Burns & Trauma, 2020, 8, tkaa019
doi: 10.1093/burnst/tkaa019
Review

Review

A Review of Skin Banking Guidelines and Standards Worldwide: Towards the Harmonization of Guidelines for Skin Banking in Therapeutic Applications for the Regions under the Asia Pacific Burn Association (APBA)

Wee Ling Heng[1], Qi Wei Wang[1], Renuka Sornarajah[2], Jacynthe Tremblay[3], Nandita Melati Putri[4], Suzina Sheikh Ab Hamid[5], Pornthep Pungrasmi[6], Hsian-Jenn Wang[7], Dong Chul Kim[8], Daizo Saito[9], Nhu Lam Nguyen[10], Wan Azman Wan Sulaiman[11], Aditya Wardhana[4], Vinita Puri[12], Hajime Matsumura[13], Niann-Tzyy Dai[14], Rajeev B. Ahuja[15], Gaoxing Luo[16], Weifeng He[16], Si Jack Chong[1,17] and Alvin Wen Choong Chua[1,17,18,*],

[1]Transplant Tissue Centre, Singhealth Duke-NUS Transplant Centre, Singapore, [2]Heart Valve and Tissue Bank, Lady Ridgeway Hospital for Children, Dr Danister De Silva Mawatha, Colombo, Sri Lanka, [3]Jacynthe Tremblay Consultation, Quebec, Canada, [4]Burn Unit, Faculty of Medicine, Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, [5]Otorhinolaryngology-Head and Neck Surgery, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, Malaysia, [6]Plastic and Reconstructive Surgery Division, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, [7]Plastic and Reconstructive Surgery, Taipei Medical University, Taipei, Chinese Taipei , [8]Plastic and Reconstructive Surgery, Bundang Jesaeng Hospital, Seongnam, South Korea, [9]Division of Traumatology, Research Institute, National Defence Medical College, Saitama, Japan, [10]Vietnam National Burn Hospital, Hanoi, Vietnam, [11]Reconstructive Sciences Programme, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, Malaysia, [12]Department of Plastic Surgery, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Mumbai, India, [13]Department of Plastic and Reconstructive Surgery, Tokyo Medical University, Tokyo, Japan, [14]Division of Plastic and Reconstructive Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, [15]Plastic and Aesthetic Surgery, Sir Ganga Ram Hospital, New Delhi, India, [16]Institute of Burn Research, Southwest Hospital, Army Medical University, Chongqing, China, [17]Department of Plastic, Reconstructive and Aesthetic Surgery, Singapore General Hospital, Singapore and [18]Musculoskeletal Sciences Academic Clinical Programme, Duke-NUS Medical School, Singapore

*Correspondence. Email: alvin.chua.w.c@sgh.com.sg

Received 29 November 2019; Revised 16 February 2020; Editorial decision 10 April 2020

Abstract

Currently, there are no harmonized guidelines which govern skin banking in the Asia Pacific region. Therefore, skin banks are either unregulated or rely on their nation's legislation or international accreditation to uphold their quality standards. A new set of skin banking guidelines was developed through a comprehensive review and collation of best international practices for the Asia

Pacific Burn Association (APBA) members, from donor screening and testing, to skin recovery, processing, storage and distribution, and quality assurance. National regulatory requirements reviewed include the European directives, Australia's Therapeutic Goods Administration and Singapore's tissue banking standards. Further technical and quality management recommendations are referenced from the American Association of Tissue Banks (AATB), the United States Food and Drug Administration standards and guidance documents, various relevant European guides, Japanese Society of Tissue Transplantation guidelines and the Asia Pacific Association of Surgical Tissue Banking. Adapted mainly from the AATB standards, the new Asia Pacific Burn Association Guidelines for Skin Banking in Therapeutic Applications offer a comprehensive manual, addressing: governance and contracts; staff responsibilities; quality management; facilities, equipment and supplies management; donor consent and testing; and recommendations of good practices pertaining to skin recovery, processing, storage and distribution. Besides complementing current generic regulations, they provide technical specifications of major aspects unaddressed in most legislations. This inaugural set of new regional skin banking guidelines would be a start for regional members of the APBA to adopt, and will hopefully culminate in a set of standards so that, in the long run, skin allografts from this region can be of similar quality, which can simplify import process and facilitate the exchange of allografts between members.

Key words: Skin banking, Skin allografts, Skin transplantation, Tissue banking, Tissue donation

Background

Transplantation of skin allografts and skin banking has made tremendous progress in the past century within the clinical setting. Girdner first presented the successful therapeutic grafting using human allografts in 1881 [1]. In 1938, Bettman used the allogenic skin grafting procedure on paediatric patients with large full thickness burns [1–3]. It was only in 1949, when the US Navy Tissue Bank was established by Hyatt, that tissue banking officially started [3–6]. This marked a breakthrough in transplantation medicine. It began with the storage of surplus bones from orthopaedic surgeries, [4,5] and soon the application extended to the storage of other tissues, including skin. Life-saving stored skin allografts became available as temporary biological dressings for treatment of severely burnt patients, whose autografts were insufficient to provide coverage to their extensive wounds. After the US Navy Tissue Bank ceased operations in 1999, its legacy and contribution to public health continued as it had laid down many important standards. These standards on donor screening, tissue recovery, processing procedures and immunological concepts in transplantation are still observed in all regulated tissue banks around the world today. Another significant milestone was the founding of the American Association of Tissue Banks (AATB) in 1975, when Sell organized the Tissue Bank Symposium during its 25th anniversary reunion [4,5]. Sell became the founding President of the AATB and continued his role on the Board of Governors until he passed away in the late 1990s [7].

Review

Practice guidelines around the world

United States The United States Food and Drug Administration (US FDA) has two divisions that deal with different aspects of allografts. The Center for Biologic Evaluation and Research manages the regulation of tissue products for therapeutic treatment. The US FDA does not issue product standards or enforce compliance to specific technical standards, but regulates by providing evidence-based oversight, recommendation of good tissue practices and timely adverse reaction reporting to ensure US health institutions produce consistently safe products [8,9].

The US FDA began to regulate tissue transplantation in the early 1990s when the Centers for Disease Control and Prevention (CDC) reported the transmission of human immunodeficiency virus following tissue transplantation and became aware of the import of tissues with positive infectious diseases into the USA. This led the US FDA to publish an interim final rule in 1993 to curb disease transmission through contaminated tissues. After extensive consultation with the public, the final rule was passed in 1997. New requirements for infectious disease testing, donor evaluation and record keeping became mandatory. Due to the complexity of issues and the necessity to consult with the public and relevant stakeholders, the laws pertaining to tissue banking and transplantation were finally implemented in 2005 [10,11]. The regulatory framework that human cells, tissues and cellular and tissue-based products (HCT/Ps) establishments must comply with are: (1) *Title 21 of the Code of Federal Regulations (CFR) Part 1271 (21 CFR 1271)* [12]; (2) *Section 361 of the Public Health Service Act (42 U.S.C. 264)* [13,14], which contain regulations to control the transmission of communicable diseases; (3) *Human Cells, Tissues, and Cellular and Tissue Based Products; Donor Screening and Testing, and Related Labeling (72 FR 33667)* [15]; (4); *Eligibility Determination of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (69 FR 29786)* [16], the donor eligibility final rule which stipulates the donor eligibility criteria and testing;

(5) *Current Good Tissue Practice (CGTP) for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement (66 FR 68612)* [17], the CGTP final rule; and (6) *Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing (66 FR 5447)* [18], the registration final rule which enforces the need for registration of tissue banks with the FDA.

