TM08-04.006 Irradiated Blood Products Policy

APPLICABILITY

Compliance with this document is required by all Alberta Precision Laboratories Ltd. (APL) employees, medical staff, students, and other persons acting on behalf of APL (including contracted service providers as necessary).

PURPOSE

This policy provides direction for the appropriate selection of irradiated blood products.

BACKGROUND

Irradiation of blood products is recommended to reduce the risk of Transfusion Associated Graft Versus Host Disease (TA-GVHD) in immunocompromised recipients.

Irradiated blood products are more costly to provide than non-irradiated products. In addition, irradiation of red blood cells (RBC) impacts the quality and integrity of the cells and reduces the shelf life of RBC units. Therefore, transfusion of irradiated RBC should be limited to patients with a clinical need.

DEFINITIONS

Cellular Therapy Product (CTP)	A somatic cell-based product that is procured from a donor and intended for processing and administration. E.g. Hematopoietic stem cell transplant (HSCT) or bone marrow transplant (BMT)
Irradiation	Treatment of a blood product using electromagnetic radiation. This inflicts irreparable DNA damage to T-lymphocytes and any nucleated cells and prevents them from replicating, thereby preventing TA-GVHD.
Irradiation equivalent	Cellular components that have been treated in a manner other than irradiation that inactivates the ability of T-lymphocyte proliferation. e.g. Psoralen treated units or units greater than 14 days old.
Transfusion Associated Graft Versus Host Disease	A rare, usually fatal complication of transfusion resulting from the transfusion of donor T-lymphocytes into a recipient whose immune system is not capable of eliminating them. These donor lymphocytes attack and cause damage to recipient tissues. Patients at highest risk include those who are severely immunocompromised, and those who receive blood products from a donor with similar human leukocyte antigen (HLA) alleles (e.g. directed donations from family members, HLA-matched platelets)

Transfusion Medicine Physician	A physician or pathologist with responsibility for Transfusion Medicine in their sector or zone.

RESPONSIBILITY

The patient's Most Responsible Health Practitioner (MRHP) and health care providers on the patient care units are responsible for:

- Identifying patients who require irradiated blood products.
- Notifying Transfusion Medicine (TM) of the requirement for irradiated blood products.
- Notifying TM when irradiated cellular blood products are no longer required.
- Informing the patient of their need for irradiated blood products.

TM Physicians are responsible for:

- Reviewing requests for irradiated blood products that fall outside of recommended indications.
- Regular reviews for all attributes without lifelong requirements; reviews should be completed:
    - At least annually ***or***
    - When the cessation of therapy is identified ***or***
    - The criterion for discontinuation is met

TM personnel are responsible for:

- Reviewing and meeting the requirements for the provision of irradiated blood products.
- Appropriately recording blood products requirements when notified by physician and patient care units.
- Monitoring the utilization of irradiated blood products for appropriateness and providing information to the TM Physicians for regular reviews
- Updating patient's history or registry file in the LIS with irradiation requirements.
- Flagging of known contraindications for review by TM physicians.

AHS Zone Clinical Department Heads are responsible for:

- Communicating and educating clinical colleagues on the appropriate use of irradiated blood products.

POLICY

APL TM shall provide irradiated blood products according to the recommendations outlined below.

Orders for irradiated blood products that fall outside of the indications listed in the tables below must be assessed by a TM physician or Cellular Therapy Medical Lead on a case-by-case basis.

The following tables are based on international guidelines and represent a minimum standard. TM and individual physicians may choose to provide irradiated products for additional patient groups based on transfusion committee / TM physician recommendations.

Included in this Policy is:

1. Products Requiring Irradiation

TM shall ensure the following blood products are irradiated, regardless of the immune status of the recipient:

- All HLA-selected/matched platelets.
- All granulocytes.
- Any products where the donor is a first- or second-degree relative of the patient. Transfusion needs for patients requiring rare blood components will be supported through CBS' Rare Blood and Specialized Cell Program.
- RBC and platelets to be transfused to a patient identified to be at risk of transfusion-associated graft-vs-host disease (TA-GVHD).
- Cellular Therapy Products (CTP) for infusion into a recipient with relapsed or refractory disease to induce graft vs leukemia effect but prevent GVHD.

