Cytotherapy, 2015; 17: 850–859

International Society for Cellular Therapy
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OCCASIONAL SURVEY

International Society for Cell Therapy Facility Sanitization Survey Laboratory Practices Committee Report

VARDA DEUTSCH[1,*], ANDREW HAVENS[2,*] & KAREN SNOW[3,*]

[1]*Tel Aviv Sourasky Medical Center, The Hematology and Bone Marrow Transplant Laboratory, Tel Aviv, Israel,* [2]*The Evelyn H. Griffin and the Judith R. Hoffberger cGMP Facilities, Program of Regenerative Medicine/University of Texas, Houston, Texas, USA, and* [3]*Massachusetts General Hospital, Boston, Massachusetts, USA*

Abstract

Background aims. Quality cell manufacturing processes require a clean laboratory environment. *Methods.* This report was aimed at describing current cleaning and sanitization practices reported by facilities that manufacture many types of cellular therapy products for clinical use. It is our hope that this report may provide the groundwork for guidance recommendations directed at developing consensus standards for cleaning and sanitization practices across the globe. Facility sanitization is a central issue to regulatory and accreditation bodies. Facilities are required to develop plans to assess sanitization practices and test cleaning effectiveness. *Results.* This document provides information on how this is performed in different facilities and may allow newer, smaller or less developed facilities to build, enhance or revise their current quality program by using experience and expertise in facility sanitization reported herein. *Conclusions.* This report summarizes the results of the latest survey and compares results with those previously reported. New and relevant trends in the field provide important information and will provide important information for establishing guidelines.

Key Words: *classification, processing facilities, regulation, sanitization*

Introduction

Maintaining a clean laboratory is an essential element of a high-quality cell manufacturing process. It is imperative to attain and maintain an extremely low number of particles of any kind, organic and inorganic, as well as the absence of microorganisms, and to demonstrate control of a clean environment. Good Manufacturing Practices (GMPs) and Good Tissue Practices (GTPs) require that any facility that processes cellular therapy products must be maintained in a clean and orderly fashion. These requirements are spelled out in the Code of Federal Regulations parts 211, 600, 820, 1271 [1] in the United States and European Commission Directive 2006/86/EC and EU Guidelines to Good Manufacturing Practice, Annex 1 01 March 2009 in the European Union [2]. Health Canada, the Therapeutic Goods Administration in Australia and other competent authorities around the world have similar requirements. The Foundation for the Accreditation of Cellular Therapy (FACT) standard D.2.4 [3] also requires the cellular processing facility to be maintained in a clean, sanitary and orderly manner. This includes all equipment used during the manufacture of cellular therapy products as well as facility itself.

In September 2003, the International Society for Cell Therapy (ISCT) announced the formation of a working group to address facility sanitization in cellular therapy processing facilities. The ISCT Laboratory Practices Committee (LPC) organized and continues to sponsor this group. A mission statement was identified to determine the focus of the project. The LPC Working Group planned to draft a document to include regulatory guidance and outline practices regarding appropriate facilities/equipment cleaning and sanitization involved in the

*These authors contributed equally to this work.
Correspondence: **Karen Snow** (ASCP)BB, CQA(ASQ), Massachusetts General Hospital, Boston, MA 02114, USA. E-mail: ksnow1@mgh.harvard.edu

(Received 15 August 2014; accepted 26 March 2015)

ISSN 1465-3249
http://dx.doi.org/10.1016/j.jcyt.2015.03.688

manufacture and processing of cellular therapy products. Input was sought from experts in the cell therapy community and pharmaceutical industries, regulatory agencies and other interested stakeholders. The Working Group agreed that a survey to collect the cleaning practices of the industry was warranted, and such a survey was developed and disseminated through the use of a web-based survey tool to the membership of ISCT, AABB and American Association of Tissue Banks in early 2005. There were 55 respondents. Because no guidance document or white paper was forthcoming and facilities have changed over time, a follow-up survey was created by the LPC in 2010 to gain a more current perspective on how facilities have modified their practices regarding approaches to facility sanitization. One hundred eight facilities (132 laboratories) responded to this new survey. Several of the same questions from the previous version were included, and additional questions were added, requesting more detail on certain topics to describe current industry practices. This report focuses on the results of 2010 survey.

There are very few and very limited descriptions of these procedures and practices; therefore, the goal in creating this document is to describe current cleaning and sanitization practices reported by facilities that manufacture all types of cellular therapy products for clinical use. This first step will provide the groundwork for guidance recommendations directed at developing consensus standards for cleaning and sanitization practices across the globe. Facility sanitization is becoming more important to regulatory and accreditation bodies, and facilities must develop plans to assess sanitization practices and test cleaning effectiveness. Maintaining a clean laboratory is a key element of a quality manufacturing process. In effect, this document may allow newer, smaller or less developed facilities to build, enhance or revise their current quality program by using the vast experience and expertise in facility sanitization reported herein. This report summarizes the results of the latest survey and compares the relevant trends in the field that provide important information for guidance with those previously reported. Ultimately, each facility should conduct its own risk-based assessments and validations regarding which practices are indicated, acceptable or feasible within that facility.

Methods

There are several terms that require definition in the context of this survey. “Sanitization” is defined as cleaning the surface to kill microorganisms that may be present. “General cleaning” is defined as cleaning of the facility and/or equipment that is regularly performed before and/or at the completion of processing as defined by each facility. “Extensive cleaning” can be thought of as “spring cleaning” and involves less frequent periodic heavy-duty cleaning and sanitization of walls, ceilings and other components. “General cleaning” of the biological safety cabinet, for example, may involve disinfecting and wiping it down before and/or after each use. Extensive cleaning may involve disassembling of the biological safety cabinets (BSC) and performing a more thorough deep cleaning and sanitization of each individual part. “Mopping” is defined as floor cleaning by means of a mop, soap and water or a mop handle and disposable sanitizing/cleaning pads.

The current survey questions were compiled in a fashion similar to the previous survey of 2005 by the members of the LPC under the leadership of Andrew Havens. The survey was submitted to memberships of ISCT, AABB and American Association of Tissue Banks. There were 108 respondent facilities (132 laboratories) in this survey compared with 55 respondents in the 2005 survey. The international distribution of the participants was 67% United States, 14% Canada, 12% Europe, 5% Australia/New Zealand and 2% Israel. The composition of the survey questions is described in Table I.

Table I. Survey composition by section and the number of questions asked in each section.

Survey section	No. of questions
General demographics, laboratory type, regulatory, quality standards, misc	14
General laboratory cleaning and reagents	8
Extensive laboratory cleaning, cleaning staff, training and supplies	10
BSCs	9
Equipment cleaning	12
Manufacturing lab accessories, clothing, personal protective equipment	12
Environmental monitoring	12

Results

Types of laboratories by air classification, products handled and regulatory status of products

In the current survey, 63 of 132 respondent laboratories (47%) reported having a standard laboratory (unclassified air); 43% have some form of classified/certified lab space (Figure 1A). In the 2005 survey, 49% reported the use of unclassified laboratory facilities, with 48% having some air classification. In this survey, a similar proportion of laboratories processing cellular products use standard (unclassified) laboratories. These results point to stability in the relative number of laboratories that use unclassified air conditions.