Thank you for providing opportunity to make comments on the new draft code of Manufacturing Practice and Standards. There has been a very long gestation period for this draft code and, unfortunately, I cannot help but feel somewhat let down now that it has finally arrived. However, we hope that the combined response of the eye, tissue, cellular therapy and blood sectors are able to provide sufficient accepted input to improve the Code and Standards.

There is general agreement that the current Code requires updating. The difficultly in doing this is, in part, due to the requirement to have so much overlap in the documents for sectors that vary so greatly. We had been lead to believe that the blood sector would once again be placed under a separate structure, but this has not occurred. We commend the authors for their effort in bringing together all the sectors, but the difficulties of accommodating small eye and tissue banks along with the large blood sector is evident in the complications that have arisen in the documents.

When the original code of GMP was being derived I was one of the few that supported it, saying it makes me do today what I had planned to do tomorrow. Over the years however my views have changed. I have found TGA auditing to be inconsistent, some sites appearing to have to meet higher demands than others. My view is that the almost exclusive use of the word “should” rather than “must” will give even more latitude for auditors to be inconsistent with their audit. Using “should” questions whether any particular clause is actually required, particularly if it is also used with “where appropriate”. I appreciate that “must” should not be overly restrictive, but this can be achieved. I had never envisaged requiring a tighter code, but I do not feel in its current form it can be best used for the stated purpose of auditing.

Because so many sectors are involved there will be advances in treatment and methods that will mean the Code and its documents will need to change. The TGA does not appear to have a facility such as the FDA federal register where amendments can be efficiently circulated, or is the Commonwealth of Australia Gazette the method? How will the TGA make amendments to any of the documents? An annual review would also seem to be appropriate with such large sectors. I think that the TGA should address these issues.

In the Code currently in force the TGA is charged with deciding, in consultation with industry, which test methods are to be used to test for infectious disease. In practice they have in the past been unable to provide a list of acceptable tests. It is with concern therefore that I see in Schedule 4, 6, a, of the infectious disease Standard, that tests must be current technology etc. There is no indication who and how current technology will be decided. I suggest that the TGA is required to provide an approved list of tests available at any time to supplement the Code. The TGA should say what is acceptable and what is not. Not to do this will result in inequity. When a test will be superseded then the TGA should say the latest time when the superseded test will be permissible.

Draft AUSTRALIAN CODE OF GOOD MANUFACTURING PRACTICE HUMAN BLOOD AND BLOOD COMPONENTS, HUMAN TISSUES AND HUMAN CELLULAR THERAPIES

Comment [p1]: The TGA is a Manufacturing Regulator and has an obligation under the Therapeutic Goods Act to regulate industries who manufacture goods for therapeutic use. Why then do even basic items such as "*101The quality system should provide a structured and organised approach for quality to be achieved"*, use "should" rather than "must"? Could an organisation have a disorganised approach?

The TGA has gone for a less prescriptive style. Whilst the general substitution of "must" for "should" does allow for greater latitude, it appears to have gone too far. It also means that there will be huge opportunity for differences of interpretation. Those of us that have dealt with the TGA over many years know that auditors have different views, using even the more prescriptive current GMP. We will be relying upon the consistency and reasonableness of auditor opinion, which is the past has not always been evident.

Comment [p2]: The guide states that the Code of GMP sets out the principles for good manufacturing practice that will be used to audit manufacturers to ensure products are safe, efficacious and have the quality that is expected. It is difficult to see how this can be achieved.

The code is principles based and, furthermore, all but four items are "should" rather than "must". It is difficult to audit against items that are not obligatory. As it is there is insufficient explanation why a "should" section of the GMP is not followed.

It is straightforward to use the Product Standards for auditing and this will also be the case for any Technical Standards.

Our advice would be that that the Code is considered as a reference only to show intent rather than be used for auditing. The Code is used in conjunction with the Standards. This is synonymous with ISO 9004 being used for principles but auditing is only done against ISO 9001.

Draft Australian Code of Good Manufacturing Practice
Human Blood and Blood Components, Human Tissues and Human Cellular Therapies

INTRODUCTION

The Australian Code of Good Manufacturing Practice (GMP) for Blood and Blood Components, Human Tissues and Human Cellular Therapies (the Code) applies to Blood, Human Tissues and Human Cellular Therapies establishments which undertake the collection, processing, testing, storage, release for supply, and quality assurance of Human Blood and Blood Components, Human Tissues and Human Cellular Therapies.

