Evaluation of Gamma Irradiated and Limited Donor Pool Human Platelet Lysate for Clinical Cell Manufacturing

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Background
- The use of fetal bovine serum (FBS) for clinical manufacturing of cell therapy products poses risks, including the potential for viral and prion transmission and the possibility of adverse immunological reactions.
- Human platelet lysate (hPL) has emerged as a viable, xenogen-free alternative to FBS in all steps of cell manufacturing.
- Differences in hPL manufacturing processes can significantly impact stem cell growth, morphology, and motility. To address these issues, Compass Biomedical has developed a highly standardized, industrial-scale production process for our PLUS™-hPL using good manufacturing practices (GMP).
- European Pharmacopoeia (Ph. Eur.) 9th Edition 5.2.2: “Because of the inherent risk of transmitting infectious agents from pooled plasma, pooled sera, or other derivatives from pooled allogenetic human blood or plasma, consideration is given to limit the number of donations which are pooled, unless sufficient methods for inactivation/removal of viruses are applied during production, where applicable.”

Infectious Disease Screening
- Each platelet unit used in the manufacturing of PLUS™-hPL has been screened for infectious diseases at AABB accredited Blood Banks using FDA approved methods and is suitable for transfusion.
- Inherent risk of transmitting infectious agents remains a concern for allogeneic blood or plasma products.
- Unknown pathogens cannot be screened at the time of blood collection.
- Gamma irradiation at 25-40 kGy is commonly applied to FBS for pathogen reduction purposes.

Methods
Gamma irradiation of three different lots of GMP PLUS™ was performed in the dose range of 25-40 kGy. The samples were kept frozen on dry ice throughout shipping and irradiation. Three lots of limited donor PLUS™ were also evaluated. Limited donor PLUS™ consists of pooling only 3 platelet apheresis units instead of the minimum 30 units. The gamma irradiated and limited donor PLUS™ were then evaluated in terms of physicochemical profile (pH, osmolality, and total protein content), concentrations of growth factors (VEGF, EGF, FGF-basic, and PDGF-BB), and ability to promote growth of bone marrow-derived mesenchymal stromal cells (MSCs).

Conclusions
- Both gamma irradiation of industrial-scale PLUS™ lots and limited donor pools (35 donors) do not compromise consistency or performance of PLUS™
- While both gamma irradiation and limited donor pooling reduce the risk of viral transmission, gamma irradiation is a preferred pathogen reduction method for hPL due to:
  - High penetration depth
  - Easily adopted into the GMP process
  - More cost-effective for end users than limited donor hPL
- Release date of GMP Gamma Irradiated hPL (PLUS™-GR): Q3 2023
- Future Plan: Complete a viral inactivation study to validate that the dose range of our GMP Gamma Irradiated hPL (PLUS™-GR) results in a 4-fold log₁₀ reduction of viral contamination.

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