

Cord Blood as a Biological Product: Implications

HRSA Advisory Council on Blood Stem Cell Transplantation



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The Regulatory Requirements

Federal Register / Vol. 72, No. 10 / Wednesday, January 17, 2007

“For use in unrelated allogeneic recipients. These HCT/Ps are regulated as biological products under section 351 of the PHS Act (21 CFR 1271.20).”

Guidance for Industry; October 2009

Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic Reconstitution for Specified Indications

Guidance for Industry; March 2014

Biologics License Applications for Minimally Manipulated, Unrelated Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System

The Regulatory Requirements

- **FDA Guidance for License: October 2009; March 2014**
- **FDA Guidance for IND: June 2011; March 2014**

HPC, Cord Blood: Hematopoietic Progenitor Cells,
Cord Blood: minimally manipulated CB product

Manufacturing: all steps from collection to release of
product to search

Licensed product: “prescription” drug with specific
indications

IND product: “investigational”; requires IRB approved
consent for use

Biologics License Application

Process Validation

Stability Studies, Product Expiration

Media Fill Validation

Laboratory Assays Validations

IT Systems Validations

Equipment Qualifications

Facility, Environmental Monitoring, Supplies

Packaging, Labeling

Product Batch Record

Quality Unit for Product Review and Release

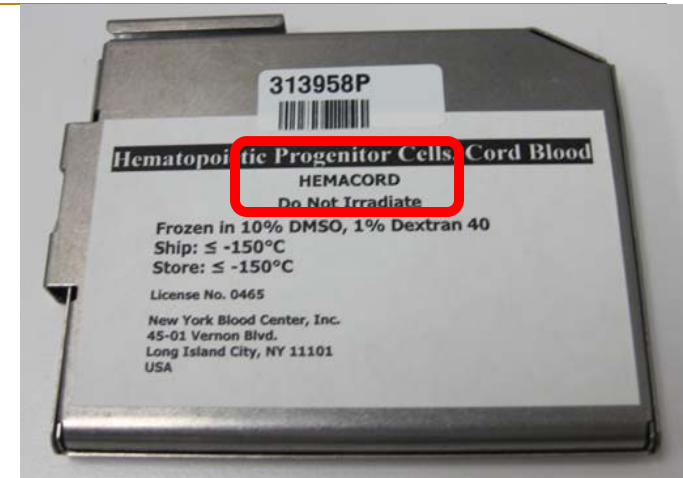
.....and many others.....

The work

Example: Stability Evaluation - Label

Apply Criteria Annually

Test	Purpose	Stability-Indicating
Visual Inspection after thawing	Determine Integrity of container / closures and Identity Label	Integrity, Identity
Total nucleated cell (TNC) count	Measure TNC content	Potency
Viable CD34+ cell content	Measure CD34+ cell number and viability	Potency
Colony-Forming Units (CFU)	Count CFU - functional progenitor cells	Potency
Microbiology	Detect microbial contamination	Integrity, Purity, Safety