The US FDA also publishes non-legal binding guidelines to express its opinions and address frequently asked questions on specific issues. These include: (1) *Guidance for Industry—CGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)* [19]; (2) *Guidance for Industry—Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)* [20]; (3) *Guidance for Industry: Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271* [21]; and (4) *Guidance Document—Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271* [22].

All US tissue banks are regulated by the US FDA. Tissue banks which fall under the jurisdiction of the states of Florida and New York are subjected to additional oversight by the respective state [23]. Many tissue banks also seek voluntary accreditation by the AATB. For these banks, the US FDA provides the broad legislative oversight, while the AATB provides a framework which covers technical specifications, organizational management and quality management that guides tissue banks on the steps required to achieve regulatory compliance.

Since its founding, the AATB has continuously evolved to keep abreast with the US FDA's changing regulations. It maintains close collaboration with the US FDA via an ongoing exchange of information [24]. The first professional standard in tissue banking was published in 1984. In 1987, tissue-specific technical manuals (including skin) were launched [4], with an emphasis on donor screening and processing methodologies. The technical manuals were later incorporated into the seventh edition of the *AATB Standards of Tissue Banking* in 1996, followed by the inclusion of new quality management systems in tissue banking, which were adapted from the ISO 9001 Quality Management System [25,26]. From 1993 onwards, when the sixth edition of the AATB Standards was published, the College of American Pathologists and the Joint Commission on Accreditation of Hospitals began referencing AATB Standards and included essential tissue banking requirements, such as donor testing and ethical issues in tissue recovery, as well as adverse reactions reporting, into their own standards [25]. Apart from the US FDA, the AATB works closely with the CDC and the American Burn Association on steps to be taken when evaluating potential donors for emerging infectious diseases and disseminating the new guidelines quickly in the form of bulletins to all member tissue banks [4]. Unlike the other standards indicated in this article, which concentrate on managing clinical tissues for transplantation, the AATB also includes ethical guidelines for handling tissues for research [26,27].

Canada In Canada, the Biologics and Genetic Therapies Directorate, Health Products and Food Branch of Health Canada and the Canadian Standards Association (CSA) jointly regulate different aspects of cells and tissue banking and transplantation [28]. Health Canada's *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* (or CTO Regulations) is legally binding [29]. The purpose of the CTO Regulations is to minimize the potential health risks to Canadian recipients of human cells, tissues and organs for transplantation. As per the CTO Regulations, source establishments, establishments that distribute within Canada and establishments that import for further distribution are required to register with Health Canada and provide assurance that they are in compliance with the CTO Regulations. Relevant guidance documents provide further suggestive insights and allow for flexibility in the approach to achieving compliance, provided they are supported by appropriate justification [30]. The documents are: (1) *Guidance Document for Cell, Tissue and Organ Establishments, Safety of Human Cells, Tissues and Organs for Transplantation*, which addresses areas pertaining to donor screening and testing, tissue retrieval, microbiological testing, tissue processing and preservation and tissue importation, among others [30]; and (2) *Guidance Document for Source Establishments—Reporting Adverse Reactions to Human Cells, Tissues and Organs*, which focuses on errors, accidents and adverse reactions reporting and investigations [31]. Vigilance and surveillance are also under the oversight of Canadian Cell, Tissue and Organ Surveillance [23].

In the 1990s, the Canadian organ and tissue banks community was concerned with the lack of standards and regulations, and in the practices followed, as highlighted by the Commission of Inquiry on the Blood System in Canada [32]. In 1996, Health Canada began to address the need for regulations and the concerns of stakeholders by establishing a working group of experts to start and develop national safety standards for cells, tissues and organs for transplantation [33].

In 2000, CSA was tasked by Health Canada to develop national standards, which mainly focused on quality management systems to further enhance the safety and quality of cells, tissues and organs for transplantation. In June 2003, the CSA published a series of six documents: *CAN/CSA Z900.1-17 Cells, tissues, and organs for transplantation: General requirements*, and five specific standards for each tissue type, including *CAN/CSA Z900.2.2-17 Tissues for transplantation*. Those standards include aspects of safety for potential and actual donors and recipients, personnel and others who might be exposed to or affected by the transplantation of cells, tissues or organs. They described the importance of quality

assurance and quality control in the establishment of an effective quality management system for the banks [25]. The CTO Regulations refer directly to sections of the CSA standards, making them mandatory.

A few large-scale tissue banks also sought AATB accreditation to facilitate transnational tissue exchange with neighbouring US banks or healthcare institutions whenever clinical need arises.

Australia In Australia, the manufacturing of blood and tissues must meet the Therapeutic Goods Administration (TGA) standards: the Australian Code of Good Manufacturing Practice for Human Blood and Blood Components, Human Tissues and Human Cellular Therapy Products. This legislation emphasized the need to perform tissue recovery, processing and other activities in strict conformity with the principles of Good Manufacturing Practices [34]. This is implemented together with other standards stated in individual Therapeutic Goods Orders (TGO) that apply to specific products [35]. These encompass: (1) The Therapeutic Goods (Manufacturing Principles) Determination 2018 [36]; (2) TGO No. 86—Standards for Human Skin, which briefly describes some concerns unique to skin banking, such as the identification of a list of specific exclusion microorganisms which mandate discard, the acceptable storage temperatures and the corresponding maximum duration of storage [37]; and (3) TGO No. 88—Standards for donor selection, testing and minimizing infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products, which sets down standards on the age limits of donors supported by validation data, physical assessment of donor, archiving of donor serum and storage duration, compulsory nucleic acid testing (NAT), assessing for hemodilution in donors' blood, use of TGA-approved test kits and methodologies in infectious disease testing, as well as time limits for blood collection and donor tissue recovery [38].

Europe Europe has probably the most comprehensive tissue banking regulations. In addition, a wide range of guidance documents have been published by several European organizations, which cover European tissue banking standards as well as standards pertaining to preclinical risk assessment and post-transplant biovigilance and surveillance. Many of these guidance documents provide advice and are not necessarily legally binding.

From the early 1990s to 2000s, tissue banking was largely overseen by systems of self-regulation. The European Association of Tissue Banks (EATB) was formed in 1991 and was instrumental in developing essential standards that led to voluntary regulation of tissue banking, collaboration and exchange of information between banks in the various European nations [39]. EATB began to collaborate with the AATB in 1992 and published the *EATB Standards for Skin Banking and Banking of Skin Substitutes* in 1998 [40]. In 1996, it cohosted the First World Conference in Tissue Banking with the Asia Pacific Association of Surgical Tissue Banking (APASTB) [39]. The British Association of Tissue Banking and the Spanish Association of Tissue Banks (Asociación Española de Bancos de Tejidos) were also set up to meet the needs of their respective countries [41], in addition to the prevailing legislations, such as the United Kingdom Human Tissue Authority's regulations [42] and the Spanish Decree [43].

