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Guidelines SFGM-TC

## Quality controls on cord blood unit contiguous segments: Recommendation of the SFGM-TC



### *Contrôle de qualité des USP via segments attachés : recommandations de la SFGM-TC*

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#### ABSTRACT

In the attempt to harmonize clinical practices between different French transplantation centers, the French Society of Bone Marrow Transplantation and Cell Therapies (SFGM-TC) set up its fourth annual series of workshops which brought together practitioners from all of its member centers. These workshops took place in September 2013 in Lille. Literature and intra-laboratories studies suggest that attached segment is representative of cord blood unit (CBU). Nevertheless, some discrepancies have been observed when analyzing large data registries. To address these issues, we have listed recommendations to increase the standardization of segment processing and quality control (QC), information on units of measurement and specifications and action to be taken in case of out of specifications QC results on segment.

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#### RÉSUMÉ

Dans une démarche qui vise à uniformiser les procédures d'allogreffe de cellules souches hématopoïétiques (CSH), la Société française de greffe de moelle et de thérapie cellulaire (SFGM-TC) a organisé les quatrièmes ateliers d'harmonisation des pratiques en septembre 2013 à Lille. Cet atelier a été consacré au segment attaché des unités de sang placentaire dans le but d'établir des recommandations quant à la standardisation du traitement de ce segment et les mesures à prendre en cas de rupture de ce segment.

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### 1. Questions

- Is the distal segment representative of thawed bag?
- How to prepare segments?

- How to thaw segments?
- What minimal quality control (QC) should be performed?
- Information to communicate to the transplant center?
- Measures taken in case of insufficient total nucleated cell viability?

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**Table 1**  
Differences between distal segment and bag.

Absolute difference in TNC viability (segment versus bag), %	Cell viability segment > bag: number of patients	Cell viability bag > segment: number of patients
0–10	22	31
10–20	2	22
20–30	4	15
30–40	3	8
40–50		5
≥ 50		5

TNC: total nucleated cell.

## 2. State of the art [1–6]

Literature and intra-laboratories studies suggest that attached segment is representative of cord blood unit (CBU).

However, some discrepancies have been observed when analyzing large data registries. We analyzed 570 CBU from the French registry (France Greffe de Moelle, FGM) that were recruited for French transplant centers from 2008 to 2012. For 117 CBU, quality control data were available for both the distal segment and thawed bag. All these CBU were infused. Divergence for total nucleated cell (TNC) viability were observed between the thawed distal segment and the thawed bag. A difference between distal segment and bag greater than 10% was noted in 64 cases. Cases where TNC viability was lower in the segment than in the bag were more frequent and of greater magnitude than the opposite way (Table 1).

These results suggest that even though the attached segment can generally be seen as fairly representative of the CBU bag, there are cases where cell viability is discordant between the segment and the bag. The causes of these discordances could be related to random variability in the thawing process, but also to specific difficulties in preparing or thawing the segment. These results also show that, confronted with a low TNC viability in an attached segment, some transplant centers nevertheless decide to use the CBU.

## 3. Methodology

- Literature review.
- French CB registry review.
- Intra-centers validation data.



**Fig. 1.** Cord blood bag showing proximal and distal segments.

Definitions: Fig. 1 depicts proximal and distal segments.

## 4. Abbreviations

CBU	Cord Blood Unit
CFU	Colony Forming Unit
QC	Quality Control
SOP	Standard Operating Procedure

## 5. Recommendations

To address the issues raised above, we have listed recommendations regarding the handling of attached segments and their QC.

- National regulations and FACT standards shall be followed. In particular, number of segments, labeling and required tests has to be closely considered in order to be fully compliant with legislation and standards.
- At the time of recruitment and before CBU release, the transplant physicians should require the expertise of HLA typing laboratory and cell therapy lab that will be in charge of CBU thawing. These teams should jointly review CBU data, including data of the thawed segment.
- Carefully validated SOP should be followed at each step:
  - before freezing. A critical step is the homogenization of DMSO and CBU, including the liquid contained in the tubing. A thorough homogenization by repeatedly (> 3 times) emptying and filling the tubing that will constitute the segment may be adopted;
  - the delay between DMSO addition and CBU cryopreservation is critical in order to avoid cell toxicity;
  - segment removal: executed by trained technical staff member in order to minimize any involuntary warning events;
  - segment thawing:
    - for a short time (< 30 s), in a defined temperature (for instance 37 °C),
    - segment disinfection, for instance with hydro-alcohol 70%,
    - slow dilution of thawed cord blood, with a defined medium volume,
    - accurate measure of the segment volume to infer cell concentration. Such a measure should be carried out after dilution to minimize imprecision.
- In case distal segment is below specifications including HLA discrepancy, after transplant center approval, thawing of proximal segment is acceptable. In such a case, the final decision on the CBU conformity should be based on data obtained from the proximal segment.
- Minimal QC on thawed segment should include:
  - HLA confirmatory typing;
  - TNC viability (%);
  - CD34 viability (%);
  - cloning efficiency: CFU-GM or CFC, expressed as % per CD34 or TNC. Calculation method shall be detailed.

In addition, the following QC can be provided:

- TNC/ $\mu\text{l}$ ;
- CD34+/ $\mu\text{l}$ .

If cell quantities are extrapolated to the whole CBU volume, it shall be clearly specified to the transplant center.

Viabilities and CD34 numeration should be performed using single platform and follow ISAGHE recommendation.

Units shall be defined and should be harmonized among registries.

CB Bank specifications should be precisely defined.

If results are below these specifications, the transplant center shall be informed. Exceptional release can be decided after joined discussion.

#### 6. Unanswered questions

- Increase standardization of segment processing (freezing and thawing).
- Proposal of specifications.

#### Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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