

CLINICAL USE of Cytomegalovirus seronegative blood products in Australia

**Position paper**

**September 2017**

Contents

[SUMMARY 4](#_Toc491245715)

[Background 6](#_Toc491245716)

[Summary of Guidelines 8](#_Toc491245717)

[Appendix 1 – Summary of current literature 10](#_Toc491245718)

[Background 10](#_Toc491245719)

[Risk of community transmission of CMV 10](#_Toc491245720)

[Risk of transfusion transmission of CMV 11](#_Toc491245721)

[Reducing the risk of Transfusion Transmission 12](#_Toc491245722)

[International decision making 13](#_Toc491245723)

[Current Australian consensus 15](#_Toc491245724)

[Conclusion 15](#_Toc491245725)

[References 16](#_Toc491245726)



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# SUMMARY

**Clinical Use of Blood and Blood Products in Australia**

Under the requirements of the *Australian Health Ministers’ Statement on National Stewardship Expectations on the Supply of Blood and Blood Products,* health providers should ensure all blood products are used in a clinically appropriate manner in accord with relevant professional guidelines and standards.

The *National Safety and Quality Health Service Standard 7-Blood Management* (1)states Health Service organisations should implement policies and procedures for blood management that address prescribing practice and the appropriate and safe clinical use of blood and blood products. The Blood Management Standard also has education and training requirements.

This position paper outlines the patient groups and indications that Health Service Organisations should consider when developing policies and protocols on the clinical use of CMV seronegative blood products. Health Service organisations should also undertake audits or compliance reviews to ensure the policy is implemented.

Transfusion laboratories are required to have written policies for the selection of CMV negative blood components. Where appropriate, the policy should include transfusion to pregnant women and for intrauterine and neonatal transfusions(2). Transfusion laboratories should review and update their policy to align with current National recommendations. Laboratories should also consider auditing their requests for CMV seronegative blood components to monitor compliance with their policy

When developing policies and protocols for CMV seronegative blood products Health service organisations and transfusion laboratories should recognise that fresh blood products in Australia are leucodepleted[[1]](#footnote-1)[[2]](#footnote-2) and the risk of acquiring CMV through a leucodepleted blood product is estimated at around 1 in 13,575,000(3). This compares to a community acquired risk where 85% of Australian adults are infected by the age of 40.

CMV ‘safe’ means through leucodepletion or antibody testing of donor blood. Neither process excludes the possibility of transfusion-transmitted infection; rather, they both provide a significant risk reduction. It is unknown whether CMV seronegative blood products provide significant additional protection over routine leucodepletion.

**Which patient groups *may be considered* for use of CMV seronegative blood products in Australia?**

The **Patient Blood Management Guidelines Module 5 Obstetrics and Maternity** (4)provides guidance suggested by the Clinical /Consumer reference group (CRG) as appropriate for Australia.

**Expert Opinion Point 12**: CMV safe blood products should be offered to all pregnant women, regardless of CMV status, when transfusion occurs in the antenatal setting in the context of an ongoing pregnancy. Preference is for CMV seronegative blood products, where available; however, life-saving transfusion should not be withheld if CMV seronegative products are not available.

The **Patient Blood Management Guidelines Module 6 Neonatal and Paediatrics** (5)provides guidance suggested by the Clinical/Consumer Reference group as appropriate for Australia.

**Expert Opinion Point 14:** CMV-negative products ***may be considered*** in the following situations:

• intrauterine transfusion

• preterm neonates (up to 28 days after expected date of delivery)

• patients with severe combined immunodeficiency (SCID) who are CMV negative

• stem cell transplantation where both donor and recipient are known to be CMV negative

• granulocyte transfusions for recipients who are CMV seronegative, or whose status is unknown.

CMV-negative products are generally not required in other clinical settings.

**Expert Opinion Point 15:** In urgent situations, if CMV-seronegative blood components are not available, CMV‑unscreened leucodepleted components should be used to avoid delays.

