

**FDA DRAFT Guidance: Cell Selection Devices for Point of Care Production of Minimally Manipulated Autologous Peripheral Blood Stem Cells (PBSCs)
[July 2007]**

Definition of Cell Selection

The term ‘cell selection’ as used in this guidance document should be clearly defined due to confusion with similar terms such as ‘cell separation.’ For example the term ‘cell separation’ was used by the Agency in responses to comments to provide examples of what the Agency considers to be minimal manipulation (see Preamble to Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, January 19, 2001). However, in the preamble to the afore mentioned rule the Agency’s mention of "selective removal" of B-cells, T-cells, malignant cells, red blood cells, or platelets are given as other examples of minimal manipulation.

Therefore, it is not clear what the Agency means when it uses the term ‘cell selection.’ For example, centrifugation is considered a form of cell separation, however the action of cell selection devices is to ‘separate’ specific populations of cells from the native HCT/P source. Would centrifugation and by extension, devices which use centrifugation, be considered within the scope of this guidance (i.e., being defined as cell selection)?

Inclusion of consideration of ‘specific clinical indication and ‘minimally manipulated’ as factors for determining an HCT/P meets the exception at 21 CFR 1271.15(b)

The Agency lists ‘five factors’ it believes must be present in order for autologous PBSCs produced at the point of care to be subject to the exception at 21 CFR 1271.15(b). Factor 1 states the cells must be intended for a “specific clinical indication” and Factor 2 states the cells are minimally manipulated. However, the exception at 21 CFR 1271.15(b) does not state or imply the in order for an autologous HCT/P to be subject to the exception that a specific clinical indication for the HCT/P must be identified nor does it make any reference to the state of ‘manipulation’ (minimal or not) that is permissible for the HCT/P. Consequently, Factors 1 and 2 should not be considered by the Agency in determining whether or not an autologous HCT/P, including PBSCs, meet the exception at 21 CFR 1271.15(b)

Devices Used to Minimally Manipulate Autologous PBSCs

This section of the guidance document states that marketing submissions for cell selection devices:

“must include data demonstrating that the device is safe and effective under the prescribed conditions of use. Demonstration of the safety and effectiveness of the device must include data on the device design, manufacturing, and performance characteristics.”

These expectations appear reasonable, however the guidance document later states that clinical trials are expected to:

“demonstrate that the device produces clinically effective cells for each specific clinical indication under consideration”

The Agency is requested to provide additional clarification and rationale on this point given that the output, autologous PBSCs produced at the point of care and returned to the patient during the same surgical procedure, are exempt from regulation since they meet the exception at 21 CFR 1271.15(b). In the absence of specific labeling claims of effectiveness of cells for a specific clinical indication, data on the device design, manufacturing, and performance characteristics should be all that is required to obtain marketing clearance or approval. It would be helpful to understand if the Agency’s guidance is dependent upon whether the medical device being employed at the point of care is cleared as a 510(k) versus a medical device that requires premarket approval (PMA).

However, the Agency should clarify exactly the basis for what data would be required regarding the cells. For example, in many cases the cells would meet the criteria described in 21 CFR 1271.10 for regulation solely under section 361 of the PHS Act, which is concerned with the prevention and transmission of communicable diseases, not clinical effectiveness of the cells. Therefore, the cell selection device should only need to provide data necessary for compliance with the regulations at 21 CFR 1271, rather than the data requirements applicable for drugs, biologics and medical devices.

Does the Agency agree in principle that if the cell selection device only claims to produce autologous HCT/Ps at the point of care with specified characteristics and does not make labeling claims about the effectiveness for use in a specific clinical indication, that clinical trials of the clinical effectiveness of the cells would not be required in order to obtain approval of the cell selection device?

Clarification of Cell Selection Devices used as Processing Equipment

Some clarification is needed to address the common situation where the same selection device is used as 'processing equipment,' one of many steps involved in producing an HCT/P that is subject to BLA/PMA premarket approval. If the cell selection device is only intended for use as processing equipment at not at 'point of care' do the requirements for preclinical and clinical studies for safety and effectiveness