European Union directives In 2004, European nations which were members of the European Union (EU) set down a common set of standards: the *European Union Tissue and Cells Directives (EUTCD)* [44]. These standards are in force in the 27 EU member states. The key objective of the EUTCD are to align the quality and safety standards of donation, recovery, testing, processing, preservation, storage and distribution of human tissues and cells across all EU states [45]. These Directives help to ensure harmonization of quality and safety standards and enables each member state to transpose these Directives into their own domestic law as "no one law can fit all" [43].

The EUTCD comprises of three Directives, and requires member states to achieve specific outcomes without dictating the way to accomplish them: (1) the Parent Directive, *2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells*, provides the framework legislation and overview [45]; and two technical directives, (2) *2006/17/EC of implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells* [46] and (3) *2006/86/EC of implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells* [47], provide in-depth requirements on specific aspects. In addition, there are three Commission Directives with amendments: (1) *2012/39/EU amending Directive 2006/17/EC* [48]; (2) *2015/565 amending Directive 2006/86/EC* [49]; and (3) *2015/566 implementing Directive 2004/23/EC* [50].

In order to achieve the EUTCD's outcomes, European states have joined hands to establish other quality management and vigilance systems, including the following.

(1) European Quality Systems in Tissue Banking

From 2004 to 2008, this EU-funded project was developed to produce a guide of technical specifications and an audit tool [23]. It was the first program for European community action in this area [51].

(2) Council of Europe Directorate for the Quality of Medicines & HealthCare (EDQM)

In 2013, the Council of Europe, which is made up of 47 European countries (27 of whom are also in the EU), published a comprehensive guidance document: the *Guide to the Quality and Safety of Tissues and Cells for Human Application* [52]. Currently in its fourth edition, it details expected quality and safety standards, explanations of the scientific principles quoting real-life scenarios as examples and technical recommendations on how to implement the EUTCD. There are ongoing discussions to include the EDQM Tissues and Cells Guidelines into the European Pharmacopoeia (personal communication with Dr Sornarajah). Such an initiative will result in greater harmonization of quality standards and promote exchange of tissues between countries [6], as the standards will become mandatory in the 47 member states.

(3) Euro-GTP II guide

The European Good Tissue Practices project was funded by the EU's Health Programme. Unlike the abovementioned standards and guides, which cover critical aspects of tissue banking, this guidance, *Euro-GTP II Guide – Good Practices for Evaluating Quality, Safety and Efficacy of Novel Tissue and Cellular Therapies and Products*, [53] focuses on the use of assessment tools in evaluating preclinical risk, and the quality and safety of critical processes that will impact the tissues and cells used in patient treatment.

(4) Biovigilance and surveillance programmes

Biovigilance is defined as the surveillance of adverse events and reactions relating to the use of tissues and cells. Surveillance is a public health activity aimed at reducing morbidity and mortality of the population [43].

The *EU Standards and Training for the Inspection of Tissue Establishment Project (EUSTITE)*, which was launched in 2009, is a landmark for the field of cell and tissue banking. Besides harmonization of technical processes, which many of the abovementioned standards strived to achieve, EUSTITE also seeks to promote standardization of inspection and vigilance processes followed by regulatory bodies and medical establishments (including tissue banks) in the EU, and create common systems for classifying, investigating and reporting serious adverse events and reactions [54].

Evolved from the EUSTITE project, the Vigilance and Surveillance of Substances of Human Origin (SOHO V&S) project was initiated in 2013. Published guidance documents provide real-life examples of what constitutes serious adverse events and reactions associated with the human application of tissues and cells, discusses the importance of investigation, appropriate follow-up actions and documentation and encourages communication between European countries for the purpose of discussion, early warning of potential incidents and quality improvement [55,56]. The project implemented essential an feedback mechanism to ensure that tissues and cells are processed appropriately, thereby maintaining tissue quality and promoting patient safety.

Other international guidelines As US, Europe and Australia were developing their own respective sets of tissues and cell banking regulations, the International Atomic and Energy Agency (IAEA) also published its own *International Standards for Tissue Banks* and *Guide for Legal and Regulatory Control* [25], based on the current standards followed by the US and EU [57]. It was authored by the IAEA expert committee and various key tissue bank specialists from the Asia Pacific region, who went on to establish the APASTB *Standards for Tissue Banking*. Published in 2003, the IAEA standards were referenced by 30 countries throughout Latin America, Asia, the Middle East and Africa [25]. This was helpful as tissue banking regulations in these nations are either underdeveloped or nonexistent. The IAEA standards reflect ideal practices relating to the management and operation of tissue banks [57].

In Central and South America, some tissue banks also follow the guidelines by the Latin American Tissue Banking Association (Asociación Latinoamericana de Bancos de Tejidos).

Prior to the time when a formal quality program was recognized as imperative, most banks adopted the ISO 9000 family of quality management standards. The AATB referred to and incorporated the ISO 9000 standards and its quality assurance and quality control recommendations into its own Standards in its seventh edition in 1996 [26]. The *ISO 9001:2015 Quality Management System* sets out quality management requirements to help organizations be more efficient and improve customer satisfaction by ensuring a traceable standardized quality system [6]. Hence, the emphasis is on developing a strong customer focus, quality improvement and delivery of consistently good quality products and services. The *ISO 19011:2018 Guidelines for Auditing Management Systems* focuses on conducting internal and external audits in accordance with ISO 9001 [58, 59].

The World Health Organization's regulations, *Aide-Memoire on Key Safety Requirements for Essential Minimally Processed Human Cells and Tissues for Transplantation* [60] and *Resolution WHA63.22 – Human Organ and Tissue Transplantation* [61], are based on the principle of noncommercialization of human cells, tissues and organs for transplantation [62]. In addition, it also addresses ethical issues relating to tissue recovery for transplantation, procedures to be followed in order to uphold the quality and safety of tissues, and encourages collaboration in information sharing, especially with regards to adverse events and post-transplantation adverse reactions.

Asia Tissue banking in the Asia Pacific regions is driven by two main organizations: the IAEA and the APASTB [63]. The APASTB standards were adapted from major international standards, with the first edition based on the standards prepared by the IAEA expert committee, with the aim of harmonizing tissue banking standards for all tissue types in Asia for all its member banks.

In Singapore, tissue donation follows the *Medical, Therapy, Education and Research Act 1972*, whereby any person with no mental disorder and of a minimum age of 18 years may donate all or any part of his or her body for the purpose of transplantation, education and/or research [63]. In 2003, the Ministry of Health released *Guidelines for Healthcare Institutions Providing Tissue Banking: Regulation 4 of the Private Hospitals and Medical Clinics Regulations* [64], providing a basic overview on the aspects of staffing and organizational requirements, facilities, donor consent and selection, quality assurance, tissue retrieval, processing and storage practices and tissue importation.