The CRG acknowledge that leucodepletion results in very low rates of transmission however the CRG identified paediatric populations, in particular SCID and stem cell transplantation patients, where the risk of CMV transmission can result in “devastating and fatal consequences”.

This paper was commissioned by the National Blood Authority under the guidance of the Jurisdictional Blood Committee Working Group. The position statement and supportive documentation were developed by a panel of expert clinicians, including Dr Jan Fizzell (Chair), Dr Marija Borosak, Dr James Daly, Dr David Forbes, Dr Joanne Pink, Dr Ian Prosser and Dr Alison Street.

**The position of the working group, based on the Expert Opinion Points in the Patient Blood Management guidelines, is that only laboratories that provide blood products to paediatric or pregnancy and birth services should hold CMV seronegative inventory**.

# Background

**What is CMV?**

Cytomegalovirus (CMV) is a human herpes virus that may be transmitted horizontally in saliva and other bodily fluids including blood or vertically with postnatal infection through breastfeeding. CMV infection in a healthy individual is often asymptomatic or results in a mild non-specific illness. However CMV infection may cause life threatening disease in susceptible groups, such as immunosuppressed individuals and neonates. Congenital infection may also occur with primary maternal infection in pregnancy.

Individuals who recover from a CMV infection develop an immune response and become CMV seropositive approximately 6- 8 weeks after contracting the virus. A CMV seropositive individual remains potentially infectious for life due to dormant (latent) infection primarily in mononuclear white cells and their precursors.

Where practitioners are concerned regarding the risk of CMV transmission they should educate their patient regarding the risks of community transmission, and simple precautions to reduce that risk especially for pregnant women and mothers of newborn babies.

**How is the risk reduced for transfusion transmitted CMV?**

Transfusion of CMV present in blood components can give rise to primary infection in CMV negative recipients - a transfusion transmitted infection (TTI). Seroselection (CMV antibody screening) of donors and leucodepletion (removal of white cells through filtration) are the two main strategies for the prevention of transfusion transmitted CMV. Although these strategies significantly reduce the risk of CMV transmission neither is 100% effective, however the risk remains many orders of magnitude lower than community transmission of these easily acquired viruses.

A recent systematic review and meta-analysis commissioned by the AABB concluded “*the scientific evidence does not favour a single strategy for reducing the risk of transfusion related CMV infection in high risk patients*”.(6)

A subsequent AABB Committee report(7) advises there is uncertainty about how to provide clinical guidance for managing blood transfusions in patients at risk for TTCMV infections and suggests alternative strategies for developing a clinical decision framework such as residual risk modelling.

This risk modelling has been completed in Australia by Seed at al(3) which estimated the residual risk for non CMV antibody screened (leucodepleted only) fresh blood components to be 1 in 13,575,000. This is considered **a negligible risk of TT-CMV associated with transfusion of these blood components in Australia.**

The major way to prevent transmission of CMV virus to pregnant women (and hence, congenital infection) is by education regarding the risk of community transmission (8).

A complete background and summary of current CMV transfusion related literature can be found in **Appendix 1.**

# Summary of Guidelines

A summary of Australian and International guidelines appears below with patient group and indications that may be considered for use of CMV seronegative blood products. All the guidelines emphasise that in urgent situations, if CMV seronegative blood components are **not** available then leucopleted blood products of unknown CMV status should be used to avoid delays. Many guidelines were developed before modelling regarding the residual risk of TTI was estimated.

*Comparison of Guidelines on the Clinical Indications for the use of Cytomegalovirus seronegative blood products*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indication** | **SaBTO[[3]](#endnote-1)**  **2012** | **PBM Guidelines[[4]](#endnote-2)**  **2015/16** | **ANZSBT [[5]](#endnote-3)**  **2016** | **NAC Canada[[6]](#endnote-4)**  **2017** |
| Intra-uterine transfusions | Yes | Yes | Yes | Yes |
| Premature neonatal transfusions | Yes | Yes[[7]](#endnote-5) | Yes | No |
| Other neonatal transfusions (≤ 28 days post EDD) | Yes |
| Granulocyte transfusions | Yes | Yes[[8]](#endnote-6) | Yes | Not specified |
| Immune deficient patients (Adult) | No | Not specified | No | No |
| Immune deficient patients(Paediatric) | SCID[[9]](#endnote-7) |
| Autologous HSCT patients | No | No | No | No |
| Allogeneic HSCT patients(Adult) | No | Not specified | No | No |
| Allogeneic HSCT patients (Paediatric) | Yes[[10]](#endnote-8) |
| Organ transplant patients | No | No | No | No |
| Pregnant women | Yes | Yes | Yes[[11]](#endnote-9) | No |

