by the sponsor to make the application.	☐
C.1.4	**Complete below:**	
C.1.4.1	Organisation : Institute of Tropical Medicine	
C.1.4.2	Name of person to contact : Dr. Emmanuel Bottieau	
C.1.4.3	Address : Nationalestraat 155, 2000 Antwerpen - België	
C.1.4.4	Telephone number : +32(0)32476450	
C.1.4.5	Fax number : /	
C.1.4.6	E-mail: EBottieau@itg.be	

C.2	**DECLARATION FOR THE ETHICS COMMITTEE**	☒
C.2.1	Sponsor	☐
C.2.2	Legal representative of the sponsor	☐
C.2.3	Person or organisation authorised by the sponsor to make the application.	☐
C.2.4	Investigator in charge of the application if applicable[2]:	
•	Co-ordinating investigator (for multicentre trial):	☐
•	Principal investigator (for single centre trial):	☒
C.2.5	**Complete below** :	
C.2.5.1	Organisation: Institute of Tropical Medicine	
C.2.5.2	Name : Dr. Emmanuel Bottieau	
C.2.5.3	Address : Nationalestraat 155, 2000 Antwerpen - België	
C.2.5.4	Telephone number : +32(0)32476450	
C.2.5.5	Fax number : /	
C.2.5.6	E-mail : EBottieau@itg.be	

D END OF TRIAL

D.1	**Date of the end of the complete trial in all countries concerned by the trial?**	
D.1.1	(YYYY/MM/DD): 2020/06/26	

D.2	**Is it an early termination?[3]**	yes ☒ no ☐

1 OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

2 According to national legislation.

3 Cf. Section 4.2. of the detailed guidance CT-1.

D.2.1 If yes, give date (2020/06/26):
D.2.2 Briefly describe in an annex (free text):
D.2.2.1 The justification for early termination of the trial;
One large multicenter randomized controlled trial found no clinical benefit of hydroxychloroquine (high dosage 9,600 mg in total over 10 days) in a late stage of COVID-19 (RECOVERY trial, UK, https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf, no full publication available). Also, the WHO stopped recruitment in its SOLIDARITY trial (with similar set up/dosage as the RECOVERY trial) because no clear benefit was apparent from its data (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments; no full publication available).

One randomized trial found no clinical benefit of hydroxychloroquine as post-exposure prophylaxis for illness compatible with COVID-19 (Boulware et al, NEJM, 2020 in USA and Canada); another trial in Barcelona reached the same conclusion, as mentioned in https://www.sciencemag.org/news/2020/06/three-big-studies-dim-hopes-hydroxychloroquine-can-treat-or-prevent-covid-19, no publication available).

To date, no randomized or non-randomized trial has provided evidence regarding early, outpatient use of hydroxychloroquine and its impact on viral shedding and infectiousness, which is the very endpoint studied in the COVIDAM trial. For that reason, the COVIDAM trial continued to enroll patients, until we became aware of an important study by a team from KU Leuven that was published as a pre-print last week (Delang, L. Antiviral treatment of SARS-CoV-2-infected hamsters reveals a weak effect of favipiravir and a complete lack of effect for hydroxychloroquine. BioRxiv, 2020.). This well-performed animal study showed that hydroxychloroquine, despite its in vitro effectiveness on Vero cells, did not have any viral benefit in hamsters. In contrast to non-human primates, hamsters with COVID-19 have a clinical disease course similar to humans. Therefore, this study, in addition to previous (non-peer-reviewed) research in macaques (Maisonnasse et al., Hydroxychloroquine in the treatment and prophylaxis of SARS-CoV-2 infection in non-human primates. 2020) is quite convincing that the benefit on viral endpoints (the ones used in COVIDAM) will probably be marginal, if not absent, in humans. Of note, early administration of hydroxychloroquine might still have some clinical, anti-inflammatory, effect beyond an antiviral action, to prevent complications and hospitalization, but this research question requires a very large sample numbers of patients (several thousands), some of which are still ongoing.

Based on these new pre-clinical in vivo data which were not available when the trial was designed three months ago, we feel that the potential risk-benefit balance of the COVIDAM trial is not in equilibrium anymore and we feel obliged to end the study.

D.2.2.2 Number of patients still receiving treatment at time of early termination in the MS concerned by the declaration and their proposed management;
Only 2 patients were randomized in the trial. Both were randomized in the Placebo arm, so received no HCQ.
Both patients completed the study on 12/05/2020 and 27/05/2020, respectively.
D.2.2.3 The consequences of early termination for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product.
As none of the participants enrolled in the study received HCQ, it is therefore not possible on the basis of the COVIDAM study to make a judgement on the evaluation of the results and risk/benefit.

E SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

E.1	I hereby confirm that/confirm on behalf of the sponsor that (delete which is not applicable): • The above information given on this declaration is correct; and • That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.[4]

E.2	**APPLICANT TO THE COMPETENT AUTHORITY** (as stated in C.1)	☒
E.2.1	Date : 29/06/2020	
E.2.2	Signature :	
E.2.3	Print name: Dr. Emmanuel Bottieau	

E.3	**APPLICANT TO THE ETHICS COMMITTEE** (as stated in C.2) :	☒
E.3.1	Date : 29/06/2020	
E.3.2	Signature :	
E.3.3	Print name: Dr. Emmanuel Bottieau	

4 Section 4.3. of the detailed guidance CT-1.