In most Asian countries, the need to deter commercialization of organs and tissues has resulted in legislation which focuses largely on regulating organ donation and detailing the legal requirements to obtain proper donor consent before transplantation of human organs and tissues. For instance in India, the *Transplantation of Human Organs and Tissues Act, 1994* marked a major milestone in the regulation of tissue banks in India as, for the first time, tissues were recognized as a separate entity from organs. The act was later amended to include regulation of tissues [65,66]. In South Korea, the *Safety, Management, Etc. of Human Tissue Act*, enacted in 2004, focuses on donor selection, and briefly touches on the quality control, documentation and importation of tissues [67].

Legislation in many Asian countries also does not address technical specifications or the quality management of tissue banking. To overcome this problem, Bangladesh's only tissue bank, the Tissue Banking and Biomedical Research Unit for instance, follows the IAEA, EATB and AATB guidelines [68]. In Japan, the Japanese Society of Tissue Transplantation (JSTT) consolidated more comprehensive guidelines in the Asia Pacific region and published three tissue banking related documents: (1) *Guideline on the Safety, Storage, and Application of Human Tissue in Medical Practice* [69]; (2) *Guideline on Ethical Issues in Application of Human Tissue to Medical Practice* [70]; and (3) *Basic Standards for Operating A Human Tissue Bank* & *Quality Assessment Form* [71].

Harmonizing skin banking guidelines in the Asia Pacific region On 10 February 2018, the Singapore General Hospital Skin Bank Unit, hosted an initial planning conference in Academia (Singapore) with the aim of formulating a set of Asia Pacific Skin Banking Guidelines for the Asia Pacific region. The 11 participating members for this initiative include Bangladesh, China, India, Indonesia, Japan, South Korea, Malaysia, Singapore, Chinese Taipei, Thailand and Vietnam. Every member agreed that having a common set of skin banking guidelines opens up research, education and clinical collaboration opportunities. In addition, during humanitarian crises, different countries can collaborate and support each other with skin allografts, knowing all are conforming to a set of common guidelines.

The inaugural workgroup meeting for the Asia Pacific Skin Banking Guidelines, co-chaired by Professor Weifeng He (China) and Assistant Professor Alvin Chua (Singapore), was held in Chongqing, China at the Radisson Blu Hotel on 18 May 2018. This meeting was hosted by Professor Gaoxing Luo, Director of the Burns Institute at the Southwest Hospital of the Army Military Medical University China, and his team. The discussion during this meeting was fruitful, as the first draft of the Asia Pacific Skin Banking Guidelines was successfully formulated, serving as a good foundation for further expansion and improvement of the harmonization exercise.

The second workgroup meeting was held in Taipei on 10 August 2018, hosted by Professor Niann-Tzyy Dai, Director of the Division of Plastic and Reconstructive Surgery at the National Defense Medical Center, Tri-Service General Hospital Chinese Taipei. This was another productive meeting as all participating members present went through the updated draft guidelines point by point and provided many valuable suggestions, taking into account the situations and context of their respective countries. During this meeting, all members agreed that this first set of skin banking guidelines should be broad-based and not prescriptive, as it would serve as a basis for a more detailed set of technical guidelines in the future.

After finalizing all the necessary inputs and suggestions put forth by all members from the first and second workgroup meetings, the final draft of the Asia Pacific Skin Banking Guidelines was presented by Assistant Professor Alvin Chua in New Delhi on 30th November 2018 on behalf of the workgroup to the Steering Committee. This Committee—chaired by Associate Professor Si Jack Chong in his capacity as President of the Asia Pacific Burn Association (APBA)—agreed with the majority of the guidelines and recommended: (1) the expansion of international standards for skin banking that the guidelines can choose to adopt and; (2) to state clearly the different types of licenses required during the importation of skin.

The final draft of the guidelines had undergone the final round of approval from all members before its promulgation in August 2019. The Guidelines was officially launched on 16 August 2019 at the 12th Asia Pacific Burn Congress held in Singapore.

The guidelines and technical and quality recommendations were formulated based on a comprehensive review of the European EUTCD; standards and guidelines from the US FDA, Australia's TGA and Ministry of Health Singapore; published guidance from the AATB; the various European guides, especially the Council of Europe's EDQM; and the APASTB and JSTT guidelines.

The new *APBA Guidelines for Skin Banking in Therapeutic Applications* was developed on the assumption that all the APBA's banks have the capacity and resources to follow the recommendations which have been set down. It assures that the minimum basic documentation of the quality management system, present in most established guidelines, is in place. This includes compliance with the relevant state regulations; oversight in quality management by responsible personnel; a quality system; contracts; process control;

presence of standard operating procedures and data control; delineated staff responsibilities and training to ensure competency in skillsets; information on donors and tissues at every stage of processing and their final destination; traceability; inspection and testing; equipment and material management; facilities monitoring and maintenance; corrective and preventive actions; and quality review [25,40].

Adapted largely from the AATB standards, European parent Directive 2004/23/EC and JSTT guidelines, the new *APBA Guidelines for Skin Banking in Therapeutic Applications* offer a comprehensive manual that addresses: governance and contracts; staff responsibilities; quality management; facilities, equipment and supplies management; donor consent and testing; and recommendations of good practices pertaining to skin recovery, processing, storage and distribution. Complementing the current generic regulations are additional technical and quality management specifications of major critical aspects, which are not addressed in most Asian legislation, such as: (1) diseases and infections contraindicated for donation; (2) reconstruction of donors' body postrecovery; (3) accreditation of testing laboratories; (4) archiving of donor serums for the purpose of future testing; (5) corrective and preventive actions procedure; (6) recall procedure; (7) environmental monitoring of skin-processing facilities; and (8) process validations prior to implementation of critical processes. (*Appendix 1*).

Discussion

The application of tissues for transplantation has increased in recent years. Transparency, evidence-based standards, consistency in the quality of human grafts and services and operation within an ethical framework are required to maintain the public's trust in state healthcare systems [62]. Upholding this is especially crucial for the Asia Pacific regions, where the public's resistance to tissue donation upon death and a misunderstanding of, and lack of trust in, the healthcare systems is widespread. Interestingly in Japan, despite potential conflicts of interest, physicians who are treating the potential recipient are permitted to seek consent for donation from the next of kin of a potential donor, in the presence of a witness. This probably reflects the level public trust in the Japanese healthcare system [69]. Other Asian countries should aim to increase public trust in order to promote tissue donation.

Currently, there are no harmonized guidelines for quality management which apply to APBA member skin banks. Member banks ensure safety of therapeutic skin allografts either by relying on the legislation of their state, which may be nonexistent, or inadequate at best, or seek prestigious international accreditation, such as from the AATB. Currently, in the event of a dispute, the version of the Asian standards written in the local languages is regarded as more authoritative than the English versions [67]. Hence, for the sake of harmonization and common understanding, this makes it all the more necessary for the new guidelines to be written in a clear and concise manner and in a common language, such as English. The guidelines have been drafted to allow some flexibility in the manner in which they can be implemented.

