

§ 1271.195

21 CFR Ch. I (4-1-06 Edition)

(c) *Operations.* You must divide a facility used in the manufacture of HCT/Ps into separate or defined areas of adequate size for each operation that takes place in the facility, or you must establish and maintain other control systems to prevent improper labeling, mix-ups, contamination, cross-contamination, and accidental exposure of HCT/Ps to communicable disease agents.

(d) *Procedures and records.* (1) You must establish and maintain procedures for facility cleaning and sanitation for the purpose of preventing the introduction, transmission, or spread of communicable disease. These procedures must assign responsibility for sanitation and must describe in sufficient detail the cleaning methods to be used and the schedule for cleaning the facility.

(2) You must document, and maintain records of, all cleaning and sanitation activities performed to prevent contamination of HCT/Ps. You must retain such records 3 years after their creation.

§ 1271.195 Environmental control and monitoring.

(a) *Environmental control.* Where environmental conditions could reasonably be expected to cause contamination or cross-contamination of HCT/Ps or equipment, or accidental exposure of HCT/Ps to communicable disease agents, you must adequately control environmental conditions and provide proper conditions for operations. Where appropriate, you must provide for the following control activities or systems:

- (1) Temperature and humidity controls;
- (2) Ventilation and air filtration;
- (3) Cleaning and disinfecting of rooms and equipment to ensure aseptic processing operations; and
- (4) Maintenance of equipment used to control conditions necessary for aseptic processing operations.

(b) *Inspections.* You must inspect each environmental control system periodically to verify that the system, including necessary equipment, is adequate and functioning properly. You must take appropriate corrective action as necessary.

(c) *Environmental monitoring.* You must monitor environmental conditions where environmental conditions could reasonably be expected to cause contamination or cross-contamination of HCT/Ps or equipment, or accidental exposure of HCT/Ps to communicable disease agents. Where appropriate, you must provide environmental monitoring for microorganisms.

(d) *Records.* You must document, and maintain records of, environmental control and monitoring activities.

§ 1271.200 Equipment.

(a) *General.* To prevent the introduction, transmission, or spread of communicable diseases, equipment used in the manufacture of HCT/Ps must be of appropriate design for its use and must be suitably located and installed to facilitate operations, including cleaning and maintenance. Any automated, mechanical, electronic, or other equipment used for inspection, measuring, or testing in accordance with this part must be capable of producing valid results. You must clean, sanitize, and maintain equipment according to established schedules.

(b) *Procedures and schedules.* You must establish and maintain procedures for cleaning, sanitizing, and maintaining equipment to prevent malfunctions, contamination or cross-contamination, accidental exposure of HCT/Ps to communicable disease agents, and other events that could reasonably be expected to result in the introduction, transmission, or spread of communicable diseases.

(c) *Calibration of equipment.* Where appropriate, you must routinely calibrate according to established procedures and schedules all automated, mechanical, electronic, or other equipment used for inspection, measuring, and testing in accordance with this part.

(d) *Inspections.* You must routinely inspect equipment for cleanliness, sanitation, and calibration, and to ensure adherence to applicable equipment maintenance schedules.

(e) *Records.* You must document and maintain records of all equipment maintenance, cleaning, sanitizing, calibration, and other activities performed in accordance with this section. You

must display records of recent maintenance, cleaning, sanitizing, calibration, and other activities on or near each piece of equipment, or make the records readily available to the individuals responsible for performing these activities and to the personnel using the equipment. You must maintain records of the use of each piece of equipment, including the identification of each HCT/P manufactured with that equipment.

§ 1271.210 Supplies and reagents.

(a) *Verification.* You must not use supplies and reagents until they have been verified to meet specifications designed to prevent circumstances that increase the risk of the introduction, transmission, or spread of communicable diseases. Verification may be accomplished by the establishment that uses the supply or reagent, or by the vendor of the supply or reagent.

(b) *Reagents.* Reagents used in processing and preservation of HCT/Ps must be sterile, where appropriate.

(c) *In-house reagents.* You must validate and/or verify the processes used for production of in-house reagents.

(d) *Records.* You must maintain the following records pertaining to supplies and reagents:

(1) Records of the receipt of each supply or reagent, including the type, quantity, manufacturer, lot number, date of receipt, and expiration date;

(2) Records of the verification of each supply or reagent, including test results or, in the case of vendor verification, a certificate of analysis from the vendor; and

(3) Records of the lot of supply or reagent used in the manufacture of each HCT/P.

§ 1271.215 Recovery.

If you are an establishment that recovers HCT/Ps, you must recover each HCT/P in a way that does not cause contamination or cross-contamination during recovery, or otherwise increase the risk of the introduction, transmission, or spread of communicable disease through the use of the HCT/P.

§ 1271.220 Processing and process controls.

(a) *General.* If you are an establishment that processes HCT/Ps, you must process each HCT/P in a way that does not cause contamination or cross-contamination during processing, and that prevents the introduction, transmission, or spread of communicable disease through the use of the HCT/P.

(b) *Pooling.* Human cells or tissue from two or more donors must not be pooled (placed in physical contact or mixed in a single receptacle) during manufacturing.

(c) *In-process control and testing.* You must ensure that specified requirements, consistent with paragraph (a) of this section, for in-process controls are met, and that each in-process HCT/P is controlled until the required inspection and tests or other verification activities have been completed, or necessary approvals are received and documented. Sampling of in-process HCT/Ps must be representative of the material to be evaluated.

(d) *Dura mater.* (1) When there is a published validated process that reduces the risk of transmissible spongiform encephalopathy, you must use this process for dura mater (or an equivalent process that you have validated), unless following this process adversely affects the clinical utility of the dura mater.

(2) When you use a published validated process, you must verify such a process in your establishment.

§ 1271.225 Process changes.

Any change to a process must be verified or validated in accordance with §1271.230, to ensure that the change does not create an adverse impact elsewhere in the operation, and must be approved before implementation by a responsible person with appropriate knowledge and background. You must communicate approved changes to the appropriate personnel in a timely manner.

§ 1271.230 Process validation.

(a) *General.* Where the results of processing described in §1271.220 cannot be fully verified by subsequent inspection