Manufacturing Licensing requirements are set out Part 3-3 of the *Therapeutic Goods Act* 1989 and include requirements to comply with both general and specific conditions of licence. It is a condition of licence that Blood, Tissue and Cellular Therapy establishments observe the Manufacturing Principles determined under Section 36 of the Act. The Manufacturing Principles require these establishments to demonstrate that manufacturing practices comply with the Australian Code of Good Manufacturing Practice for Human Blood and Blood Components, Human Tissues and Human Cellular Therapies.

The revision of the Code was undertaken by the TGA Manufacturing Regulator in consultation with Medsafe NZ and the Australian and New Zealand Human Blood and Human Tissue establishments. The structure of the document has been changed and is written in a less prescriptive style. It describes the way in which Human Blood and Blood components, Human Tissues and Human Cellular Therapies should be manufactured to ensure that they consistently meet specifications and are safe to use.

Product Standards are to be established separately which will set out specifications addressing product safety and efficacy. Manufacturers will be required to develop Technical Standards Files for product groups to demonstrate that these Standards are met.

This Code does not intend to deal with common or statute law requirements, such as Occupational Health and Safety, or the requirements for building construction.

It is not intended that the Code be used to replace procedures that are already in place, but that it be used to ensure that procedures in place meet the requirements of the Code. The Code sets out all the requirements for good manufacturing practice (GMP) which collectively ensure that the final human blood and blood components, human tissues and human cellular therapies consistently meet specifications. While the Code descr ibes benchmark practices that should be followed, alternative approaches are permitted provided it can be demonstrated that the intent of the Code is met in a timely and effective manner in order to meet quality objectives.

Comment [p3]: The guide states that products are ensured to be efficacious.

The Code introduction states that *"Product Standards are to be established separately which will set out specifications addressing product.....efficacy".* Also section 103 of the code states, *"Management should define objectives pertaining to the quality, safety, efficacy..".*

The only reference however to efficacy in the Ocular Product standard is, " *no absolute guarantee of efficacy'".* Reconciling these items to an auditor may be difficult. Furthermore measurement of efficacy may only be that no complaints come back. Class 2 banked items do not appear to require proven efficacy, although for eye tissue there can be no doubt.

Comment [p4]: There are no other references regarding a Technical Standards file. We are wondering how the TGA will implement requiring a TSF? Should it not be better defined?

You would be relying on the good will of the manufactures it would seem.

Comment [p5]: There should be a clearer indication of this is the code itself. If "should" means "must" - unless you can justify otherwise, this must be more positively set out in the code itself.

Section 1

QUALITY MANAGEMENT

Principle

100. Quality management is that aspect of the overall management function which directs and controls an organisation with regard to quality. This should include every aspect of manufacture to ensure that the quality objectives will always be achieved.

A quality system should be established, documented, implemented and maintained to ensure that finished products are safe, are of appropriate quality, and meet regulatory requirements. The quality system should take into account the appropriate elements outlined in the Code and incorporate risk management principles.

Comment [p6]: Could there be any alternative available here? Cannot a regulatory body say must?

General

101. The quality system should provide a structured and organised approach for quality to be achieved. There should be resources at all levels to enable objectives to be met effectively.

Comment [p7]: Using "should" rather than "must"? Could an organisation have a disorganised approach?

106. Deviations and any action taken should be approved by an authorised person within the quality unit.

Comment [p8]: What is the 'quality unit"? This seems a rather vague term. If there has been a deviation from the quality system then this is an important event. We would suggest that as is used later it should be "by the quality manager, or delegate"

107. If applicable, corrective or preventive action should be taken to eliminate the cause of nonconformities in order to prevent recurrence or occurrence.

113. Regular periodic quality reviews of all products should be conducted with the objective of verifying the consistency of processes and the appropriateness of current specifications for both starting materials and finished product.
Trends should be highlighted to identify necessary product and process improvements. Such reviews should be conducted and documented annually, taking into account previous reviews, and should include, as applicable:

Comment [p9]: We do not understand why this is specified. Since the reviews are periodic then there appears to be no reason to add this issue.

Deleted: Quality reviews

Deleted: may be grouped by product type where ¶ scientifically justified.

