Session number: 3872/G350 Animal Welfare Enhancements for ePPND Studies

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Background and Objective

- The enhanced pre- and postnatal developmental (ePPND) toxicity study design is based on experience of biologics and primarily utilizing non-human primates (NHPs). This study integrates elements of the embryo-fetal developmental (EFD) and pre- and postnatal developmental (PPND) toxicity assessments, focusing on newborns and infants rather than fetuses.
- Evaluating offspring viability, growth, and survival in ePPND studies requires an extended observation period and significant investment in terms of animal resources and costs. Optimizing animal welfare and improving animal care are crucial to minimize risks and potential abnormalities.
- To ensure the efficient execution of the ePPND study, we explored various measures aimed at enhancing animal welfare under experimental conditions, which can influence the accuracy and reliability of study data positively.

Methods

• Animal Cohabitation Ratio:

The male-to-female ratios were 1:1 (62 females) or 1:2 (18 females), cohabitating in housing cages, mating for three consecutive days with sexually mature males starting from the 12th to 14th day of the female's menstrual cycle. The second day of cohabitation was recorded as GD0 (Gestation Day 0).

• Space for Pregnant Animal: From approximately GD130, each pregnant animal was provided with a "channel cage", allowing free movement between two vertically stacked cages. Corresponding indicators were monitored and recorded to assess the impact of these channel cages on gestation duration and parturition outcomes.

- Nutritional Support: To supplement nutrition, additional feed, welfare foods, vitamin C or vitamin D are provided according to the needs at different stages of pregnancy.
- Emotional Care: When separating the baby from the maternal animal, gently pat the female's back for comfort. For females unresponsive to calming efforts, precautions should be taken to prevent self-harm. If these measures are ineffective, closely monitor the female's behavior and provide appropriate welfare food.
- Social and Entertainment Measures: Provide soft towels to mimic maternal embrace and toys for entertainment. For monkeys with 3 months age, place two juvenile animals with similar age in adjacent cages to enable visual interaction. More than 3 months of age, monkeys with similar ages were kept together. Additionally, offer regularly animated videos to maintain pleasant mood. Monitor the stereotyped behaviors for longer housing.







