Indiana State Department of Health
Health Care Quality and Regulatory Commission
Division of Acute Care

Testing of Blood/Blood Products and Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

ISDH HCQRS: Program Advisory Letter
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ADVISORY SUMMARY

- **Effective Date: September 10, 2012.**
- **Donations used in the manufacturing of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) licensed by the U.S. Department of Health and Human Services, Food and Drug Administration (FDA) are subject to the testing requirements and timeframes established by the FDA.**
- **Blood Centers that collect donations for HCT/Ps must maintain a list of licensed products, by manufacturer, for which the blood center collects donations.**
- **All donations not used for a HCT/P, whether allogenic or autologous, remain subject to the testing requirements of Ind. Code § 16-41-12.**

Purpose

The purpose of this program advisory letter is to inform Blood Centers of the Indiana testing requirements for donations of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). Specifically, Blood Centers that collect donations that are registered with the Food and Drug Administration (FDA) as HCT/Ps are not required to test the HCT/Ps donations under Indiana Code. This does not alter the Blood Center's requirements to test HCT/Ps pursuant to federal law.

Background Information

The Indiana State Department of Health, Acute Care Division (Division) is the licensing authority for Blood Centers conducting business within Indiana. The Division has been made aware that some Indiana Blood Centers collect various blood and tissue components from donors for the production of HCT/Ps registered by FDA. Blood Centers are concerned that the testing and labeling required by the FDA for HCT/Ps is in conflict with Ind. Code § 16-41-12.

Analysis

Indiana Code § 16-41-12 governs the Precautionary Measures for Use of Human Tissues and Blood Products and Regulation of Blood Centers. Indiana Code defines screening tests, blood, and autologous donations, but is silent regarding HCT/Ps. Additionally, the Indiana Code requires testing for the human immunodeficiency virus (HIV) for both autologous and non-autologous blood donations. (*See* Ind. Code § 16-41-12-13(a) and Ind. Code § 16-41-12-11.) Pursuant to Ind. Code § 16-41-12-13, "[a] blood center shall perform a screening test on a donor's blood and obtain the results of the test before blood, plasma, a blood product, or a blood derivative is distributed for use."

FDA licensed manufacturers of HCT/Ps are required to test HCT/Ps for HIV types I and II; Hepatitis B and C; and *Treponema Pallidum* (syphilis); and in certain circumstances for Human T-lymphotropic virus types I and II; cytomegalovirus (CMV); *Chlamydia trachomatis*; *Neisseria gonorrhea*; and transmissible spongiform encephalopathy. (*See* C.F.R. §1271.85; C.F.R. §1271.90 and "Guidance for Industry, Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue Based Products (HCT/Ps)" located at http://www.fda.gov/cber/guidelines.htm). In addition to these testing requirements the FDA requires numerous other tests; however, it is outside the scope of this analysis to expand on each and every one. In addition to the requirements already cited, the FDA has regulatory authority to inspect HCT/Ps programs for adherence to 21 C.F.R. § 1271. Upon review of the FDA requirements for HCT/Ps, it is evident that the FDA requires much more extensive testing than would be required if HCT/Ps were subject only to Ind. Code § 16-41-12.

The term "blood" is defined by the Indiana Administrative Code (IAC), 410 IAC 1-4-1, as "human blood, human blood components, and products made from human blood" and by the Code of Federal Regulations (CFR) as "a drug which consists of human whole blood, plasma, or serum or any product derived from human whole blood, plasma, or serum, hereinafter referred to as "blood product..." 21 C.F.R. § 607.3(b). The IAC definition is materially similar to the CFR definition. Specifically, "human blood" is equivalent to "human whole blood", "human blood components" is equivalent to "plasma or serum", and "products made from human blood" is equivalent to "any product derived from human whole blood, plasma, or serum".

As stated above, the Indiana Code does not define and is silent regarding testing of HCT/Ps. The CFR defines HCT/Ps as:

> [A]rticles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue. The following articles are not considered HCT/Ps:
> . . . (2) Whole blood or blood components or blood derivative products subject to listing under parts 607 and 207 of this chapter, respectively; . . .

21 C.F.R. §1271.3(d). The CFR specifically excludes blood from the definition of HCT/Ps.

Given equivalent federal and state definitions of blood products, the federal exclusion of blood products as part of HCT/Ps and the silence of Indiana Code in regards to HCT/Ps, is reasonable to conclude that:

1. 21 C.F.R. § 1271. 3(d) *et. seq*. excludes blood products from inclusion as an HCT/Ps.
2. Given the equivalent federal and state definitions of blood/blood products, it is reasonable to presume state statute would follow the federal exclusion.
3. State statute and rules are silent in regards to HCT/Ps.
4. Federal regulation is controlling in regards to HCT/Ps.
5. 21 C.F.R. § 1271, through administration by the FDA, sets forth a registration and licensing process which imbeds the performance of required testing, timing of the testing, labeling of the donation, processing, manufacturing and test reporting for donations used in the manufacture and use of HCT/Ps.
6. FDA required testing of donations used for HCT/Ps exceeds testing required by the state.
7. Blood/Blood products remain subject to state statute at Ind. Code § 16-41-12.

With respect to autologous testing of blood/blood products, the FDA does not require testing of autologous blood/blood product donations. However, Ind. Code § 16-41-12 *et. seq.* does require the testing of autologous blood/blood products. Therefore, except for donations used for HCT/Ps, blood centers must follow state statute for allogenic and autologous blood/blood product donations including adherence to testing before the blood/blood product is distributed for use in accordance with Ind. Code §16-41-12-11 and Ind. Code § 16-41-12-13.

Policy

Donations used in the manufacturing of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) licensed by the U.S. Department of Health and Human Services, Food and Drug Administration (FDA) are exclusively subject to the testing requirements and timeframes established by the FDA license.

In order for state surveyors to appropriately apply state statute when inspecting blood centers that collect donations for HCT/Ps, the blood center must maintain a list of licensed products, by

manufacturer, for which the blood center collects donations. This will prevent the application of state statute to donations that are controlled exclusively by federal regulation and inspection.

All donations not used for a HCT/Ps, whether allogenic or autologous, remain subject to the testing requirements of Ind. Code § 16-41-12.

Questions

Questions about this program advisory letter may be addressed to Lorraine Switzer, Program Director, (317) 233-7502, email: lswitzer@isdh.in.gov or Randy Snyder, Division Director, (317) 233-1286, email: rsnyder1@isdh.in.gov.

Approved by:

/s/
Terry Whitson, Assistant Commissioner
Health Care Quality and Regulatory Commission