Most Asian countries have basic laws that govern the ethical aspects of consent-taking for tissue donation to curb commercial organ/tissue trading and encourage the reporting of post-transplantation adverse reactions. The problem with these non-specific laws is they are often combined with regulations for organ donation, which may not be applicable.

Many Asian tissue banks find it difficult to afford the high cost of international accreditation and ongoing costs to maintain accreditation. Also, for many banks, there is no real benefit to obtain and maintain accreditation, as hospitals in most Asian countries continue to obtain tissues from unaccredited banks. The costs of accreditation and maintenance, and periodic reaccreditation inspections on top of the regular audits by regulatory bodies in the respective states, is a major strain for smaller banks with less financial resources and manpower [11]. Another limitation is the mandatory compliance to guidelines which may not apply within the Asian context.

For example, Singapore's experience in attaining AATB accreditation for their tissue bank was challenging [72]. Examples include the requirements to: (1) comply with infectious disease testing methods using US FDA–approved cadaveric donor screening kits; (2) test for communicable diseases which are rare or nonexistent in Singapore, such as human T-cell lymphocytic virus (HTLV); and (3) engagement of testing labs certified by Clinical Laboratory Improvement Amendments (CLIA) and the US FDA's 42 CFR part 493, as there are very few CLIA-certified labs outside of the USA [9]. However, the AATB did accept most of the proposals by the Singapore tissue bank seeking justification for noncompliance. Their acceptance was based on the fact that local laboratories in Singapore lacked the capacity to perform specific tests, the irrelevance of these requirements in the local context and the fact that tissue grafts recovered from Singapore would not be exported to the USA.

In the new harmonized set of guidelines there is an emphasis on donor screening and testing. This is due to the higher inherent risk associated with tissue recovery from deceased donors as compared to living donors. Information to assess a donor's health status is obtained from family members, that is, third parties, which may not be accurate. This limitation means there must be a greater reliance on accurate laboratory testing. Nevertheless, the importance of identifying recent infections, which can be undetectable during the window period, should not be underestimated. Blood collected postmortem is subject to unique considerations, such as time lapse from death to collection, volume, extent of haemolysis, presence of hemodilution and integrity of blood samples [73]. To ensure reliable test results, this is why US, Australian and European facilities performing organ and tissue transplantation specifically require the use of test kits that are US FDA-approved, TGA-approved or with Certification Mark (CE-marked) which indicates that the test kits are manufactured in compliance with health, safety, and environmental protection

standards stipulated by the European Economic Area (EEA), respectively.

The new guidelines separate clauses to allow for flexibility to determine which diseases to screen for in different centers. Actual transmission of infectious agents can be categorized into three areas: (1) agents requiring mandatory tests, which all donors worldwide must be screened for, as the microorganisms are present around the world and transmission will have serious adverse effects on recipients; (2) agents requiring discretionary tests, which are only for donors who have been exposed to potential risks, for instance, when they live or visit a country where the disease in question is endemic, or present with suspected signs of infection; and (3) rare or unknown conditions, which are handled on a case-by-case basis. Stored archived serum can be potentially very useful in these cases [73].

The new guidelines also state that the skin banks shall exercise prudence in determining which tests are required for all donors and which should be discretionary according to prevalence and the impact of transmission. Some infections, including cytomegalovirus (CMV), do not fall into the "mandatory test" category even though they are significant for organ transplant recipients, and are "easily transmissible" to immunocompromised burns patients. This is because there is little evidence that this seroconversion will have any clinical impact. The benefit of using skin allografts for life-saving treatment hugely outweighs the minute risk of CMV transmission [4].

Another example is HTLV. Under the AATB standards, HTLV I and II testing is a mandatory test for all tissue donors [74] However, it was amended to a "discretionary test" for all donors of viable leukocyte-rich tissue, or if it was deemed to be required by state regulation [75]. For Australian banks, it remains a mandatory test according to state law [38]. Being the first oncogenic human retrovirus to be discovered, the prevalence of HTLV remains low. However, clusters of endemicity exist throughout the world, including Japan [76], hence the necessity of screening Japanese donors for the presence of HTLV [67]. Similarly, donors testing positive for parvovirus B19 are also contraindicated in Japan and member banks following the APASTB guidelines. This is because parvovirus B19 infections can occur following blood transfusion and transplantation. It can cause significant morbidity, presenting as refractory anaemia in immunocompromised organ transplant recipients [77]. For other Asia Pacific countries, such as Singapore, donors are not tested as these infections are extremely rare.

In Singapore, besides conforming to the AATB's requirement of malaria screening, further steps are taken to exclude any clinical history and manifestation of dengue as well. It is included in the guidelines because dengue fever is rampant in tropical and subtropical countries, including many Asian countries. Despite rare occurrence of transmissions [78] following transplantation of grafts, there have been reported cases of dengue transmission through solid organ transplantation [79,80] and blood transfusion [81], increasing post-operative risk of thrombocytopenia, haemorrhage and other associated comorbidities in immunocompromised patients [79]. As there is no specific antiviral drug to treat dengue infections and there is evidence of serious adverse reactions due to transmission to recipients [78], it is recommended that all donors in dengue-endemic regions be tested using the dengue PCR method. Zika and Chikungunya are two other related mosquito-borne infections. While the latter is associated with mild illness [78], the former poses new public health challenges due to its apparent correlation with severe congenital microcephaly and neurological implications [82]. The necessity of Zika testing should also be evaluated with proper consideration, as little is known about the risk of transmission in transplantation. At present, only an expensive Zika PCR method can be used for testing as cadaveric serological test kits are not currently available. In Europe, most tissue banks take a precautionary approach and have developed screening criteria in their donor history questionnaires to detect and defer donors with recent travel history to Zika-endemic regions (e.g. Latin America and Asia). Nevertheless, the US guidelines recommend that the risk of such donor-derived infection should be reviewed based on a risk-versus-benefit assessment, instead of outright deferment, to avoid unnecessarily depriving life-saving allografts to recipients [78].

While the new guidelines do not stipulate a need for molecular screening using NAT, it is recommended to use NAT in conjunction with, not as a replacement, mandatory serological testing. This is because, while NAT offers higher sensitivity in detecting early infection within the window period, serological tests are more effective in revealing existing and previous infections [73], providing a more complete overview of the health status of donors. Currently, US and Australian standards mandate NAT, while the other established standards or guidelines strongly advocate its use.

Although it is not mentioned in the guidelines, it is suggested to formalize time limits for skin recovery and preservation in the standard operating procedures. Realistic shortest possible time limits for the various processes should be formulated based on best practices and the in-house validation of the tissue banks to support the preservation of biological properties of tissues and slow down the rate of intraluminal bacterial translocation to the rest of the body after death. This can be challenging for larger countries, where recovery centers and processing laboratories are far apart and the logistics of transportation may be hard to control. Establishing a postrecovery time limit is critical, as a delay in the removal of tissues from deceased donors can result in a higher risk of bacterial translocation from the gastrointestinal tract to the tissues and blood, thus increasing the probability of contamination by resistant pathogens. Eastlund reported a rise in the rate of positive blood culture results from deceased donors when the time after death became greater [83]. Hence, most banks complete tissue recovery within 24 hours of death of the donor, while some more stringent professional standards, like those of the AATB, require recovery to take

place within 15 hours of death if the body is not refrigerated within 12 hours of death [26].

