

ABSTRACT - The Study Data Technical Conformance Guide (TCG) v5.5 section 4.1.3.4.3 states that, “...maternal and fetal EFD end points measured during the gestational phase of an ePPND study can be modeled under SEND DARTv1.1.” This poster will examine the issues with determining data scope, challenges with current variable definitions, and Controlled Terminology (CT) limitations for the Embryo Fetal Development (EFD) end points in Enhanced Pre and Post Natal Development (ePPND) studies. Results for this project will include considerations for implementers as well as outstanding questions for CDISC and regulators.

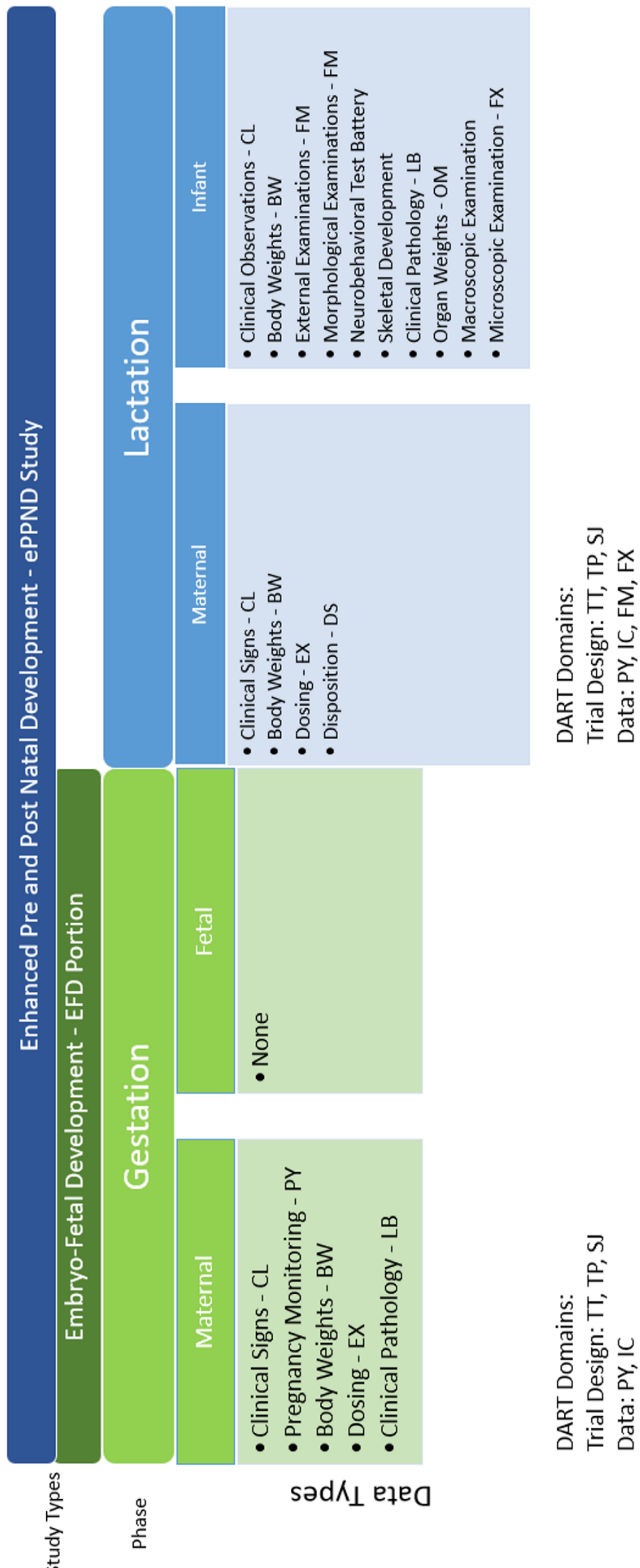


Fig 1 Typical ePPND Study Design

INTRODUCTION - ePPND studies evaluate embryo-fetal development in infants rather than in a fetus. These studies will typically have at least a gestation and lactation phase with most of the data being collected outside of gestation. [see Fig 1] Though the DARTIG v1.1 models EFD study designs only, the TCG states that gestational end points for ePPND studies can be included in a SEND dataset. The considerations discussed in this poster come from the analysis of several ePPND studies conducted at Labcorp Inc. The most significant issues that were observed from creating an solely EFD end point study were regarded closely and evaluated from two perspectives: an EFD-mindful approach seeking to adhere strictly to current TCG guidelines and a more improvisational approach to encompass the entirety of ePPND study data.