In 2016 the **AABB** prepared a Committee report on reducing transfusion transmitted CMV rather than develop clinical practice guidelines[[12]](#endnote-10)

# Appendix 1 – Summary of current literature

## Background

Cytomegalovirus (CMV) is a common herpes virus that results in chronic and mostly asymptomatic infection in the majority of adults worldwide(5). The estimated prevalence of CMV antibodies in the general adult population ranges from 45% to 100% globally (9, 10). In Australia, the estimated CMV seroprevalence among 20 to 69 year olds is 76.12%(9).

## Risk of community transmission of CMV

CMV is a common viral infection, especially amongst children(11). By young adulthood, 50% of people have already been infected with CMV and close to 85% by the age of 40(11). CMV seroprevalence amongst Australian adults (approximately 80%) is comparatively higher than that of other developed parts of the world such as Western Europe and the USA(9). This is likely due to cultural, sociodemographic and climatic differences. CMV seroprevalence is higher amongst females and is similar to results of other seroepidemiologic studies conducted abroad(9). This is thought to be due to maternal exposure to young children with a high incidence of primary CMV infection and viral shedding.

CMV is transmitted from person to person through close contact with an individual excreting the virus in their saliva, nasal mucous, urine or other bodily fluids(11). CMV may be transmitted through handling children’s toys that have saliva or mucous on them, or contaminated items like dirty tissues or soiled nappies then touching the eyes, nose or mouth without first washing hands, through sexual contact as well as through vertical transmission as a result of maternal infection during pregnancy or breast feeding(11). The latter two are important routes of CMV transmission for infants. Babies are vulnerable to CMV and it is a common cause of congenital infection and malformation (12, 13). A reported 0.3% to 2.4% of neonates are born with congenital CMV in different countries (13). In Australia, studies have demonstrated that 6 infants out of 1000 live births have congenital CMV infection(11). Congenital CMV is associated with serious clinical sequelae, prematurity, intrauterine death or neonatal death in infants each year(12) An estimated 20% of infants with congenital CMV die and up to 12% and 10% of infected babies develop sensorineural hearing loss and cerebral palsy respectively(14).

Low birth weight infants and fetuses of pregnant women newly infected with CMV are especially susceptible to CMV. Breast milk in particular poses a significant risk for transmission of CMV in infants (15).

A prospective study by Josephson et al in 2014 evaluated both blood transfusion (CMV seronegative (CMV-N) and leucoreduced[[13]](#footnote-3) transfusions) and breast milk sources of postnatal CMV infection in very low birth weight infants and found that breast milk was the primary source of postnatal CMV infection in this population(15). Whilst there were 2061 transfusions (CMV seronegative and leucoreduced products) amongst 310 infants none of these babies had a CMV infection linked to transfusion. In contrast, 27 of 28 post-natal infections occurred amongst infants fed CMV-positive breast milk (12-week incidence, 15.3%; 95% CI, 9.3%-20.2%)(15).

These findings were recently supported by a study conducted by Yamagishi et al (2016) verifying that breast milk poses a substantial risk for transmission of postnatal CMV infection in very low birth weight infants(16). In this study, a very low birth weight infant (689g) was transfused with leucoreduced red blood cells (RBCs) that were later found to be CMV seropositive and CMV DNA positive. In addition to this, the infant was fed CMV DNA-positive breast milk and developed CMV disease. CMV DNA sequence analysis including deep sequence analysis was conducted to determine the route of transmission. CMV DNA sequence-matching rates for the leucoreduced RBCs and the patient's blood were 64.6% for the UL139 gene and 68.6% for the UL146 gene. Conversely, the sequences of these genes in the patient's blood were 100% matched with those in the breast milk. Moreover, the CMV strain found in the patient's blood was not detected in the transfused leucoreduced RBCs based on deep sequence analysis(16).