These guidelines serve as minimum requirements to help member skin banks kickstart the processes that lead to better quality management of services and products. As these guidelines are only the beginning, with the aim of getting all APBA members to agree on the basic principles and practices on skin banking, the next step is to come out with more detailed technical guidelines on skin banking for the region. This will be done using a stepwise approach by the various APBA members. The aim is for such a plan to be presented for discussion at the APBA central committee meeting in May 2021. Various experts will be assigned to spearhead the reviewing and finetuning of the various key processes. Once these non-mandatory guidelines are adopted by a majority of the skin banks within the APBA members' jurisdictions, a set of skin banking standards under APBA will then be considered in terms of mechanisms for review of policies, oversight, resources, personnel and role of government and other agencies. However, at this juncture, this is not being considered as it will depend on the adoption rate of the recently promulgated skin banking guidelines.

Conclusion

With the set of inaugural skin banking guidelines established (*Appendix 1*), it is hoped that these will pave the way for harmonized standards for the region that can facilitate the provision of uniform-quality skin allografts among the regional members of the APBA. This in turn will simplify the import process when skin allografts are transferred between them. Maintaining similar quality and safety principles for procured, processed and stored tissue will help to fulfil the altruistic wishes of donors and donor families who aim to give a new lease of life to other patients and ensure all recipients have access to similar quality grafts in times of clinical need.

Supplementary data

Supplementary data are available at Burns & Trauma.

Abbreviations

AATB: American Association of Tissue Banks; US FDA: United States Food and Drug Administration; CDC: Centers for Disease Control; HCT/Ps: human cells, tissues and cellular and tissue-based product; CFR: Code of Federal Regulations; CSA: Canadian Standards Association; CTO Regulations: Health Canada's Safety of Human Cells, Tissues and Organs for Transplantation Regulations; TGA: Therapeutic Goods Administration; NAT: nucleic acid testing; EATB: European Association of Tissue Banks; APASTB: Asia Pacific Association of Surgical Tissue Banking; EU: European Union; EUTCD: European Union Tissue and Cells Directives; EUSTITE: EU Standards and Training for the Inspection of Tissue Establishment Project; IAEA: International Atomic and Energy Agency; APBA: Asia Pacific Burn Association; HLTV: human T-cell lymphocytic virus; CLIA: Clinical Laboratory Improvement Amendments; CMV: cytomegalovirus; PCR: polymerase chain reaction.

Acknowledgements

The authors are grateful to the organizers of the various cities—Singapore, Chongqing, Taipei and New Delhi—for kindly hosting the Working Group Committee and the Steering Group Committee meetings so that the first edition of *Guidelines for Skin Banking in Therapeutic Applications (Appendix 1)* was made possible for APBA. In addition, the authors would like to thank Professor Aziz Nather from National University Hospital, Singapore, for sharing the second edition of the APASTB as a reference.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Authors' contributions

NMP, SSAB, PP, HJW, DCK, DS, NLN, WAWS, AW, VP, HM, NTD, RBA, GXL, WFH, SJC and AWCC all contributed equally to conception and design and acquisition of data. WLH and QWW drafted the manuscript. RS, JT, SJC and AWCC revised it critically for important intellectual content. All authors approved the final manuscript version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

This study was exempt from institutional review board approval.

Conflicts of interest

None declared.

References

1. Dziewulski P, Wolf SE. The use of allograft skin in burn surgery. In: Warwick RM, Brubaker SA (eds). *Tissue and Cell Clinical Use – An Essential Guide*. United Kingdom: Wiley-Blackwell, 2012, 236–57.
2. Carter JE, Holmes JH. The surgical management of burn wounds. In: Albanna M, Holmes JH (eds). *Skin Tissue Engineering and Regenerative Medicine*. USA: Elsevier Inc. Academic Press, 2016, 289–98.
3. Voigt CD, Williamson S, Kagan RJ, Branski LK. The skin bank. In: Herndon DN (ed). *Total Burn Care*, 5th edn. Netherlands: Elsevier Inc, 2018, 158–66.
4. Strong DM. The contribution of Kenneth W. Sell to the progress of tissue banking. In: Philips GO, Von Versen R, Strong DM,