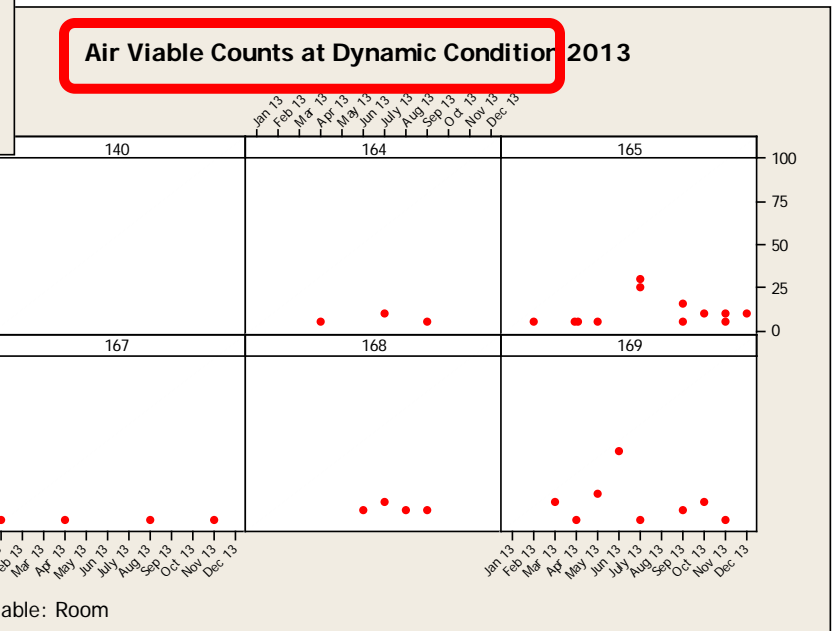
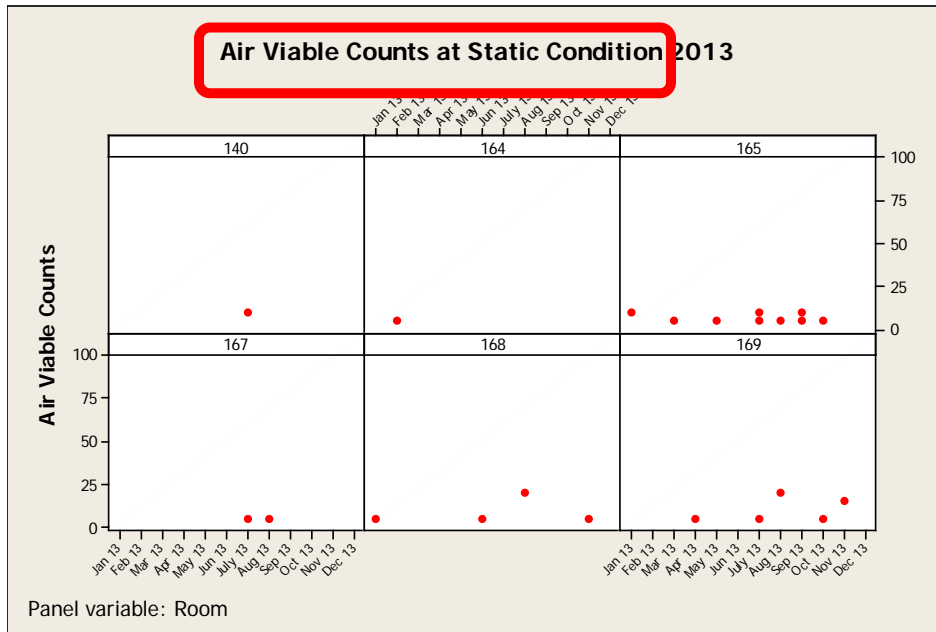
HEMATOPOIETIC PROGENITOR CELLS, CORD BLOOD	
HEMACORD	
<i>Injectable Suspension</i>	
HEMACORD ID: 123456P	NDC 76489-001-01
RECIPIENT: Last, First	SEARCH ID: 11111
TNC/kg: 2.3×10^7	
HLA match with recipient: one B locus mismatch <small>(HLA matching is assigned considering low resolution typing for HLA class I A and B loci, and high resolution typing for HLA DRB1 alleles.)</small>	
For Intravenous Administration Only	
Do Not Irradiate	
Rx only	
Cryopreservative (concentration): DMSO (10%) / Dextran 40 (1%)	
Volume: Approx. 25 mL	
Storage: < -150°C	
Expiration Date: 10/11/2020	