Current Australian public health preventative strategies focus on reducing the risk of transmission to vulnerable individuals such as pregnant women and women of child bearing age including those that work in child care centres, preschools and health care settings e.g. obstetric and paediatric units(11, 17). These include infection control measures such as good hand hygiene especially after close contact with young children, handling children’s toys or blowing noses; not sharing eating utensils or personal items such as toothbrushes with young children; avoiding contact with saliva when kissing a child; or cleaning of objects that come into contact with children’s mucous, urine or saliva such as toys or countertops(11). The two main methods of preventing CMV transmission through blood donation include leucoreduction (LR) and selection of CMV seronegative donors (seroselection). Transfusion transmitted infection is thought to be very rare. Whilst there is currently no vaccine available to protect against CMV infection, several are currently under development including recombinant vaccines, live attenuated vaccines, and chimeric vaccines (13).

## Risk of transfusion transmission of CMV

The risk of community transmission of CMV is far greater than the risk of transfusion transmission of CMV.

CMV can be transfusion transmitted mainly through latent viruses that are located in white blood cells (WBCs) found in cellular blood components(6). Following blood transfusion, the virus may result in primary infection in CMV negative recipients (transfusion transmitted CMV) or reinfection in individuals previously infected with the virus(14). CMV is able to be transmitted from blood donors with active (primary/reactivated) or latent forms of the infection(14). Whilst the transfusion of CMV- positive blood has minimal impact on immunocompetent recipients, more severe disease however may occur in immunocompromised patient populations (9, 14). These mainly include low birth weight infants and/or premature neonates, fetuses requiring intrauterine transfusion, pregnant women, transplant recipients, patients with primary immunodeficiencies and chemotherapy recipients (7, 9).

Advancements in diagnostic tools such as robust CMV PCR assays have improved the ability to detect TT-CMV (9, 18). Furthermore, routine virological surveillance of some high-risk patient groups such as stem cell transplant recipients and the use of pre-emptive or universal ganciclovir therapy in vulnerable individuals have proven very effective in CMV disease prevention including transfusion transmission of the virus (7, 9, 10). In addition to this, several promising vaccines against CMV are under development as mentioned above (13).

## Reducing the risk of Transfusion Transmission

Leucoreduced and seroselection signify the two main strategies for the prevention of transfusion transmitted CMV (TT-CMV) (9, 10, 18). These methods have enabled a reduction in the incidence of TT-CMV by approximately 10 fold in high-risk subpopulations over the past three decades(9).

Leucoreduced cellular blood components including red blood cell and platelet products have been available in Australia since 2008(9). In other developed countries such as the UK and Canada, universal LR has been in use since the late 1990 following studies that demonstrated that it was effective in reducing the risk of TT-CMV (10, 18). These include the landmark study by Bowden et al (1995) that showed LR was as effective as CMV seronegative (CMV-N) blood products in preventing TT-CMV infection in hematopoietic stem cell transplant (HSCT) recipients (19).

Findings of these earlier studies is supported by more recent studies including those by Wu et al (2010), Thiele et al (2011), Nash et al (2012) and Kekre et al (2013) all of which reaffirm the equivalent safety of CMV untested (CMV-U), leucoreduced blood components (10, 20-22). The studies by Thiele and Nash demonstrated the absence of clinical TT-CMV infection (0% risk of TT-CMV) amongst study participants despite a combined transfusion of approximately eight thousand CMV-U, leucoreduced component (20, 21). The risk of TT-CMV reported by Wu et al was 6.5 % (95% CI 1% -18%) per transfusion recipient (3 cases of probable TT-CMV were reported in this study although not confirmed from donor follow up) (22). Kekre and colleagues did not find any significant difference in TT-CMV viraemia or disease in patients receiving only leucoreduced versus CMV-N and leucoreduced blood products in HSCT recipients (10).

