Designation: E2888 – 12 (Reapproved 2019)

Standard Practice for Process for Inactivation of Rodent Retrovirus by pH[1]

This standard is issued under the fixed designation E2888; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This practice assures 5 log10 inactivation of non-defective C-type retroviruses, which are endogenous to murine hybridoma and CHO cells and are potentially present in the production stream of biopharmaceutical processes that use rodent derived cell culture.

1.2 The process parameters specified in this practice consistently assure 5 log10 inactivation of murine retrovirus by adjusting the pH of a process solution after initial affinity capture chromatography purification.

1.3 This practice is applicable to mAb, IgG fusion, or other recombinant proteins produced from rodent cell lines (for example, CHO or murine hybridoma), which do not target retroviral proteins. Additionally, the low pH step is performed on a cell-free intermediate, post initial capture using protein A chromatography.

1.4 The 5 log10 inactivation of murine retrovirus claimed by using this practice will be utilized in conjunction with other clearance unit operations (for example, chromatography and virus retentive filtration) to assure sufficient total process clearance of murine retroviruses, which will be supportive of early phase regulatory filings.

1.5 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.6 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Terminology

2.1 *Definitions of Terms Specific to This Standard:*

2.1.1 *IgG fusion protein, n*—a dimeric protein comprised of two monomers, each monomer consisting of a peptide sequence (usually a human receptor-like protein or protein fragment) fused to the carboxyl-terminal of the Fc-domain of a human IgG antibody.

2.1.1.1 *Discussion*—Dimerization occurs by way of the Fc domain.

2.1.2 *immunoglobulin G (IgG), n*—an antibody molecule composed of four peptide chains — two γ heavy chains and two light chains.

2.1.2.1 *Discussion*—Each IgG has two antigen binding sites. IgG constitutes 75 % of serum immunoglobulins in humans. IgG molecules are synthesized and secreted by plasma B cells. There are four IgG subclasses (IgG1, 2, 3, and 4) in humans, named in order of their abundance in serum (IgG1 being the most abundant). Only human IgG1, IgG2, and IgG4 show significant affinity to protein A.

2.1.3 *log10 reduction value (LRV), n*—typically used to describe the degree of reduction of a population, in this case rodent retrovirus, by the treatment process.

2.1.3.1 *Discussion*—Each log reduction (10^{-1}) represents a 90 % reduction in the population. So a process shown to achieve a 6-log reduction (10^{-6}) will reduce a population from a million (10^{6}) to 1.

2.1.4 *monoclonal antibody (mAb), n*—monospecific antibodies which have affinity for the same antigen and are made from a master cell bank, cloned from a parent cell.

2.1.5 *murine leukemia virus (MuLV), n*—retroviruses named for their ability to cause cancer in murine (mouse) hosts.

2.1.5.1 *Discussion*—MuLV is a member of the genus *Gammaretrovirus*. MuLV is an enveloped spherical RNA virus which has a diameter of 80–110 nm and has low chemical resistance. MuLV is used as a model for non-defective C-type endogenous retrovirus or retrovirus like particles produced by murine hybridoma and CHO cell lines. MuLV is used to assess rodent retrovirus clearance of protein purification processes that use rodent cells for production.

2.1.6 *recombinant protein, n*—produced from the expression of recombinant DNA within living cells.

2.1.6.1 *Discussion*—Recombinant DNA is genetically engineered by inserting foreign DNA into the DNA of an appropriate host so that the foreign DNA is replicated along with the host DNA.

[1] This practice is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.12 on Process Applications.

Current edition approved Feb. 1, 2019. Published March 2019. Originally approved in 2012. Last previous edition approved in 2012 as E2888 – 12. DOI: 10.1520/E2888-12R19.