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Comments on:

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

General comments

This Draft Code of GMP contains many elements which are already underway in Australian hospitals. However, it's implementation as written will require an upgrading of the processes involved in production of a variety of human tissues for therapeutic use. These will require an appropriate level of funding for the currently woefully underfunded areas of quality management, process development, facilities structure, review and training. Since many hospitals are already trying to introduce these practices with inadequate funding, a major increase in human resources and funding will be essential if this code is adopted. Implementation without enhancement will impact adversely on patient care.

Introduction

"Product standards to be established." The definition of a technical standards file needs to be clarified as soon as possible, as it is important that the TGA again understands there is no point of comparison between a drug and an HPC product.

Nowhere is this code does it refer to the intention to list some of these products on the ARTG.

1. How many products is the TGA talking about?
In 2009, my Unit transplanted 33 children. These consisted of :
17 patients undergoing autologous peripheral blood stem cell infusions (including 9 patients who had 20 sequential infusions)
6 matched sibling allogeneic bone marrow from minors
6 unrelated cord blood donors from Australia
3 unrelated peripheral blood stem cell transplants with CD 34 selection in vitro.
1 related peripheral blood stem cell transplant with CD 34 selection in vitro.
In all of these cases, cells went through our BMT laboratory.

Is this 1 product for the ARTG register and one technical standards file (for HPCs), or 3 (HPC-BM, HPC-cord, HPC-A) , or 5? (HPC-A related, HPC-A, unrelated, manipulated; HPC-A, related, manipulated; HPC-BM; HPC-cord.) And what if we had planned to do a CD 34 selection, but the cell yield was inadequate and we elected not to proceed with CD 34 selection? That decision, taken on receipt of the HPCs, would have to be made on the spot, and then we would have used a

product that isn't on the register. With the small volume of product in any individual centres, it will be easy to swamp the ability of any transplant unit to perform any transplants.

2. How will be the sponsor?
Who will sponsor this product? Will we expect the > 23 registries in other countries that our products come from to sponsor them?
Will CHW be prepared to invest in registering a matched sibling bone marrow product for 6 patients a year?

Exceptional release – the SAS A category has been widely used for patients undergoing HPC transplant in the past, and could easily apply to the majority, or even all the products that we use, and such a system will be used if the TGA imposes a system which is too expensive, too complex and impractical, this calling into question whether this process has any value at all.

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.
Quality systems are required for clinical transplantation and is an area which has been recognised by clinicians active in transplantation, but a major barrier is lack of perceived need by underfunded hospitals and area health authorities. The systems required are complex, time consuming and need prolonged input from senior clinicians to educate quality staff about how human clinical HPC transplantation works. It is extremely rare to find any quality staff that have any knowledge or experience in this area; often the skills they do have need to be unlearnt before they can understand what is involved in this area. This will require massive funding support for quality systems, including senior medical staff as this will take them away from their clinical roles.

104.
Bullet point on supply of therapeutic product.
Nearly one half of all products used for unrelated allogeneic HPC transplantation in Australia have been sourced from overseas. The most widely used system of verification that these products have been produced and controlled adequately is an international standard, the FACT standard, which is already being used in several centres in Australia. Since TGA will have no control over half of the material we use; many Australian centres are already in the process of implementing the FACT standard, and the FACT standard includes the clinical process of transplantation, not just manufacture of the product, then implementation of any system through the TGA is ineffective for many of our products, duplicates some elements of what is being done, and falls short of a standard already being adopted. It has nothing to offer except significant cost.

205.
The quality and production nominees should have a relevant tertiary level qualification, (eg. in medicine, science, medical laboratory science, nursing), and have had practical experience, at management level, in the manufacture of therapeutic products.
This will be possible for whoever is designated as Head of the BMT Lab. For quality nominees, this will be almost impossible to achieve as there are not sufficient staff to be able

to achieve this. The current and past experience in several centres has taught us that, for example, Quality managers coming from a Blood manufacturing background have almost no idea of what is involved in clinical transplantation and have a perspective which requires significant re-education before such staff can start working usefully in these positions. (See point 101 above)

207
The duties laid out in 207 are duties of the manufacturing staff, not the Quality staff, as all these items must be completed before each product is released.

Section 7
The working in this section reflects the drug product origin of the whole document. It is too late to issue a recall for a product which has already been infused into a patient. I assume no work on this section has been done; it needs to be looked at from an HPC perspective, not a drug manufacturer perspective.

Section 8
Collection – almost all of these points are so general that they are of no value when compared to the NPAAC standard or FACT standard.

905
It is very difficult to work out what sort of laboratories will be adequate to carry out the Infectious Disease markers in BMT patients. Terms used include “Competent lab” and “Licensed lab”. There is a lot of overlap with the NPAAC document; it would be better to stick to one type of lab standard (eg NATA, as per NPAAC) than TGA talking about ‘certified”. Most/all of these testa re already done, in local hospital labs (without an adequate, or indeed any, item number). Limiting these tests to other labs will involve more and more cost.

914.
All products for human allogenic transplantation are infused after completing pre-defined acceptance criteria. Ill informed, incorrect and unnecessarily complex regulatory requirements have the ability to stop patients undergoing life-saving procedures, or even dying if a product is not released for an individual patient.

With kind regards,

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