Product Expiration Date



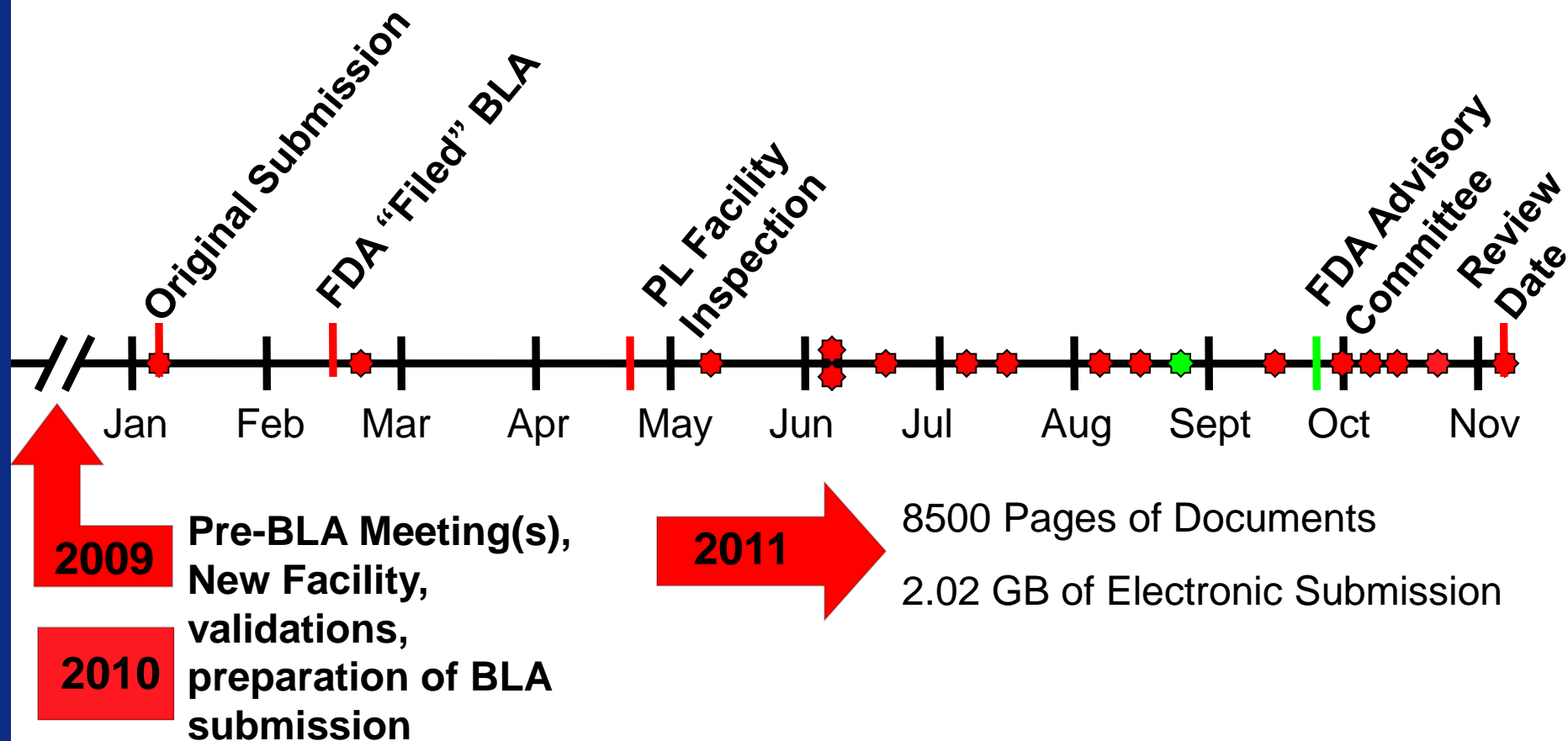
The work

Example: Environmental Monitoring of the Facility



Annual cost appx. \$35,000

The Time: Biologics License Timeline - NCBP



- ★ Amendments Completed; Package Insert
- ★ Advisory Committee Briefing Book Submission

Nov. 10, 2011

HEMACORD™
(hematopoietic progenitor cells, cord blood)

The aim

Biologics License

The goal is for ALL banked CB units to be of consistent high Quality, and to have reliable Identity, Safety, Purity and Potency, so that there will be maximum Safety and Efficacy at Transplant

The challenges

CB Licensure: benefits

Cord Blood Banks

Regulatory oversight and guidance

Quality Systems in Manufacturing and Testing

Consistently safer, high quality products

Close Monitoring of Adverse Events

Transplant Community

Experience with and easier/faster access to high quality HPC-C products

Enhanced safety of transplant procedures

More patients can benefit from the treatment

NCBP presentation: Cellular, Tissue and Gene Therapies Advisory Committee Meeting, Sep. 22, 2011