In 2012 the UK Department of Health’s Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) recommended that solely leucoreduced blood be considered sufficient risk reduction for TT-CMV in high-risk patient populations with the exception of intrauterine transfusion recipients, pregnant women and neonates who should be transfused with CMV-N products (14).

Whilst LR prior to transfusion is an effective strategy to reduce the risk for TT-CMV (current methods can achieve very low viral levels <0.1 viral copies per mL), it cannot completely eliminate CMV transmission most likely because free virus, i.e. virus not harboured in WBCs, is usually not retained by LR filters (7).

The use of blood from donors seronegative for anti-CMV is an alternative strategy used to reduce the risk of TT-CMV in high-risk populations (9). This method has been the standard of care for patients considered to be at risk of TT-CMV since the pivotal study by Bowden et al (1986) that found the use of CMV-N blood products significantly decreased the absolute risk of CMV infection by 21% in CMV-seronegative HSCT recipients when compared with the use of non-leucoreduced blood products (23). With the introduction of universal LR however, there has been a shift from this standard practice by some transplant centres although others still favour using CMV-N products over solely leucoreduced components based on evidence of improved TT-CMV prevention efficacy (10, 21, 24).

As with LR, seroselection is unable to completely eliminate TT-CMV. Seronegative donors have the potential to transmit CMV DNA to the transfusion recipient, particularly during the long window period following infection (10, 18, 21). CMV serological testing during this period fails to detect a donor who is CMV positive as the antibody test remains negative (10). Thus the sole use of CMV-N products paradoxically can increase the risk of TT-CMV if blood donated in the window period is used (10). The use of CMV-N blood components is further compounded by the financial costs associated with ongoing testing of donors (due to the relatively high CMV seroprevalence in the general population) and the requirement of hospitals to manage a separate inventory of leucoreduced and CMV-N products as is the case in Australia (9, 18).

These and other factors including LR, effective pre-emptive or universal treatment with antivirals such as ganciclovir for high-risk patient groups and, routine virological surveillance of susceptible individuals have raised questions regarding the continuing need to use CMV-N blood products in high-risk patients (9, 10, 18). Certainly in Australia, the optimal strategy for managing CMV-safe inventories remains a topic of current debate for these and other reasons including the issue of sustainability of the current approach of dual LR and seroselection(9). There is evidence that the annual CMV-seronegative component excess in Australia significantly reduced between 2008/9-2012/13 and that if current trends continue there may be a future deficit of CMV-N component inventories where demand exceeds supply by 2017/18 (9).

The necessity of CMV-N products has been called into further question by a recent report by Seed et al (2015) that demonstrated the relative safety of leucoreduced only components using a modelling approach to estimate the residual risk of TT-CMV associated with the use of leucoreduced blood components in Australia20. Based on their model, the estimated combined residual risk of leucoreduced-only Red Blood Cells (RBCs) and platelet units was extremely low (1 in 13 575 000 (95% CI: 1 in 1,344,167,000 – 1 in 730,000 as were the individual residual risk estimates for leucoreduced-only RBCs and leucoreduced platelets (1 in 7,790,000 (95%CI: 1 in 771,307,000 – 1 in 993,000) and zero (95% CI: 0 – 1 in 1,074,000) respectively) (3).

## 

## International decision making

Approaches to providing CMV-safe cellular blood components for transfusion vary substantially amongst clinicians globally (7). This is most likely due to the challenges associated with LR and seroselection described above and possibly as a consequence of the paucity of data needed to inform a meaningful conclusion on the optimal strategy for the prevention of TT-CMV (7). In Canada for example, the practice is currently divided as half of the transplant centres continue to require CMV-N blood products for allogenic HSCT recipients whilst the remainder have moved away from this practice following the introduction of universal leucoreduction (10).

