Medicines & Healthcare products Regulatory Agency

MHRA

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10/03/2025

Dear Dr Pamela Sandu,

NOTICE OF NON-ACCEPTANCE OF AMENDMENT

Our Reference:	CTA 24712/0060/001-0003
Eudract Number:	2021-006886-39
Product:	Noradrenaline (Norepinephrine), Plasma-Lyte® 148, Compound Sodium Lactate Solution for Infusion BP
Protocol number:	GN20AE342
Substantial Amendment Code Number:	SA_09

THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 1031

I refer to your notice of amendment received on 04/02/2025 concerning a proposed amendment to the terms of your request for a Clinical Trial Authorisation or to the particulars or documents that accompanied it. The Licensing Authority has carefully considered the proposed amendment but has decided, in accordance with regulation 24(5) of the Regulations, not to accept it on the following grounds.

Grounds for Non-Acceptance:
MEDICAL - Remarks: *MEDICAL – Rejection points:

The present substantial amendment is rejected. Should you wish to respond to this notice, a new substantial amendment should be submitted via MHRA submissions that addresses the following:

1.-The last version of the protocol approved by the MHRA is version 2.0 dated 16/12/2022.

During this CTA the sponsor has not declared or provided to the MHRA details of all substantial amendments perform to the protocol from the last version approved by the MHRA (version 2.0 dated 16/12/2022) and the submitted version 4.0 dated 09/12/2024. This is not acceptable; therefore, the application is rejected.

The sponsor has only declared and provided a tracked-changes document detailing the changes between version 3.0 dated 14/02/2024 and version 4.0 dated 09/12/2024. The sponsor has not provided details of the changes performed to the protocol from the last version of the protocol approved by the MHRA (version 2.0 dated 16/12/2022) and version 2.1 dated 10/10/2023 and version 3.0 dated 14/02/2024 which according to the information in page 118 of the protocol were considered “substantial” changes.

The sponsor is required to provide details of all the substantial changes conducted to the protocol since the last version approved by the MHRA (version 2.0 dated 16/12/2022), including justification of the changes and tracked-changes

version of the protocol showing all the changes between each version of the protocol issued by the sponsor (version 2.0 vs version 2.1, version 2.1 vs version 3.0, and version 3.0 vs version 4.0).

2.-The sponsor must clarify if the substantial changes performed between version 2.0 dated 16/12/2022 and version 2.1 dated 10/10/2023 and version 3.0 dated 14/02/2024 have been implemented by the sponsor without MHRA approval.

If the Sponsor resubmits the application, the revised protocol (updated tracked changes versions as well as a clean signed versions) must be included with the application. The covering letter and application form should indicate that the application is a resubmission

*REMARKS

Clinical Remarks.

1.- The sponsor is reminded that substantial changes to the protocol can only be implemented after approval by the regulatory agency, and non-substantial amendments should be declared and contained in the documentation when it is subsequently submitted, for example in the subsequent notification of a substantial amendment. Please note that compliance with these requirements will be subject to specific scrutiny in any future GCP inspection.

If you believe it is possible to modify or adapt the proposed amendment to the protocol in order to address the concerns set out in the grounds for non-acceptance, you may respond, up to at least 14 days before the amendment is to be made, by giving written notice to the Authority and the relevant ethics committee in accordance with regulation 25(2). Any other modifications to the original notice of amendment that are required to address the grounds for non-acceptance will need to be submitted as a new valid notice of amendment.

Yours sincerely,

Clinical Trials Unit
MHRA