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Figure 3. Nursery room

Results

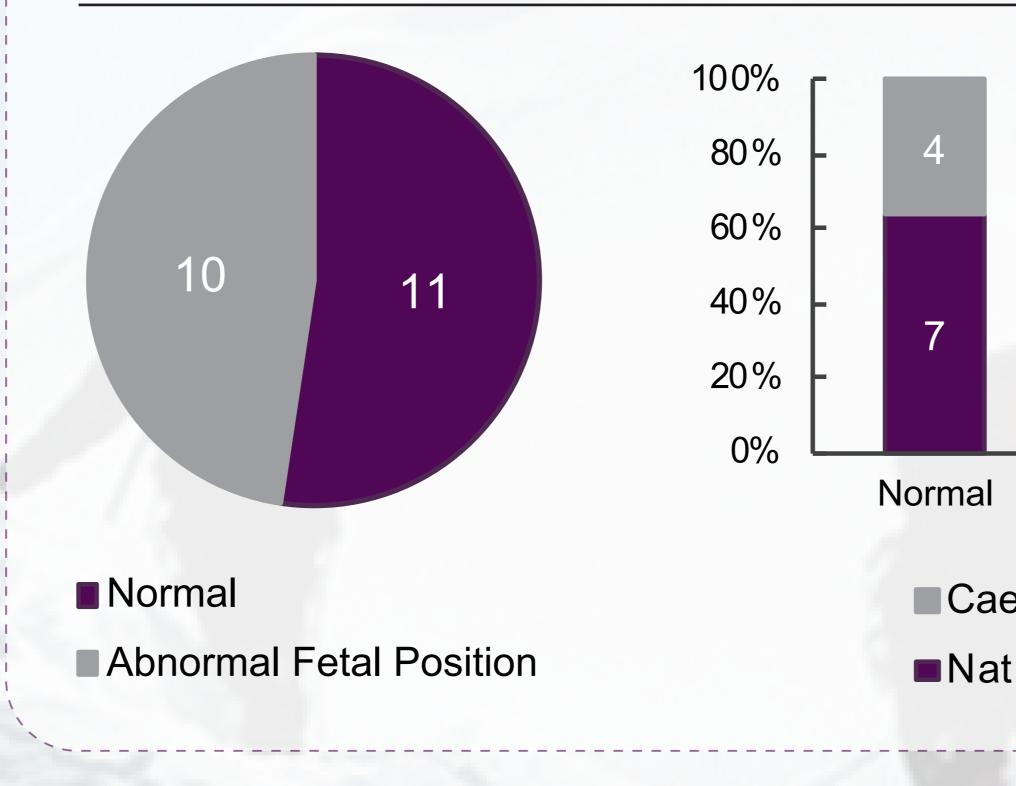


Table 1. Information from using of "channel cage"

Index	Normal	Abnormal Fetal Position	Total
Pregnant animals (n)	11(52.4%)	10(47.6%)	21
Start using (GD)	143.7±11.2	134.9±8.4	139.5 ± 10.7
End of use (GD)	162.5±3.0	155.5±10.6	159.1±8.2
Usage duration (day)	17±10.8	22.1±5.0	20.3±9.0
(Final)Head position (n)	11(100.0%)	7(70.0%)	18(85.7%)
Natural infant (n)	7(63.6%)	6(60.0%)	13(61.9%)
Caesarean section (n)	4(36.4%)	4(40.0%)	8(38.1%)
F1 survival (n)	10(90.9%)	9(90.0%)	19(90.5%)
F1 deaths (n)	1(9.1%)	1(10.0%)	2(9.5%)

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Gestation day obtained under different welfare circumstances of pregnant animals. It can improve the ratio of pregnancy, decrease the ratio of caesarean section:

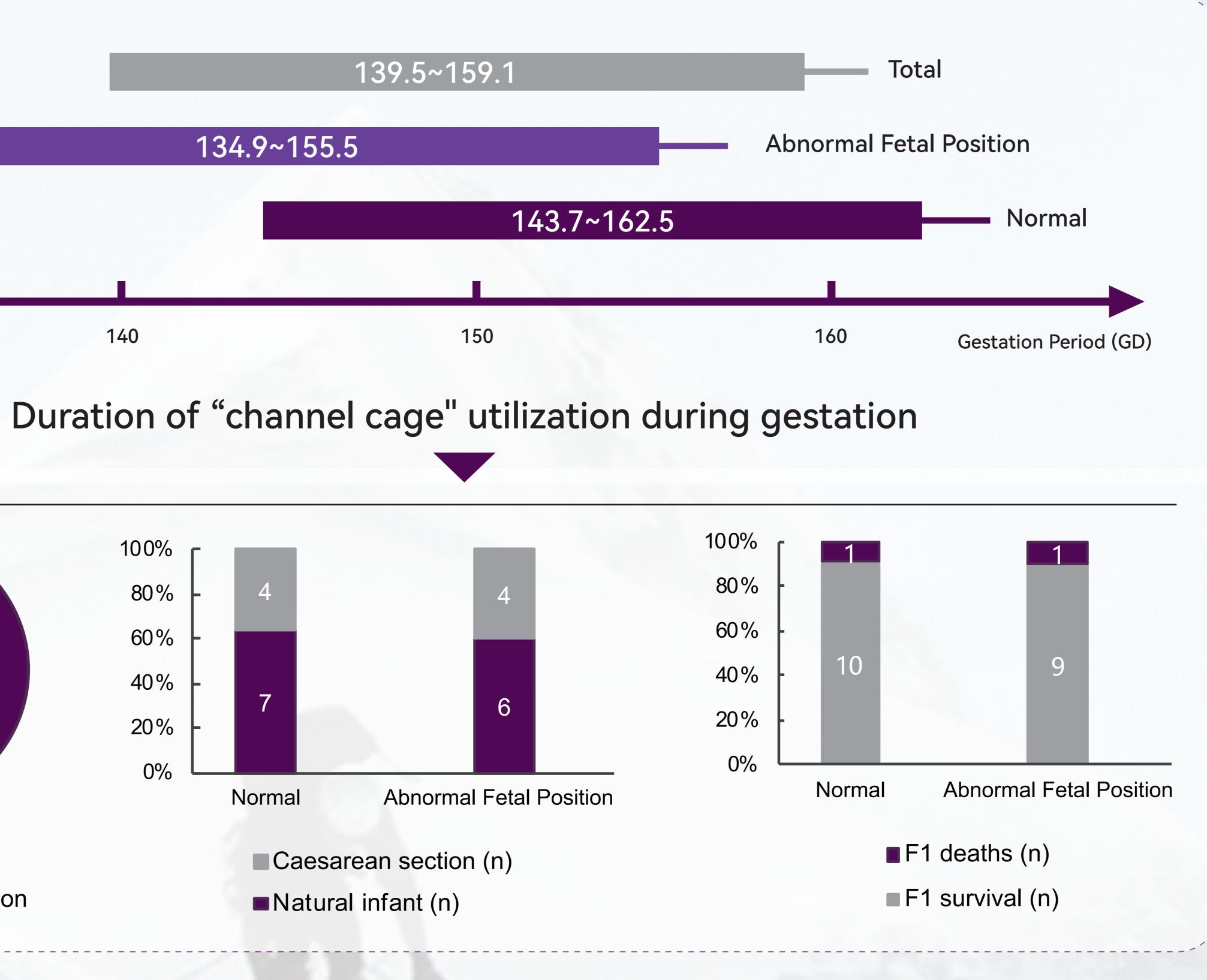


Figure 4. Delivery mode summary

- Enhance pregnancy rate:
- Decrease the risk of dystocia:
- social enrichment for the offspring.



Conclusion

Through mock exploratory research, we further demonstrate that prioritizing animal welfare during the ePPND study is crucial for minimizing risks during pregnancy and lactation, enhancing conception rates, reducing difficult labor occurrences, and producing reliable data.

TriApex Laboratories Co., Ltd. has distinguished itself through groundbreaking advancements in animal welfare innovation, capitalizing on its core competencies in NHP facility optimization, methodologies, cutting-edge instrumentation, GLP-compliant quality management systems, and multidisciplinary expertise. The facility has provided an industry-leading research platform for NHP reproductive and developmental toxicity assessments, establishing rigorous scientific safeguards to ensure data integrity and methodological validity.



Ultrasound results from GD18 to GD20 indicated that under the 1:2 cohabitation condition, 7 of 18 females were confirmed to be pregnant(38.9%). Conversely, under the 1:1 cohabitation condition, 27 out of 62 females were confirmed to be pregnant, yielding a total pregnancy rate of 43.5%. This demonstrates that the 1:1 cohabitation could enhance pregnancy rate and mating efficiency.

The implementation of "channel cages" demonstrated significant benefits:11 animals exhibited no abnormal fetal positions at the end of gestation among 21 females, with 7 females delivering naturally and 4 females with cesarean sections due biparietal diameter or prolonged labor (36.4%). The remaining 10 females showed fetal malposition, with 7 transitioning to the head position (70%), resulting in 6 natural births and 4 cesarean sections due to malposition or prolonged labor (40.0%). The average gestation period was 159 days, with a stillbirth rate of 9.5%.

• The reliable data from animals under well-being condition:

By introduction of psychological comfort, restraint measures, and enrichment measures during in-life phase, the animals exhibited less stress responses, increased cooperation, and a decreased incidence of abnormal behavior with their offspring, for instance, hair plucking. No stereotypical behaviors were observed by providing toys and

Figure 5. Animal welfare measures