Nather A (eds). *Advances in Tissue Banking*, Vol. 2. Singapore: World Scientific, 1998, 1–19.
5. Strong DM. The US Navy tissue bank: 50 years on the cutting edge. *Cell Tissue Bank*. 2000;1:9–16.
6. Tognetti L, Pianigiani E, Ierardi F, Mariotti G, Perrotti R, Di Lonardo A, *et al*. Current insights into skin banking: storage, preservation and clinical importance of skin allografts. *Journal of Biorepository Science for Applied Medicine*. 2017;5:41–56.
7. Joyce MJ. American Association of Tissue Banks – the present and future. In: Philips GO, Von Versen R, Strong DM, Nather A (eds). *Advances in Tissue Banking*, Vol. 2. Singapore: World Scientific, 1998, 29–35.
8. Fragale DA. Regulatory models for safety and quality of allografts: USA (heart valves). In: Philips GO, Von Versen R, Strong DM, Nather A (eds). *Advances in Tissue Banking*, Vol. 1. Singapore: World Scientific, 1997, 13–21.
9. *Tissue & Tissue Products*. Available at: https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products. 2019 Accessed 3 Jun 2019.
10. *FDA Regulation of Human Cells and Tissues*. Available at: http://www.fda.gov/media/81676/download. Accessed 30 May 2019.
11. *US Department of Health and Human Services, Office of Inspector General – Oversight of Tissue Banking*. Available at: http://www.hhs.gov/oig/oei. 2001 Accessed 10 Jun 2019.
12. *CFR – Code of Federal Regulations Title 21*. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=1271. 2019 Accessed 30 May 2019.
13. *42 U.S.C. §264. Regulations to Control Communicable Diseases* Available at: https://www.govinfo.gov/content/pkg/USCODE-2011-title42/html/USCODE-2011-title42-chap6A-subchapII-partG.htm. 2011 Accessed 24 Sep 2019.
14. *FDA Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P's) Product List*. Available at: https://www.fda.gov/vaccines-blood-biologics/tissue-tissue-products/fda-regulation-human-cells-tissues-and-cellular-and-tissue-based-products-hctps-product-list. 2018 Accessed 30 May 2019.
15. *Human Cells, Tissues, and Cellular and Tissue-Based Products; Donor Screening and Testing, and Related Labeling*. Available at: https://www.federalregister.gov/documents/2007/06/19/E7-11795/human-cells-tissues-and-cellular-and-tissue-based-products-donor-screening-and-testing-and-related. 2007 Accessed 30 May 2019.
16. *Eligibility Determination of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products*. Available at: https://www.federalregister.gov/documents/2004/05/25/04-11245/eligibility-determination-for-donors-of-human-cells-tissues-and-cellular-and-tissue-based-products. 2004 Accessed 30 May 2019.
17. *Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and Enforcement*. Available at: https://www.federalregister.gov/documents/2004/11/24/04-25798/current-good-tissue-practice-for-human-cell-tissue-and-cellular-and-tissue-based-product. 2004 Accessed 30 May 2019.
18. *Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing*. Available at: https://www.federalregister.gov/documents/2001/01/19/01-1126/human-cells-tissues-and-cellular-and-tissue-based-products-establishment-registration-and-listing. 2001 Accessed 30 May 2019.
19. *Guidance for Industry – Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)*. Available at: https://www.fda.gov/media/82724/download. 2011 Accessed 30 May 2019.
20. *Guidance for Industry – Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)*. Available at: https://www.fda.gov/media/73072/download. 2007 Accessed 30 May 2019.
21. *Guidance for Industry: Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271*. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigating-and-reporting-adverse-reactions-related-human-cells-tissues-and-cellular-and-tissue. 2016 Accessed 30 May 2019.
22. *Guidance Document – Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271*. Available at: https://www.fda.gov/media/107703/download. 2017 Accessed 30 May 2019.
23. Brubaker SA, Fehily D. Development of vigilance and surveillance systems. In: Warwick RM, Brubaker SA (eds). *Tissue and Cell Clinical Use – An Essential Guide*. USA: Wiley-Blackwell, 2012, 48–71.
24. Joyce MJ. American Association of Tissue Banks: a historical reflection upon entering the 21st century. *Cell Tissue Bank*. 2000;1:5–8.
25. Brubaker SA. Establishing a quality system. In: Galea G (ed). *Essentials of Tissue Banking*. Netherlands: Springer Science & Business Media, 2010, 191–215.
26. American Association of Tissue Banks. *Standards for Tissue Banking*, 14th edn. 2016.
27. *AATB Non-transplant Anatomical Donation Organizations (NADOs) Guidance Documents*. Available from: https://www.aatb.org/standards/nado-guidance-documents. Accessed 24 Sep 2019.
28. *Cells, Tissues and Organs*. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/information-health-product/cells-tissues-organs.html. Accessed 7 Jun 2019.
29. *Profile Page for Guidance Document for Cell, Tissue and Organ Establishments – Safety of Human Cells, Tissues and Organs for Transplantation*. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/regulatory-initiatives/cells-tissues-organs/guidance-document-safety-human-cells-tissues-organs-transplantation.html. Accessed 7 Jun 2019.
30. *Guidance Document for Cell, Tissue and Organ Establishments, Safety of Human Cells, Tissues and Organs for Transplantation*. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/regulatory-initiatives/cells-tissues-organs/guidance-document-safety-human-cells-tissues-organs-transplantation/document.html. Accessed 7 Jun 2019.
31. *Guidance Document for Source Establishments – Reporting Adverse Reactions to Human Cells, Tissues and Organs*. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submi

ssions/guidance-documents/reporting-adverse-reactions-human-cells-tissues-organs.html. Accessed 7 Jun 2019.
32. *Final report / Commissioner: Horace Krever* Available from: http://publications.gc.ca/site/eng/9.646740/publication.html. Accessed 19 Sep 2019.
33. *The Evolution of Eye Banking and Regulatory Standards in Canada* Available from: http://eyebankingjournal.org/wp-content/uploads/2015/12/53-1040-1-PB.pdf. Accessed 19 Sep 2019.
34. Therapeutic Goods Administration. *Australian Code of Good Manufacturing Practice for Human Blood and Blood Components, Human Tissues and Human Cellular Therapy Products*, version 1.0; April 2013. https://www.tga.gov.au/sites/default/files/manuf-cgmp-human-blood-tissues-2013.pdf. Accessed 12 Jun 2019.
35. Wright C, Velickovic Z, Brown R, Larsen S, MacPherson JL, Gibson J, *et al*. Raising the standard: changes to the Australian code of Good Manufacturing Practice (cGMP) for human blood and blood components, human tissues and human cellular therapy products. Pathology. 2014;46:177–83.
36. *Therapeutic Goods (Manufacturing Principles) Determination 2018*. Available from: https://www.legislation.gov.au/Details/F2017L01574. Accessed 12 Jun 2019.
37. *Therapeutic Goods Order No. 86 – Standards for Human Skin (08/07/2011)*. Available from: https://www.legislation.gov.au/Details/F2011L01492. Accessed 12 Jun 2019.
38. *Therapeutic Goods Order No. 88 – Standards for donor selection, testing, and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products*. Available from: https://www.legislation.gov.au/Details/F2013L00854. Accessed 12 Jun 2019.
39. *History of the European Association of Tissue Banks (EATB)* Available from: https://www.eatb.org/images/pdf/1.3history_of_eatb.pdf. Accessed 31 May 2019.
40. Monig HJ, Versen RV. Standards, Regulatory and Quality Systems, Within a Global Context. In: Philips GO, editor. *Radiation and Tissue Banking (IAEA)*. World Scientific. 2000. p. 1–55.
41. Freelander E, Boyce S, Ghosh M, Ralston DR, MacNeil S. Skin banking in the UK: the need for proper organisation. *Burns* 1998; 24: 19–24.
42. *Human Tissue Authority – Guidance for Professionals*. Available from: https://www.hta.gov.uk/guidance-professionals. Accessed 24 Sep 2019.
43. Marazuela R, Garrido G, Matesanz R. European Union and Spanish regulations on quality and safety of tissues and cells: overview and biovigilance. *Transplant Proc* 2009; 41: 2044–6.
44. *European Union. EU Tissue and Cells Directives*. Available from: https://www.hta.gov.uk/policies/eu-tissue-and-cells-directives. Accessed 10 Jun 2019.
45. European Union. *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells*. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:en:PDF. Accessed 10 Jun 2019.
46. European Union. *Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells* Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:038:0040:0052:EN:PDF. Accessed 10 Jun 2019.
47. European Union. *Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells*. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:294:0032:0050:EN:PDF Accessed 10 Jun 2019.
48. European Union. Commission Directive 2012/39/EU of 26 November 2012 amending Directive 2006/17/EC as regards certain technical requirements for the testing of human tissues and cells. Available from: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:327:0024:0025:en:PDF. Accessed 10 Jun 2019.
49. European Union. Commission Directive (EU) 2015/565 of 8 April 2015 amending Directive 2006/86/EC as regards certain technical requirements for the coding of human tissues and cells. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015L0565&from=EN. Accessed 10 Jun 2019.
50. European Union. Commission Directive (EU) 2015/566 of 8 April 2015 implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells Available from: https://www.legislation.gov.uk/eudr/2015/566/pdfs/eudr_20150566_2015-04-08_en.pdf. Accessed 10 Jun 2019.
51. Kaminski A, Uhrynowska-Tyszkiewicz I, Miranda B. Design and validation of a specialised training model for tissue bank personnel as a result of the European quality system for tissue banking (EQSTB) project. *Transplant Proc*. 2007;39:2698–700.
52. Europe Directorate for the Quality of Medicines & HealthCare (EDQM); Council of Europe. *Guide to the Quality and Safety of Tissues and Cells for Human Application, 4th edn*. September 2019. https://www.edqm.eu/en/organs-tissues-and-cells-technical-guides. Accessed 10 Jun 2019.
53. Euro-GTP II Guide: Good Practices for evaluating quality, safety and efficacy of novel tissue and cellular therapies and products. Available from: http://www.goodtissuepractices.site/docs/EuroGTP_II_Guide.pdf. Accessed 11 Jun 2019.
54. *European Union Standards and Training for the Inspection of Tissues Establishments (EUSTITE)*. Available from: https://www.notifylibrary.org/content/european-union-standards-and-training-inspection-tissue-establishments-project-eustite. Accessed 11 Jun 2019.
55. *SOHO V&S Guidance for Competent Authorities: Communication and Investigation of Serious Adverse Events and Reactions Associated with Human Tissues and Cells*. Available from: https://www.notifylibrary.org/sites/default/files/SOHO%20V%26S%20Communication%20and%20Investigation%20Guidance.pdf. Accessed 11 Jun 2019.
56. *Vigilance and Surveillance of Substances of Human Origin (SOHO V&S), SOHO V&S Guidance for Healthcare Professionals on Vigilance and Surveillance of Human Tissues and Cells*. Available from: https://www.notifylibrary.org/sites/default/files/SOHOV%26S%20Vigilance%20Guidance%20for%20Healthcare%20Professionals%20-%20Part%201%20Tissues_0.pdf. Accessed 11 Jun 2019.

