



## American Association of Tissue Banks

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March 29, 2013

European Commission  
DG Health and Consumers  
Unit D5 'Medicinal products – authorisations, EMA'  
SANCO-ADVANCEDTHERAPY-REPORT@ec.europa.eu

***In Re: Public Consultation on the Regulation on Advanced Therapy Medicinal Products***

Dear Madams and Sirs:

The American Association of Tissue Banks [hereinafter referred to as the “AATB” or the “Association”] submits these comments in response to your request for public consultation regarding the proposed Regulation 1394/2007 of the European Parliament and of the Council on Advanced therapy medicinal products and amending Directive 2001/83/EC.

### **I. THE INTEREST OF THE AATB**

The AATB is a voluntary, professional, scientific and educational organization. The Association is nonprofit and tax-exempt under Section 501(c)(3) of the United States Internal Revenue Code. It was founded in 1976 by a group of doctors and scientists who had started in 1949 the United States Navy Tissue Bank, our nation’s first tissue bank.

The AATB’s mission is public health. The Association is dedicated to ensuring that human tissues intended for transplantation are safe and free of infectious disease, of uniform high quality, and available in quantities sufficient to meet patient needs. To further that mission, the Association has, since 1984, published the only standards for tissue banks, the AATB’s *Standards for Tissue Banking*. This document, in its 13<sup>th</sup> edition, is the recognized authoritative source for the profession.

Beginning in 1986, the AATB initiated a voluntary Accreditation Program to ensure that tissue-banking activities are being performed in a professional manner in compliance with these *Standards*. All of the AATB’s institutional members must be accredited and re-inspected and re-accredited every three years. The Association’s membership currently includes nearly 1,000 individual members and more than 120 accredited tissue banks engaged in the recovery, processing, storage and/or distribution of human tissue. Annually, these tissue banks handle

tissue recovered from an estimated 30,000 donors and distribute in excess of 2 million allografts for transplant.

The AATB has consistently advocated and publicly supported balanced governmental regulation aimed at safeguarding human tissues from disease transmission. With the publication of the Food and Drug Administration's (FDA) first regulations in 1993 [62 *Federal Register* 40,429], the AATB publicly supported establishment of interim disease transmission requirements for human tissues. The Association continues to support reasonable U.S. Food and Drug Administration (FDA) regulation of tissue banking as well as reasonable recommendations provided by the U.S. Centers for Disease Control and Prevention (CDC) in the form of guidelines or recommendations.

The AATB's *Standards* contain extensive requirements for donor screening, testing, and processing to promote safety and avoid disease transmission. With the exception of ocular tissue, AATB-accredited banks provide most of the commonly used structural tissues for clinical use in the United States. The Association is, therefore, extremely interested in the proposed regulation and its potential effects on the supply of human tissue for transplantation.

While the Association primarily focuses on issues related to tissue distribution within the United States, given AATB-accredited tissue banks export tissue to more than 40 countries, including Member States of the European Union, the Association feels that it is important to provide information on this important topic.

## **II. RECOMMENDATIONS**

Given the interest of the AATB, the Association's comments will focus on ensuring that in enforcing the directive for advanced therapy medicinal products, authorities do not inadvertently adversely affect availability of human tissues currently covered by Directive 2004/23/EC of the European Parliament and Council.

***The AATB strongly urges The Commission to ensure that tissues and cells currently covered by standards of quality and safety in the Directive (and Commission Directives) 2004/23/EC and where applicable additional national jurisdiction in Member States of the European Parliament and the Council are unaffected by a decision to provide a framework for the marketing authorization for advanced therapy medicinal products (ATMPs).*** In creating Directive 2004/23/EC related to human tissues, the European Council recognized the transplantation of tissues and cells as a promising field of medicine offering excellent opportunities for the treatment of as yet incurable diseases. The high quality and safety standards for tissues and cells of human origin established by this directive aim to minimize the infection risk involved in transplant operations and therapies through the regulation of tissue and cell donation, procurement, testing, processing, preservation, storage and distribution. Since the

Directive came into effect in 2006, Member States have made progress in undertaking the requirements of the Directive, particularly in regards to inspections and monitoring. In reviewing the proposed framework and definitions, the Association has the following specific concerns.

**Explicitly exclude DBM.** The Directive should explicitly exclude demineralized bone matrix (DBM) added to a carrier agent as an ATMP whereas now they are regarded as “tissue” under Directive 2004/23/EC and further assessed under national law by each Member State.

**Provide greater detail regarding the transparent process.** The Association fully supports a transparent process for determining the regulation of ATMPs. Therefore, we are encouraged by provision (23) of the preamble which describes a process of seeking advice from the Agency; however, we hope that the Agency provides additional clarification about how that process will occur in future discussions.

**Add demineralization and decellularization to Annex 1.** Annex 1 describing manipulations which are not considered “substantial manipulation” does not include two common manipulations -- demineralization and decellularization. The Association encourages you to amend the Annex to incorporate these two common, non-substantial manipulations.

**Clarify intent of “concentration” in Annex 1.** Annex 1 also includes the descriptions “cell separation, concentration, or purification,” which are not well defined, especially related to concentration. Therefore, we suggest that you provide additional specificity regarding the intent.

**Exclude non-viable cells within key definitions.** Article 1.1 provides a definition of “combined advanced therapy medicinal product” which includes a reference to “non-viable cells” that seems overly broad and likely to incorporate products which are currently not regulated as ATMPs or combination ATMPs. Therefore, we request that you revise such definition to narrow the scope. If, however, you are unwilling to revise the scope, we strongly urge you to revise requirements related to clinical trials (detailed under Chapter 2, Article 4, Section 1), given that those currently may make it overly burdensome to provide allograft products with non-viable cells to the patient.

**Clarify the application of Article 2.2.** Article 2.2 states “[w]here a product contains viable cells or tissues, the pharmacological, immunological or metabolic action of those cells or tissues shall be considered as the principal mode of action of the product.” This statement should only apply as a derivative of Article 2.1 (b) or (c). If the statement in 2.2 is considered separately, it could have the potential effect on the provision of human tissue grafts with viable cells preserved for purposes of enhanced clinical outcome but where there is no systemic or metabolic effect (e.g., restricting the ability for the provision of fresh cartilage grafts).

**Encourage traceability for less than 30 years.** The Association strongly supports processes by which to provide appropriate traceability of human cells and tissues, and ATMPs. However, we are concerned with the requirement that such traceability is rather excessive when stating that records must be maintained “for a minimum of 30 years after the expiry date of the product, or longer if required by the Commission as a term of the marketing authorization.”.

**Provide final report before taking further action.** Finally, while the Association understands that you are performing this public comment period to comply with the requirements outlined in Article 24, Report and review, the AATB strongly urges you to ensure that the final report is available, including the “comprehensive information on the different types of advanced therapy medicinal products authorised pursuant to this regulation,” before taking any final action on this Directive. Without this public information, it will be difficult for the Association and others to ascertain whether this proposed directive for ATMPs inadvertently alters the current regulation of human tissues.

### **III. CONCLUSION**

The AATB thanks the European Commission for the opportunity to comment on the regulation of advanced therapy medicinal products. As was described at the outset, the AATB has a long and valued history of working with government entities to develop appropriate oversight and guidelines in this evolving field of medicine. These comments are intended to continue that collegial and cooperative spirit. The AATB stands ready and willing to assist the European Commission in any way you deem appropriate.

Sincerely,



Frank S. Wilton  
Chief Executive Officer