-
- A review of all quality-related returns, complaints and recalls and the investigations performed at the time.
- A review of adequacy of any other previous product process or equipment corrective actions.
- The qualification status of relevant equipment and utilities, e.g. HVAC, water, gases, temperature controlled equipment;
- A review of Contractual Agreements to ensure that they are up to date.

Comment [p10]: This section on the stability monitoring program does not appear applicable to eyes, blood, tissue sectors. If the TGA does require it to be included then there should be a definition.

Deleted: If applicable, a review of the results of the stability monitoring program ¶ and any adverse trends

Deleted: .

Comment [p11]: Should be named in full and not abbreviated.

117. The potential impact of the proposed change on the quality of the product should be evaluated and should be approved by the quality manager,

Deleted: or

before implementation.

Section 2

PERSONNEL AND TRAINING

Principle

200. The establishment and maintenance of a satisfactory system of quality assurance and the correct manufacture of therapeutic products relies upon people. For this reason there should be sufficient competent personnel to carry out all the tasks in accordance with documented procedures. Individual responsibilities should be clearly understood by the individuals and recorded. All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training relevant to their needs.

Key Personnel

Quality and Production Nominees

203. The responsibility for quality and production should be allocated to persons specified on the manufacturing licence.

204. The nominees should be different persons, neither responsible to the other. They should have the authority to ensure that quality measures are employed in the manufacture (including testing) of product.

207. The Quality nominee generally has the following responsibilities:
- to approve or reject, as appropriate, materials and therapeutic products;
- to evaluate process records;
- to ensure that all necessary testing is carried out;
- to approve specifications, sampling instructions, test methods and other quality procedures;
- to approve and monitor any subcontractors and suppliers;
- to ensure the maintenance of the quality department premises and equipment;
- to ensure that the appropriate validations are done;
- to ensure that the required initial and continuing training of the quality personnel is carried out.

Training

209. Beside the basic training on the theory and practice of Good Manufacturing Practice, newly recruited personnel should receive training appropriate to the duties assigned to them. Continuing training should also be given, and its practical effectiveness should be periodically assessed. Training programmes should be available, approved by either the head of Production or the head of Quality Control, as appropriate. Training records should be kept.

210. Personnel working in areas where contamination is a hazard, (e.g. clean

Comment [p12]: The use of delegate means many things. It may allow adverse changes to be made to the quality system that may be picked up too late.

Deleted: delegate

Deleted: ,

Comment [p13]: Here an throughout where there is reference to the principles of GMP. Do the authors mean this code in this context? If this is the case then it should be stated thus. If the authors means the general principles of GMP then there should be a formal reference to the text in question.

Comment [p14]: . We completely agree that production and quality nominees should not be responsible to the other. In practice it is the case in some organisations that one is a line manager of the other. We believe that the use of should allows this to occur and this does not allow for the best quality management. If the TGA has the strength to implement must, this would be an improvement.

Comment [p15]: There is a discrepancy here between terms. In 206 and 207 the Production and Quality Nominees have their roles defined. In 209 the Heads of Production and Quality are given a role.
There needs to be some consistency here.

Comment [p16]: Again use of the word "generally" means that the code is really just guidelines.

Comment [p17]: In this section quality premises are mentioned but there is no similar statement about production premises. Only facilities are mentioned in the former section. Surely quality is part of production.

Comment [p18]: As in the above comment why use head of quality and production whereas you have used the quality and production nominee? There needs to be consistency.

Comment [p19]: I do not agree that training should be approved by the production or quality head. All training should be approved by both positions. Quality is part of production and cannot be separated in this way.

areas or areas where infectious materials are handled), should be given specific training.

211. Visitors or untrained personnel should not be taken into the processing and Quality Control areas. If this is unavoidable, they should be given appropriate information in advance and they should be closely supervised.

Comment [p20]: It is never unavoidable to do this, but it is undesirable.

Section 3

PREMISES AND EQUIPMENT

Principle

300. Premises, facilities and equipment should be located, designed, constructed, adapted, maintained, and suitable for its intended purpose. Their layout and design should aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid contamination, and, in general, any adverse effect on the quality of products.

In order to minimise the risk of microbiological, particulate or pyrogenic contamination, the manufacture of sterile products, or products required to have a low bioburden, should be subject to special environmental controls (e.g. Clean rooms, biological safety cabinets). Where required, applicable code clauses in Annex 1 of the mandated Code of GMP for Medicinal Products should apply.