Note: It is not necessary to irradiate fresh frozen plasma, pathogen inactivated blood products, or fractionated plasma products.

Irradiated Product Availability

- Not all hospitals in Alberta have the ability to irradiate on-site, or stock irradiated products in regular inventory.
- In the event of emergency transfusion, when irradiated RBC are indicated but not available, RBC that are older than 14 days shall be provided if possible.
- Prolonged storage of pre-irradiated units is associated with high potassium levels, in vitro hemolysis, and decreased post-transfusion recovery. Therefore, TM shall avoid maintaining large inventories of irradiated RBC which may result in potentially harmful transfusion of irradiated RBC to patients who do not require them.

2. Contraindications

Due to the risk of increased potassium and in vitro hemolysis in irradiated RBC units, irradiated RBC should not be issued to the following patient types unless the patient has a specific clinical indication requiring irradiated products:

- Patients with a history of renal disease
- Patients with elevated potassium or creatinine
- Patients at high risk of hyperkalemic arrest
- Patients on dialysis
- Patient in cardiac intensive care units
- Patient known to be using rapid infusers (e.g. trauma or massive hemorrhage)

When inventory pressures require the use of irradiated RBC for patients who do not have a patient attribute necessitating irradiation, TM will attempt to limit these units from being issued to the above patient populations. This exclusion may be based on the location of the patient (e.g. dialysis unit) or clinical indication that is readily available or included with the order.

If inventory pressures require irradiated RBC to be given to the above patient populations, consult the TM physician. *Exception:* in MHPs, 1 out of 4 RBC units in kits for patients greater than 25 kg may be irradiated without TM physician approval.

3. Patients Approved for Irradiated Blood Products

Table 1: Fetal and Neonatal Patients

- Neonates less than 14 days old should receive units irradiated within the last 24 hours. If these are not available, then non-irradiated units greater than 14 days old should be provided.

Patient	Scenario	Recommended Duration
Fetus	Intra-uterine transfusion (IUT)	During the entire pregnancy
Neonate	All	Up to 14 days of age (regardless of gestational age or low birthweight)
Neonate	Exchange transfusion	Up to 4 months of age
Neonate	Previously received IUT	Until 6 months of age
Neonate	Congenital T cell immunodeficiency suspected or confirmed	Until congenital T cell immunodeficiency is excluded* Indefinitely if confirmed.
Neonate	Complex cardiac malformation / Chromosome 22q11 deletion /	Until 22q11 deletion is excluded* Indefinitely if confirmed.

*The presence of a congenital cardiac abnormality identified in a neonate or infant may raise the suspicion of chromosome 22q11 deletion syndrome, commonly associated with a congenital T cell immunodeficiency.

Since newborn screening in the province of Alberta identifies patients with this risk within the first two weeks of life the provision of irradiated products on suspicion secondary to cardiac abnormality will be restricted to patients from outside of Alberta until testing is completed. Irradiated products will be provided until T lymphocyte immunodeficiency syndrome has been excluded.

Cardiac abnormalities most frequently associated with chromosome 22q11 deletions include: Tetralogy of Fallot, ventricular septal defect, interrupted aortic arch, combined pulmonary atresia and ventricular septal defect, and truncus arteriosus.

There is no need to irradiate red cells or platelets for infants undergoing cardiac surgery unless clinical or laboratory features suggest a coexisting T lymphocyte immunodeficiency syndrome.