The challenges

CB Licensure: challenges

Cord Blood Banks

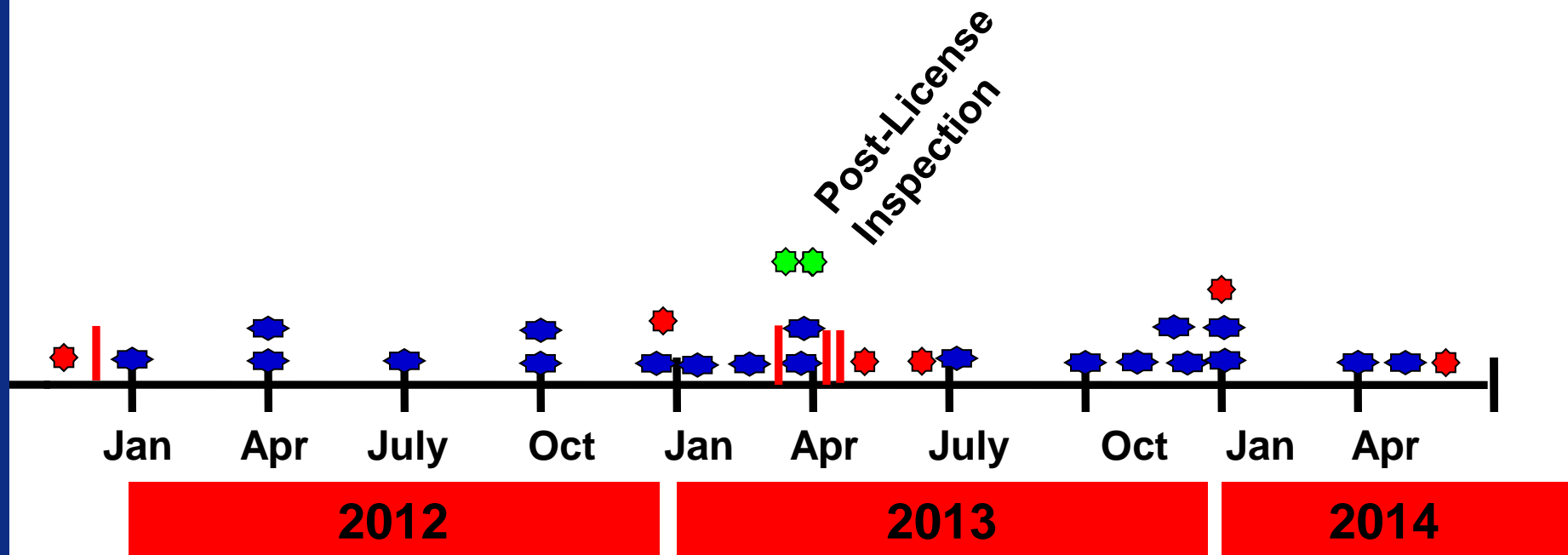
Substantially Increased Costs of:

Documentation - Facilities - Operations - Personnel -
Testing - Equipment

Licensure will be beneficial for the transplant community if it contributes to broader utilization of the higher quality HPC, Cord Blood products

NCBP presentation: Cellular, Tissue and Gene Therapies Advisory Committee Meeting, Sep. 22, 2011