Premises, facilities and equipment which is critical to the control of processing should be formally qualified.

Comment [p21]: Here we have premises delimited from facilities whereas only facilities are mentioned in production and only premises in quality (section 206 nd07).

Comment [p22]: Again using should but meaning must unless a reason is given seems unhelpful. Premises (i.e. building etc according to the Therapeutic Goods Act definition) have usually not been designed and built for the purpose. It would seem unnecessarily onerous to imply this.

Deleted: build

Comment [p23]: This seems rather an inappropriate term. Surely dirt is explained enough in the next section, microbial, particulate etc.

Deleted: up of dirt

Comment [p24]: Since this is going to cease to be used by July 2010 why cite it in this way and what is to replace it.

PREMISES

General

301. The manufacture of products should be carried out under appropriate and specified conditions, and each area, including mobile sites, should be designed and maintained to suit the operation(s) to be performed.

302. The design of premises should be appropriate and the premises should be equipped so as to afford sufficient protection against the entry of insects or other animals.

303. Steps should be taken in order to prevent the entry of unauthorised people to premises and restricted access areas. Precautions should be taken to check visitors to the premises, including external maintenance people and contractors, and to provide an appropriate level of access and supervision for their activities.

304. Where appropriate, contingency plans for breakdowns in critical services or equipment should be developed and regularly reviewed. For example, in the event of power failure, where necessary there should be access to a power source to allow the maintenance of critical services and equipment to permit the safe conclusion of activities in progress.

Comment [p25]: Not all premises are specifically designed for the purpose, but they can be suitably used. It seems unnecessary to say that they should be specifically designed for the purpose (here I am following the premise in the code that should means must unless it can be justified).

Deleted: P

Deleted: designed

Deleted:

Comment [p26]: It is not appropriate to say maximum protection. Maximum protection might mean no windows and a single door. A single mosquito entering premises would not be maximum protection, but in most cases it would be an acceptable risk.

Deleted: maximum

305. Lighting, temperature, humidity, air quality and ventilation should be appropriate and such that they do not adversely affect either the products during their manufacture and storage, or the correct functioning of equipment.

306. Premises for the manufacture of products should be specifically designed and used so as to avoid mix-ups or contamination.

Comment [p27]: Premises means normally means buildings and these will usually not have been designed for the purpose, but the facility will nonetheless still be acceptable.

307. Donor interview facilities should enable interviews to be conducted in private.

Processing areas

308. Materials of construction should not pose a source of contamination to the product. Critical surfaces in processing areas should be non-porous, smooth, and easily cleanable.

Storage areas

314. Storage areas should provide adequate space, suitable lighting, and be arranged and equipped to allow dry, clean and orderly placement of stored material under monitored environmental conditions (eg temperature, light, humidity)

Comment [p28]: The way this is written all stored material should be environmentally monitored in some way. For some items this may not be necessary. A metal tin for example may not need any environmental monitoring as it could withstand any condition.

315. Storage areas should provide for suitable and effective segregation of quarantined, rejected and released material.

316. If despatch areas are physically different locations from the storage areas, there should be provision for appropriate storage while awaiting transport.

317. Storage facilities should be secured to ensure that quarantined or released product cannot be tampered with or removed by unauthorised persons. Product storage facilities should not be used for any other purpose.

EQUIPMENT

323. Processing equipment should be used according to documented procedures.

324. There should be contingency plans in place for instances where routine equipment cannot be used. In such instances, the contingency plan equipment should meet the same acceptance criteria as for routine.

Comment [p29]: As it is written there have to be other alternatives available if routine equipment is not available. This is not the case.

328. Where controlled temperature conditions (including during transport, where appropriate) are required, the environment should be monitored as follows:

- there should be temperature recording devices, and records kept and reviewed;
- there should be an alarm to indicate that a temperature control system has failed. The alarm should permit resetting only by authorised personnel, and should be checked at regular defined intervals;

Comment [p30]:

Comment [p31]: The way it was written the temperature control system could not be reset e.g. there should be system so that ice could not be changed in a box which is hardly practical.

Deleted: system

329. Water systems used in the manufacturing should be sanitised according to

336. Preventive maintenance should be carried out on premises, facilities and equipment at defined regular intervals.

Comment [p32]: Preventative maintenance may not be appropriate for all equipment. Some equipment is used until failure or is used for a set period and then discarded before expected failure. How can preventative maintenance be carried out on a metal spatula.