SCOPE/EXCLUSIONS - Generators of ePPND studies need to take careful consideration of each phase of data collected on the study. As the purpose of ePPND studies is to take the most impactful tests from EFD studies and instead study them in newborns, there is no data for the fetal animals and minimal data for the maternal animals during Gestation. Instead, most of the fetal data is present in the Lactation phase and the same is true for maternal animals. Suggested exclusions are to exclude the entire 'Lactation' phase from the study in order to keep strictly to EFD end points or to keep entire study data which would result in risks that are discussed further in this poster.

Note: The opinions expressed in this poster are those of the authors and do not necessarily represent the opinions of their respective organization. Author emails:
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TRIAL DESIGN MODELING - Modeling the trial design essentially narrows down to two different approaches (1) limiting the trial design to EFD end points or (2) comprehensive for entirety of the study design. The Trial Design consideration chart [see Fig 2] discusses a few different aspects of the trial design to note for each different approach.

CONTROLLED TERMINOLOGY - To capture data in the Lactation Phase, the dataset generator could choose to to create a user-defined NCDPHASE [see Fig 3]. This solution provides the most data to the reviewer but may pose a challenge to cross-study analysis once more DART study types come into scope for SEND.

The more conservative approach is to leave lactation undefined and therefore exclude all Lactation Phase data. This solution means that the majority of data will be excluded which may pose a different challenge to cross-study analysis with the introduction of more DART studies. It is up to the stakeholders to choose whether to bear the cost of compilation now with planned future data rework or generate currently out-of-scope data in the future with a more mature DART standard.

CONCLUSION - There are several limitations to both possible options to generate EFD end points for ePPND [see Fig 4]. If end points are strictly contained to EFD data, then the data would have no fetal data and very minimal maternal data. Taking into consideration the purpose of DART studies, no information would be present regarding a treatments' risk to developing fetal animals. However, there are a few significant setbacks in the current CT that would not allow for the data to come out in the SEND Datasets. Carefully consider which approach makes sense for your organization and stakeholders.

Option 1 – EFD-only	Option 2 – ePPND
- Potentially no fetal data and very little maternal data - Limited value outside of standard EFD endpoints - Adjustments to methods in define file - nSDRG statement for missing lactation data - No DS domain	- Potential incompatibility with future DART implementation - Adjustments to methods in define file - nSDRG statements for CT - Data collection not optimized for SEND - Stakeholders unprepared to handle ePPND studies - Software, Resource, Education limitations

Fig 4 Drawbacks and Considerations for each Implementation

Trial Design Domain & Variable		Option 1 - EFD-only	Option 2 - ePPND
TS	TRMSAC	Option 1 – TRMSAC encompasses only period from first day of dosing to end of Gestation	Option 2 – TRMSAC encompasses entire period from first day of dosing (Gestation) to last day on study (Lactation)
TE		Option 1 – Dosing elements only encompass Gestation phase therefore TEDURs will not go beyond Gestation phase	Option 2 – Dosing Elements encompass entirety of study and therefore TEDURs would go beyond Gestation Phase
TT	RSTAGE	Option 1 – Only includes RSTAGE of GESTATION	Option 2 – Includes both RSTAGES of 'GESTATION' and a stage for Lactation Phase (See Controlled Terminology for discussion on this)
TP	RPATH	Option 1 – Only includes RPATH that describes 'GESTATION'	Option 2 – Includes an RPATH that describes both Gestation and Lactation phases
SJ		Option 1 – Only includes RPATH that describes 'GESTATION'	
		Option 2 – Includes an RPATH that describes both Gestation and Lactation phases and SJSDTCTs as anchors for each phase	

Fig 2 Two Options for Trial Design Modeling

Codelist Name	Code	Submission Value
NCDPHASE	C124602	GESTATION
NCDPHASE	C124603	PAIRING
NCDPHASE	C124604	POSTNATAL
NCDPHASE	C124605	POSTPAIRING
NCDPHASE	C124606	PREMATING

Fig 3 NCDPHASE Codelist 2023-12-15

DISCUSSION - This investigation has raised the following questions to regulators and CDISC:

- With current CT, is it acceptable to deliver a dataset without a DS domain? It may be necessary for CDISC to develop CT to cover 'Lactation' ahead of PPND studies coming into scope to facilitate EFD end point ePPND deliveries.
- What is the benefit of ePPND studies with just EFD end points? Further insight into how these data are used may help guide individuals to make more strategic choices.
- Which option do regulators prefer considering the limitations of each implementation?