Medicines & Healthcare products Regulatory Agency

MHRA

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Prof C Butler
UNIVERSITY OF OXFORD
NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES,
RADCLIFFE OBSERVATORY QUARTER, WOODSTOCK ROAD
OXFORD
OX2 6GG
UNITED KINGDOM

10/03/2022

Dear Prof C Butler,

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

Our Reference:	CTA 21584/0452/001-0003
Eudract Number:	2021-005748-31
Product:	Molnupiravir, Paxlovid
Protocol number:	PANORAMIC
Substantial Amendment Code Number:	Substantial Amendment 2.0

NOTICE OF ACCEPTANCE OF AMENDMENT

I am writing to inform you that the Licensing Authority accepts the proposed amendment to your clinical trial authorisation (CTA), received on 03/03/2022.

COMBINED REVIEW MEDICAL - Remarks: The substantial amendment request to add the Paxlovid arm and a viral sub-study to the PANORAMIC trial is approved with the following conditions;

1. The SmPC provided with this application is Pfizer (UK) Limited, 31 Dec 2021. The SmPC that should be referenced in the protocol (as the RSI) and provided as a substantial amendment is the revised SmPC, dated 02/2022 (Ref: PX 3_0). The SmPC itself, and not a link to the GOV.uk website must be provided. The current protocol must be reviewed in line with the updated SmPC and subsequent protocol substantial modifications made as and where applicable.

2. The protocol must be modified to provide additional clarity on the risk mitigation and safety monitoring in place for concomitant medications that require adjustment with Paxlovid in the PANORAMIC trial (as described in List B in Appendix F of the current protocol). Details around enhanced safety follow up and questions asked about clinically significant drug interactions using the standard script (as provided as supporting information, by the applicant, in an email dated the 9th March 2022) must be provided.

3. Regarding List B ‘Details of Paxlovid drug interactions and implications for eligibility for drugs that are not recommended or require adjustment with Paxlovid in the PANORAMIC trial’ the protocol states; ‘The list will be

updated as new information becomes available (without protocol amendment)'. The protocol must be amended to state that a protocol substantial amendment will be submitted for regulatory approval when List B is modified as this has a direct impact on trial eligibility and trial participant safety.

The Sponsor is required to address the above points as a matter of urgency following receipt of this approval letter to align with regulatory and GCP requirements.

For further information email; lisa.campbell@mhra.gov.uk

This amendment may therefore be made.

If applicable, you should ensure your trial details have been updated on the database where you have registered your trial.

You are reminded that where it is appropriate, the Ethics Committee should also be notified of amendments.

You are reminded that from 1 January 2022 you will need to comply with the requirements specified in the following guidance, where applicable:

- ***Import of IMPs from listed countries to GB:***

https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries

- ***Supply of IMPs to Northern Ireland:***

https://www.gov.uk/guidance/supplying-investigational-medicinal-products-to-northern-ireland

- ***Substantial amendments to clinical trials:***

https://www.gov.uk/guidance/guidance-on-substantial-amendments-to-a-clinical-trial

Any required substantial amendment to your Clinical Trial Authorisation should be submitted and approved as soon as possible and before 1 January 2022.

Yours sincerely,

Clinical Trials Unit
MHRA