Section 4

DOCUMENTATION

401. All processes and associated activities in the manufacture of product should be documented and the documentation controlled.

Records should be taken for all critical points in the manufacture of product and these should be retained.

Comment [p33]: It seems as if records will not have been dealt with adequately without a separate entry.

402. Documentation should be legible, accurate, readily identifiable and retrievable.

403. Documentation should not include superfluous data and should be written in the imperative (i.e. as instructions rather than statements of what is desired or should happen).

Comment [p34]: It seems rather ironic to have this statement. The code is not written in the imperative.

407. Any alteration made to the entry on a document should be signed and dated in permanent ink; the alteration should perm it the reading of the original information. Where appropriate, the reason for the alteration should be recorded.

Comment [p35]: Surely all changes should be explained if they are changes to a document.

409. The retention period and storage conditions for all documents should be defined and, comply with legislation.

Comment [p36]: As it was written there was an opportunity that documentation need not comply with legislation. I do not believe the TGA would support not following legislation.

Deleted: where applicable

Section 5

CONTROL OF MATERIAL

512. Products returned from the customer and which have left the control of the manufacturer should be destroyed unless their quality is satisfactory. They may be considered for re-supply only after they have been critically assessed by the Quality Control Department in accordance with a written procedure. The nature of the product, any special storage conditions it requires, its condition and history, and the time elapsed since it was issued should all be taken into account in this assessment. Where any doubt arises over the quality of the product, it should not be considered suitable for re-supply. Any action taken should be appropriately recorded.

Comment [p37]: This seems rather strange terminology. It means that there must be no doubt that reissued material meets quality specification. That in its own right is OK, but why not therefore say tissue that has not been reissued without doubt meets quality? For this reason without doubt appears superfluous.

Deleted: without doubt

Section 6

SUBCONTRACTING

Principle

600. Subcontracting should be correctly defined, agreed and controlled in order to avoid misunderstandings which could result in a product or work of unsatisfactory quality. There should be a written agreement between the manufacturer and the contractor which clearly establishes the duties of each party.

Comment [p38]: There needs to be consistency in 600, 601 and 602. Subcontractor, contractor and contract acceptor are all used, whereas it is believed they are all the same thing. Furthermore in 603

General

601. The contractor (eg testing, irradiation, pest control, cleaning, calibration, preventive maintenance) should be subject to an initial evaluation and regular review to ensure compliance with the quality system. Subcontracting should be covered by a formal documented agreement specifying the responsibilities of both parties. If applicable, subcontracted personnel should be trained in GMP or supervised whilst on the licensed premises. Records should be maintained.

Deleted: sub

602. The contractor must not subcontract any work without written authorisation from the manufacturer.

Deleted: acceptor

Deleted: contract giver

Section 7

COMPLAINTS, ADVERSE EVENTS AND RECALLS

Principle

700. All complaints and other information concerning potentially defective products and adverse events should be carefully reviewed according to written procedures. In order to provide for all contingencies, a system should be designed to promptly and effectively recall products known or suspected to be defective, from the market.

Comment [p39]: An adverse affect should be recorded even if there is not a complaint.

COMPLAINTS AND ADVERSE EVENTS

701. There should be a procedure established, implemented and maintained for the investigation of adverse events and product complaints and how they can be avoided or minimized in future.

Comment [p40]: There needs to be these additional words, otherwise the investigation only looks at what happened and not how it could be avoided in future.

Section 8

COLLECTION AND PROCESSING

PRINCIPLE

800. Collection and processing activities should follow clearly defined procedures; they should comply with the principles of Good Manufacturing Practice in order to obtain products of the requisite quality and be in accordance with regulatory requirements.

Collection and processing should be conducted in a manner that minimises the risk of contamination and errors.

COLLECTION

805. A procedure should be established implemented and maintained for obtaining medical and other required information prior to donation.

806. There should be a documented procedure for defining the medical assessment requirements for live and deceased donors, including the acceptable timeframe for assessment,

For a live donor, the donor selection records, including consent and medical history, signed by the donor should be witnessed and signed by an authorised person.

The medical assessment records examined should be documented and there must be a statement of acceptability of the donor signed by a nominated authorised person. The medical assessment should be made as close as possible to collection.

808.