The Time: Events after License - NCBP

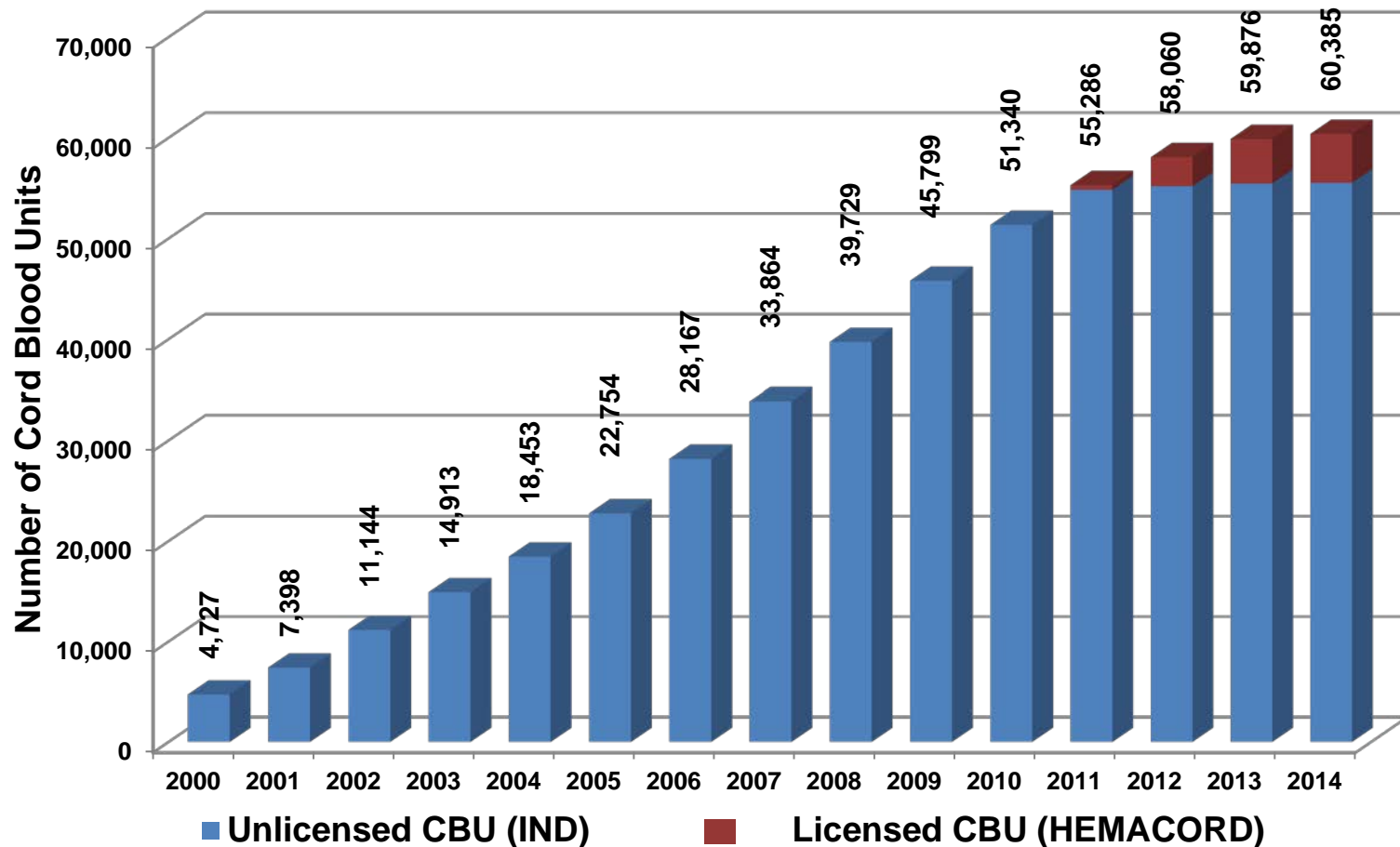


- ★ Amendments
- ★ License-related Reports (PAER, Distribution, Annual, Events)
- ★ Post-License FDA inspection
- | Package Insert and Label submissions/revisions

Maintaining the License is an ongoing process..

The current NCBP Search Inventory

Investigational and Licensed CB products



The current situation

- **CB Banks are using all (limited) resources to meet FDA Requirements – increased cost of Banking – higher cost of CB products**
NCBP CBU price (2008): \$35,000
NCBP IND CBU (2012): \$42,500
HEMACORD CBU: \$45,000
- **As a result of changes related to cost and higher TNC at collection, the CB Inventory is growing at a lower rate – the decreased growth affects primarily the licensed products**
- **Overall, utilization of CB products for transplantation is decreasing, at the same time when the clinical results are improving**

FDA-licensed CB products

Will we be using them to their full potential?



**HRSA subsidy covers part of the cost of the NCBI CBU
– still, provides important revenue for the CB Banks**

**Increases in HRSA subsidy will impact significantly the
future inventory and the sustainability of the CB Banks**

Increased funding is needed