

RESPONSE TO CBER COMMUNICATIONs REGARDING SUBMISSION OF CLINICAL DATA SETS TO SUPPORT AN EUA SUBMISSION RECEIVED ON OCTOBER 28, 2020

The Sponsor acknowledges CBER's communication regarding the submission of clinical data sets to support an EUA submission (email subject ****IND 19745 - Submission of Clinical Data Sets to Support an EUA Submission****). Reference is also made to the email from CBER with the subject ****IND 19745.52 - RE: Data Sets**** which references the cover letter for Amendment 52.

This document provides the Sponsor's response to FDA's request (in **Bold**).

This communication is regarding the requirement of clinical data sets in support of an EUA submission. Please note that clinical data sets will be required in support of an EUA submission.

Sponsor Response:

The Sponsor acknowledges the request from CBER and wishes to clarify that it has relied on the Emergency Use Authorization of Medical Products and Related Authorities Guidance for Industry and Other Stakeholders (<https://www.fda.gov/media/97321/download>), which reads, in section III.D.3, *"FDA expects material to be provided in a reviewable form and sufficiently complete to permit substantive review. Nevertheless, FDA recognizes that, in rapidly developing or unexpected emergency circumstances, or when previously unanticipated or unavailable MCMs are being considered, it may not be possible for a sponsor to provide all of the requested data or to provide it in the format suggested in a timely manner. In such circumstances, FDA will accept and evaluate the request for an EUA based on data in the form the sponsor is able to submit."*

The Sponsor has put together a proposal for CBER's consideration. However, the Sponsor wants to clarify that the P301 analyses envisaged for EUA entail unique challenges:

- The proposed P301 EUA data package is based on results from Data Snapshots (DS) to support EUA
- A data snapshot is not a database lock. Data are therefore not fully cleaned, rather as clean as possible. It is therefore anticipated that validation errors may be triggered.
- The generation and publishing of these datasets in a format that would be suitable and usable by CBER will require additional time after the generation of the summary tables and listings that were planned initially to form the core of the EUA submission, as described in the EUA Pre-Submission Briefing Document, submitted on November 4th 2020 (IND19745 SN#0063)

The phase 3 P301 study will provide the vast majority of the safety data for this program (approximately 15,000 exposed subjects), whereas the phase 2 data will only add information on 400 exposed subjects. Although we will submit the complete set of summary tables and listings from the P201 study, in the interest of time our proposal is to submit datasets for P301 only.

Below is a brief description of the content of the proposed data package:

Case Report Tabulation (CRT) data package:

- Annotated CRFs (aCRFs)
- Clinical Study Data Reviewers' guide (cSDRG), including information on:
 - Protocol description including study data standards and dictionary inventor
 - Subject data description and SDTM subject domains
 - Data conformance summary
- CDISC SDTM domains in xpt format
- Define.xml

Analysis package:

- Analysis Data Reviewers' Guide (ADRG)
 - Includes basic and required information
- ADaM datasets as listed below:
 - ADSL, ADDV, ADRISK, ADIS, ADEX, ADSYMP, ADEFF, ADTTE, ADTTEA, ADMB, ADAE, ADCM, ADAR, ADARP7D, ADARSUM, ADCM, ADVS
 - Define.xml