809. Donor selection records, including informed consent and final assessment, should be reviewed and recorded by an authorised person to ensure the suitability of the donor.

810. Where State/Federal requirements require consent for the collection, of blood, tissue or cells, the consent should be obtained.

811. Procedures for donation should be established, implemented and maintained.

Comment [p41]: Without this change it would be allowable for particulate contamination to take place so long as it was sterile.

Deleted: microbial

Comment [p42]: There seems to be no value in having statutory after required has been used.

Deleted: statutory

Comment [p43]: 806, 807 and 808 appear to separate tissues from cellular therapies for a reason we cannot understand. Furthermore blood is excluded which following the wording would mean it need not follow the code. It is therefore sensible to remove the reference to a single sector and have a blanket requirement that covers all the sectors.

Comment [p44]: Without this change all collections other than tissues would not need to document when a medical assessment needs to be done.

Deleted: For

Deleted: Tissue Collections

Deleted: t

Deleted: if not able to be

Comment [p45]: Even if the medial assessment is done on the day of death there should be a statement as to what is acceptable.

Deleted: done on the day of donation

Deleted: 807. For Tissue Collections, in the case of the deceased donation, the

Formatted: Indent: Left: 101 pt

Deleted: For Cellular Therapies, there should be a documented procedure for ¶
defining the medical assessment requirements including the acceptable ¶
timeframe for assessment, if not able to be done on the day of ¶
procurement.

Comment [p46]: Without removing the next sentence it would appear that the authors might be approving actions that went against state or federal requirements, even legislation. If there is a state or federal requirement this should be followed.

Formatted: Indent: Left: 132.15 pt

Deleted: In

Deleted: exceptional circumstances ¶
where consent cannot be obtained at collection, the consent should be ¶
obtained before tissue or cellular therapies can be released. ... [1]

818. Collection should be performed aseptically.
Equipment and containers coming into contact with the blood, cells or tissue should be sterile.
and used n a manner which will minimise contamination.

819. Collection documentation records should include:
- The donor identity
- The date, time and place of the procedure
- The identity of the person(s) performing the procurement
- For Cellular Therapies; the Cells retrieved, Donor and cell selection information
- For Tissues; The tissue(s) retrieved, Donor and Tissue selection information, Details of the physical examination of the donor prior to collection

Confidentiality of the donor should be maintained unless otherwise approved.

820. If applicable, documented procedures for the transport of donations should be established, implemented and maintained. The procedures should ensure that the integrity of donations is protected and traceability is maintained.

PROCESSING

822. Before any processing operation is started, steps should be taken to ensure that the work area and equipment are clean and free from any starting materials, blood or blood component, tissue or cellular therapy product residues or documents not required for the current operation. Records should be maintained.

823. There should be documentation which defines the material, procedures and controls used in the processing of product.

Section 9

QUALITY CONTROL

901. Samples for quality testing should be taken in a manner so as to avoid risk of microbial contamination of the product and mix-up of samples.

902. Documented procedures for quality control should be established, implemented and maintained. The procedures should ensure that the product meets specifications

903. Solutions which are in direct contact with the product during manufacture should be sterile. If prepared in-house, they should be prepared in an appropriate environment and should comply with the requirements of the test for sterility.

Comment [p47]: Again why should cells and tissues be different to blood or blood products?

Comment [p48]:

Deleted: of cells and tissues

Deleted:

Deleted: and carried

Comment [p49]: What is a controlled condition? Either this needs to be defined or removed. There is ample reference to the conditions of the retrieval that should be ensured.

Comment [p50]: Some equipment used in collection might not be sterile, but so long as it does not come into contact with the tissue it would be acceptable. A drill for example might not be sterile, but a drill bit would be sterile.

Deleted: out under controlled conditions

Deleted: .

Deleted: used

Deleted: Retrieved tissue and cellular therapies should be packaged using sterile ¶ containers

Deleted: i

Comment [p51]: In some cases the donor may not wish for confidentiality and if legislation permits there may be no need to maintain this.

Comment [p52]: This does not require change but it would contradict the sterile collection of earlier.

Comment [p53]: Surely any sample for testing should not be contaminated, not only laboratory samples.

Deleted: laboratory

Testing

905. Screening tests for donor suitability should be carried out by competent laboratory. Where required by legislation the laboratory must be licensed by the regulatory authority for therapeutic products.

906. Screening tests should be conducted according to documented procedures and should include (or refer to) the acceptance criteria for individual tests.