57. Pedraza JM, Gajiwala AL, Pardo MEM. A review of the International Atomic Energy Agency (IAEA) international standards for tissue banks. *Cell Tissue Bank*. 2012;13: 15–25.
58. *ISO 9000 Family – Quality Management*. Available from: https://www.iso.org/iso-9001-quality-management.html. Accessed 24 May 2019.
59. Du Pont JS. Regulatory Models for Safety and Quality of Allografts: Europe. In: Philips GO, von Versen R, Strong DM, Nather A (eds). *Advances in Tissue Banking*, Vol. volume 1. Singapore: World Scientific, 1997, 3–12.
60. World Health Organization. *Aide-Memoire on Key Safety Requirements For Essential Minimally Processed Human Cells and Tissues for Transplantation*. Available from: https://www.who.int/transplantation/AM_HCTTmin_requirements.pdf. Accessed 27 Jun 2019.
61. World Health Organization. *Resolution WHA63.22 Human Organ and Tissue Transplantation*. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R22-en.pdf. Accessed 27 Jun 2019.
62. Biller-Andorno N, Wilson D, Kerridge I, Chapman JR. Ethical issues regarding the use of human tissues and cells. In: Warwick RM, Brubaker SA (eds). *Tissue and Cell Clinical Use – An Essential Guide*. USA: Wiley-Blackwell, 2012, 1–22.
63. Nather A, Foong SYM, Tan N, Wang K. Tissue banking in Asia Pacific region – past, present and future. *Cell Tissue Bank*. 2018;19:229–40.
64. Ministry of Health Singapore (2003) *Guidelines for Healthcare Institutions Providing Tissue Banking: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (CAP 248, RG 1)*. Available from: https://www.moh.gov.sg/docs/librariesprovider5/licensing-terms-and-conditions/guidelines-for-private-healthcare-institutions-providing-tissue-banking.pdf. Accessed 25 Sep 2019.
65. Gajiwala AL. Regulatory aspects of tissue donation, banking and transplantation in India. *Cell Tissue Bank*. 2018;19: 241–8.
66. Sahay M. Transplantation of human organs and tissues act – "simplified". *Indian Journal of Transplantation*. 2018;12:84–9.
67. *Korean's Safety, Management, etc. of Human Tissue Act*. Available from: http://www.moleg.go.kr/english/korLawEng?pstSeq=58339&brdSeq=33&searchCondition=AIIButCsfCd&searchKeyword=urba. Accessed 7 Jun 2019.
68. Aktar N, Rahman MS, Jamil HM, Arifuzzaman M, Miah MM, Asaduzzaman SM. Tissue banking in Bangladesh: 12 years of experience (2003-2014). *Cell Tissue Bank*. 2016;17:189–97.
69. Japan Society of Tissue Transplantation. *Guideline on the Safety, Storage, and Application of Human Tissue in Medical Practice*. Available from: http://www.jstt.org/htm/topics/Safety.pdf.Accessed27Jun2019.
70. Japan Society of Tissue Transplantation. *Guideline on Ethical Issues in Application of Human Tissue to Medical Practice*. Available from: http://www.jstt.org/htm/topics/Ethical.pdf. Accessed 27 Jun 2019.
71. *Japan Society of Tissue Transplantation. Basic Standards for Operating A Human Tissue Bank & Quality Assessment Form*. Available from: http://www.jstt.org/htm/topics/Standards.pdf. Accessed 27 Jun 2019.
72. Heng WL, Heng WL, Seck T, Tay CP, Chua A, Song C, *et al.* Homograft banking in Singapore: two years of cardiovascular tissue banking in Southeast Asia. *Cell Tissue Bank*. 2013;14:187–94.
73. Kitchen A, Barbara J. Testing the donor. In: Galea G (ed). *Essentials of Tissue Banking*. Springer Science & Business Media, Netherlands, 2010, 141–65.
74. American Association of Tissue Banks. *Standards for Tissue Banking*, Netherlands, 12th edn, 2008.
75. American Association of Tissue Banks. *Standards for Tissue Banking*, 13th edn, 2012.
76. European Centre for Disease Prevention and Control. *Technical Report: Geographical distribution of areas with high prevalence of HTLV-1 infection*. Available from: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/geographical-distribution-areas-high-prevalence-HTLV1.pdf. Accessed 27 Jun 2019.
77. Eid AJ, Brown RA, Patel R, Razonable RR. Parvovirus B19 infection after transplantation: a review of 98 cases. *Clin Infect Dis*. 2006;43:40–8.
78. Darrigo LG, Carvalho AM, Machado CM. Chikungunya, dengue, and Zika in Immunocompromised hosts. *Curr Infect Dis Rep*. 2018;20:5.
79. Tan LSF, Loh LSKD, Prabhakaran K. Dengue haemorrhagic fever after living donor renal transplantation. *Nephrol Dial Transplant*. 2005;20:447–8.
80. Cedano JA, Mora BL, Parra-Lara LG, , Manzano-Nuñez R, Rosso F, *et al.* A scoping review of transmission of dengue virus from donors to recipients after solid organ transplantation. *Trans R Soc Trop Med Hyg*. 2019. https://doi.org/10.1093/trstmh/trz024 (Epub ahead of print).
81. Tambyah PA. Dengue haemorrhagic fever transmitted by blood transfusion. *N Engl J Med*. 2008;359:1526–7.
82. Musso D, Gubler DJ. Zika virus. *Clin Microbiol Rev*. 2016;29:487–524.
83. Eastlund T, Winters MK. Testing the Tissue and the Environment. In: Galea G (ed). *Essentials of Tissue Banking. Springer Science+Business Media*; 2010. p. 167–187.