Similarly, in the US, many centres continue to transfuse CMV-N components to CMV-seronegative allogenic SCT recipients due to the uncertainty about the safety of CMV-U blood products in reducing the risk of TT-CMV in this group of patients (18). A web-based survey of American Association of Blood Banks (AABB) physician members in 2007 demonstrated a gap between perception and practice with respect to current blood banking and clinical practices for prevention of TT-CMV in the country (7). The majority (65%) of the 183 participating institutions indicated that they considered CMV-N and leucoreduced products equally effective in preventing TT-CMV; however, the view of equivalence expressed by most responders was not consistent with reported practices (7). For example, more than 33% of responders reported preferentially transfusing CMV-N components particularly to fetal and neonatal patient groups whilst two thirds of physicians managing adult solid organ transplant recipients considered leucoreduced products equivalent to CMV-N components.

In the UK, many transplant centres have changed their practice following recommendations by SaBTO that solely leucoreduced products are sufficient for HSCT recipients and that routine post-transplant CMV PCR monitoring be conducted to detect an increase in TT-CMV for CMV-seronegative allogenic SCT recipients (18).

The AABB CMV Prevention Work Group recently commissioned a systematic review in 2015 in an attempt to address the lack of clarity regarding which is the optimal strategy for preventing TT-CMV i.e. LR versus CMV serological testing and LR (7). Eleven studies met the inclusion criteria, however one was subsequently excluded as it compared two different types of LR. Analysis of the 10 remaining studies indicated no significant difference between treatment groups when comparing LR to transfusing CMV-U cellular blood components (5 studies); LR to transfusing CMV-N cellular components (3 studies) and, LR alone to combined LR and CMV testing in high-risk patient groups (2 studies) (6, 7). The review concluded that current scientific evidence does not favour a single strategy for reducing the risk of TT-CMV in high-risk patients. It is important to note however that most of the studies included in the meta-analysis were outdated (from 1980’s and 1990’s) and thus their relevance to modern practice is uncertain as they relied on low sensitivity techniques to detect TT-CMV and LR methods that were not as efficient as those currently available.

Following the release of the systematic review, the AABB published a committee report (7)where the committee decided not to publish clinical practice guidelines regarding the appropriate usage of leucoreduced and /or CMV seronegative units to reduce the risk of TT CMV because the data from the systematic review was of poor quality and it is unclear whether leucoreduction of cellular blood components is sufficient to reduce TT- CMV or whether CMV serological testing adds additional benefit to leucoreduction. The committee report also notes there is a wide variation in practices of using leucoreduced components alone or combining CMV serology and leucoreduction to prevent TT-CMV for at risk patients.

An editorial by Strauss(25) in the same edition of Transfusion as the AABB committee report suggests it is reasonable to conclude that leucocyte reduction of Red Blood Cells and platelets by any method capable of consistently achieving a White Blood Cell count of <5 x 106 White Blood Cells/unit optimally reduces the risk of TT-CMV.

Finally, the most recent statement from the National Advisory Committee on Blood and Blood Products Canada (February 14 2017) <http://www.nacblood.ca/resources/guidelines/CMV.html> regarding appropriateness of use of CMV seronegative vs CMV safe product recommends

Recommendation #1

The National Advisory Committee recommends that CMV safe (leucoreduced) and CMV IgG seronegative products be considered equivalent except for intrauterine transfusion.

Recommendation #2

The National Advisory Committee recommends that Canadian Blood Services stop their current process for testing and provision of CMV seronegative units issued to hospital facilities and develops a new process to maintain a small inventory of CMV seronegative blood components for the sole purpose of intrauterine transfusion.

Recommendation #3

The National Advisory Committee recommends that Canadian Blood Services explores the feasibility of providing a small boutique inventory of dually tested (seronegative and NAT) CMV negative blood components for the sole purpose of intrauterine transfusion.