913. In order to ensure both the reliability of the manufacturing process and the quality of the final product there should be routine microbial contamination testing. Where contamination is demonstrated, records should show the corrective action taken.

Product release

915. The manufacturer should ensure that where Tissue and Cellular Therapies does not meet the product specifications a review of the product should be undertaken. Only when a risk based approach and/or regulatory requirements have been met can such products be released.

916. Products not released should be identifiable from those which conform to specification and have received their final inspection. Appropriate records should be maintained. In the event that a product fails release, and where applicable, a check should be made to ensure that other products from the same donation and products prepared from previous donations (where applicable) given by such donors have been identified. There should be an immediate update of the donor record to ensure that the donor cannot make a further donation, if appropriate.

917. Where applicable, with autologous Blood or Blood Components and Cellular Therapies from donors with reactive mandatory screening tests, intended to be reintroduced into that donor, records should be available to demonstrate the rationale for this use. Such product should be appropriately labelled. Authority for the release of this product should be documented.

918. There should be a documented procedure which defines the disposal requirements for product not used. Product which is to be discarded should be labelled to reflect its status, stored in a dedicated and secure area, and disposed of. There should be a record of discarded product, including the reason for discard.

Deleted: a

Comment [p54]: Again use of laboratory seems unnecessary. Also use of should seems ridiculous Why if it is required by legislation is not it obligatory. Is the TGA saying that it might accept tests done where legislation is not followed?

Deleted: should

Comment [p55]: 913 indicates that there should be routine microbiological testing, whereas in the infectious diseases standard corneas are exempt from this requirement Why then have 913 section without exemption. If the TGA is not to have an exemption then what would the contamination for eye tissue be reviewing since there is no standard for the natural colonisation and the eye is not sterile.

Comment [p56]: typo

Comment [p57]: I support the risk assessment of this section However this section which is based on risk assessment would seem contrary to that on reissue of product where there must be no doubt of quality.

Deleted: are

Comment [p58]: We do not see the distinction here. A final product is one that can be released. All other products are in quarantine. If any item fails a quality assessment then consideration ea should be given how this might affect others. It is not the case that only final products are important.

Deleted: the final

Comment [p59]: Surely there should be a procedure for any use of donor product that has reactive serology?

Deleted: repeatedly

Comment [p60]: Does not read

Deleted: Where applicable,

Comment [p61]: There should be a procedure for any product disposed of, whether it is suitable for use or not.

Deleted: suitable

Deleted: for use

References

1. Australian Code of Good Manufacturing Practice – Human Blood and Tissues. 2000. TGA.
2. Australian Code of good Manufacturing Practice for Medicinal Pr oducts, 2002
3. Guide to the preparation, use and quality assurance of blood com ponents. 14 th ed, 2008. Council of Europe
4. Recommendations on Validation Master Plan, Installation and Operation Qualification, Non-Sterile Process Validation, Cleaning Validation. PI 006-2, 1 July 2004. PIC/S.
5. Guide to Good Manufacturing Practice for Medicinal Products. PE 009-5, 1 August 2006. PIC/S.

Comment [p62]: The document states that to assist in the reading of the Code there are references and recommended standards and publications. These would seem superfluous unless they are directly referenced in the code.

Of the five, 1) Australian Code of Good Manufacturing Practice – Human Blood and Tissues. 2000. TGA will be out of date when the Code comes into force and so has only historical interest; 2) the Australian Code of good Manufacturing Practice for Medicinal Products, 2002 concerns a separate sector and so has little relevance; 3) the Guide to the preparation, use and quality assurance of blood components. 14th ed, 2008. Council of Europe may have some value; 4) the Recommendations on Validation Master Plan, Installation and Operation Qualification, Non-Sterile Process Validation, Cleaning Validation. PI 006-2, 1 July 2004. PIC/S shows most value for the sectors; 5) and again the Guide to Good Manufacturing Practice for Medicinal Products. PE 009-5, 1 August 2006. PIC/S also concerns a separate sector and so has little reference.

Whilst some might say having references included does no harm, auditors have in the past indicated that they must be followed. Only Codes, and Standards should have to be followed. Guidelines, certainly and Recommendations, probably, were never designed to be required for audit.

exceptional circumstances
where consent cannot be obtained at collection, the consent should be
obtained before tissue or cellular therapies can be released.