

PER E-MAIL TO BI@CCMO.NL
Attn. Competent Authority
Parnassusplein 5
2511 VX Den Haag,
The Netherlands

Bucharest, Date: 10 May 2021

Subject: Digital submission of a substantial amendment for approval:
Temporary halt of the trial

EudraCT no.: 2018-004233-33
Novartis study no.: CMHS552A12101
ToetsingOnline NL71107.056.19
Dossier no.:
Study title: A first-in-human, randomized, subject-blinded, placebo-controlled, single ascending dose study to investigate the safety, tolerability and pharmacokinetics of MHS552 in healthy volunteers

Dear Madam, dear Sir,

On behalf of the Sponsor, **Novartis Pharma AG**, Parexel International Romania s.r.l. herewith submits a substantial amendment to the above-mentioned clinical trial for review and authorization.

The changes in this amendment relate to:

- Temporary halt of the trial starting 07-May-2021

Two subjects in this FIH study experienced hypersensitivity-like reactions assessed as CTCAE AEs grade 2 or higher that were considered drug-related and therefore study-stopping rules were met as agreed by both the Investigator and Sponsor. Enrollment is placed on hold. A full safety review will be conducted.

No patients are in active treatment, 60 have been treated: 40 having completed the study, 20 remain in follow-up.

Please find the following study documents supporting this request for approval attached to this e-mail:

CCMO numbering	Document	Version/Date
A1	Cover letter	10-May-2021
B5	EudraCT Annex 2 form for amendments	10-May-2021

With this submission we declare that all relevant documents in the present submission dossier are signed by the persons authorized for this task.

We trust that the information provided in the application is sufficient, however if you require any further information, please contact us.

Yours faithfully,

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Parexel International Romania SRL

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