## Current Australian consensus

Universal LR has been in practice in Australia since 2008 (9) Following a 2004 meta-analysis that found seroselection has a modest higher efficacy over LR in prevention of TT-CMV, the Australian Red Cross Blood Service recommended the use of CMV-N blood components for susceptible groups including transplant recipients, chemotherapy recipients, intrauterine RBC transfusion recipients, premature or immunocompromised neonates and, pregnant women. The current practice in Australia therefore includes combined leucoreduction and seroselection (9)

## Conclusion

CMV is a common infection and one that is easily acquired in the community setting. In immunocompromised individuals, CMV infection can be devastating; however, this has become less of a problem partly due to selection of seronegative donors and leucoreduction as core strategies to prevent TT-CMV. The optimal strategy for managing CMV-safe inventories has been debated since the introduction of leucoreduced blood products in many countries. Newer diagnostic tools and effective antiviral regimens have further fuelled the current debate regarding the continuing need to transfuse blood products from CMV-N donors to high-risk patients. Whilst there is some evidence for improved TT-CMV prevention efficacy with selection of seronegative donors, these data have since been superseded by more recent studies affirming the equivalent safety of solely leucoreduced blood products. The safety of such products has been further demonstrated by a modelling approach used by Seed et al(3) that estimated the residual risk of leucoreduced-only products in Australia is negligible (1 in 13 575 000). This risk is very low compared to the risk of acquiring CMV in the community.

In the absence of an international consensus on the optimal strategy to prevent TT-CMV and given the low likelihood of future large scale clinical trials to determine which approach is superior i.e. LR, seroselection or a combination of both, the variation in practices of LR versus combining LR and seroselection is likely to persist. Whilst the latter approach forms the current Australian strategy for preventing TT-CMV, the growing evidence-base supporting the effectiveness of LR alone, as well as improved diagnostic ability to detect TT-CMV and effective antiviral therapy, affirms the necessity for this stance to be reassessed. Furthermore, the potential for demand for CMV-N components to exceed supply by 2017 if current trends continue, calls into question the future sustainability of this dual approach for managing CMV-safe inventories. Finally, if Australia is to continue managing a separate CMV-N inventory, substantial additional resources will be required to maintain this approach in the long term.

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1. granulocytes are not leucodepleted [↑](#footnote-ref-1)
2. removal of white cells through filtration during manufacture [↑](#footnote-ref-2)
3. **Notes**

   SaBTO Cytomegalovirus tested Blood Components Position Statement https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/215125/dh\_133086.pdf [↑](#endnote-ref-1)
4. Patient Blood Management Guideline Module 5 Obstetrics and Maternity and Patient Blood Management Guidelines Module 6 Neonatal and Paediatrics

   <https://www.blood.gov.au/pbm-guidelines> [↑](#endnote-ref-2)
5. Australian and New Zealand Society of Blood Transfusion guidelines for Transfusion and Immunohaematology Laboratory Practice 2016 <https://www.anzsbt.org.au/data/documents/guidlines/GuidelinesforTransfusionandImmunohaematologyLaboratoryPractice_1ed_Nov20_.pdf> [↑](#endnote-ref-3)
6. National Advisory Committee’s statement regarding appropriateness of use of Cytomegalovirus (CMV) seronegative vs CMV safe product

   <http://www.nacblood.ca/resources/guidelines/CMV.html> [↑](#endnote-ref-4)
7. The PBM Guidelines Module 6 Neonatal and Paediatrics – preterm neonates (up to 28 days after expected date of delivery [↑](#endnote-ref-5)
8. Granulocyte transfusions for CMV negative patients (or unknown CMV status) [↑](#endnote-ref-6)
9. Patient with Severe Combined Immunodeficiency who are CMV negative (paediatric population) [↑](#endnote-ref-7)
10. Stem cell transplants where donor and recipient are CMV negative (paediatric population) [↑](#endnote-ref-8)
11. Pregnant women regardless of CMV status who require regular elective transfusions during pregnancy (not during delivery) [↑](#endnote-ref-9)
12. AABB Committee Report: reducing transfusion-transmitted cytomegalovirus infections

    <http://dx.doi.org/10.1111/trf.13503> [↑](#endnote-ref-10)
13. Terminology: leukoreduced (LR)and leucodepleted (LD) are terms used interchangeably for the filtered removal of white cells from blood components. In Australian leucodepleted is the preferred terminology. [↑](#footnote-ref-3)