Table 2: Specific Diagnoses and Treatments

<table>
<tr><th colspan="2">Diagnosis / Treatment</th><th>Recommended Duration</th></tr>
<tr><td colspan="2">Hodgkin’s Disease (Hodgkin lymphoma)
From diagnosis and following completion of curative therapy. Required for a minimum of 6 months following achievement of remission</td><td>Can be removed at the request of the MRHP following remission or at direction of TM physician</td></tr>
<tr><td colspan="2">Suspected or confirmed (T cell) congenital immune deficiency (i.e. Wiskott-Aldrich, Di Georges, SCID)
Required until immunodeficiency ruled out, or life-long if proven immunodeficiency</td><td>Lifelong
Can be removed at the request of the MRHP if immunodeficiency is ruled out.</td></tr>
<tr><td rowspan="2">Aplastic Anemia</td><td>If patient has ever received ATG (Anti-thymocyte globulin)
No defined duration
ATG in the context of other diagnosis may not require irradiated components, the request should be reviewed and approved by TM physician.</td><td>Lifelong
Can be removed at the request of the MRHP following cessation of therapy or at direction of TM physician.</td></tr>
<tr><td>If patient has ever received alemtuzumab (CD52)
Required a minimum of 6 months after cessation of therapy</td><td>Can be removed at the request of the MRHP following cessation of therapy or at direction of TM physician.</td></tr>
<tr><td>Patients treated with certain Chemotherapy/ immunosuppressive agents</td><td>Fludarabine, Cladribine, Deoxycoformycin, Nelarabine
and
Other purine-like analogues (e.g. clofarabine, Bendamustine)*
Required during therapy and for a minimum of 6 months after cessation of therapy</td><td>Can be removed at the request of the MRHP following cessation of therapy or at direction of TM physician.</td></tr>
<tr><td colspan="3">Other immunosuppressive agents not listed - This is not an exclusive list of diagnoses or immunosuppressive agents that may warrant provision of irradiated products. Consult with a TM physician is recommended.
Physician to review annually - The decision to provide irradiated blood for patients on immunosuppressive agents should be made with consideration given to perceived risks and benefits of irradiated blood transfusion, the availability of the irradiated products, and the immunosuppressive potency of the agent. Discussion between the patient’s most responsible physician and a TM physician is advised.</td></tr>
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Note: Consult the AHS Parenteral Monographs for drug information, including trade vs. generic names.

Table 3: Transplant Recipients and Donors

Patient / Donor	Approval Begins	Recommended Duration
Allogeneic bone marrow or stem cell transplant recipient	From start of conditioning chemotherapy	Until meets criteria for discontinuation*
Donors (including autologous) of bone marrow and peripheral blood stem cells receiving allogenic transfusions	7 days prior to harvest	Until harvest of bone marrow/stem cells
Donor lymphocyte infusion (DLI) in the context of their post-allogeneic transplant therapy. The duration of irradiated blood transfusion post-DLI is contingent upon clinical factors related to engraftment post HSCT, the presence of acute or chronic GVHD and ongoing immunosuppressive therapy.	Upon booking of planned infusion if allogenic requirements have been removed.	Until meets criteria for discontinuation*
Patients with transplant associated graft-versus-host disease (GVHD)	At diagnosis	Until meets criteria for discontinuation*
Autologous bone marrow or stem cell transplant recipient	From start of conditioning chemotherapy	Until 6 months post-transplant
Patients undergoing peripheral blood lymphocyte collections for future CAR-T cell re-infusion	7 days prior to and during the harvest	6 months post CAR-T cell infusion

* The indication for ongoing transfusion of irradiated blood components should be reviewed at least yearly. May consider lifting the requirement for irradiated blood components at the direction of a TM physician with consultation with MRHP if all of the following criteria are met:

a. More than 6 months have elapsed since the transplant date;
b. The lymphocyte count is more than 1 x 10^9/L;
c. There is no evidence of active GVHD; and,
d. All immunosuppression has been discontinued.

REFERENCES

Clinical Guide to Transfusion, Chapter 15 Irradiated, Washed, and CMV Seronegative Blood Components. Canadian Blood Services On-line Edition, 2 March 2021. https://professionaleducation.blood.ca

Recommendations for use of irradiated blood components in Canada, National Advisory Committee on Blood and Blood Products, A MAN and CCNMT Collaborative Initiative: 2023-10-16 . www.nacblood.ca

Supplement to the NAC-CCNMT Recommendations for Use of Irradiated Blood Components in Canada 2023-11-02. https://nacblood.ca/en/resource/supplement-nac-ccnmt-recommendations-use-irradiated-blood-components-canada

CSA. Blood and Blood Components. National Standard of Canada. CAN/CSA-Z902:20. Ottawa, ON. Standards Council of Canada; 2020.

CPSA. Standards for Diagnostic Laboratory Accreditation: Transfusion Medicine v9 April 2021.

Government of Canada. Health Canada. Health Products and Food Branch. *Blood Regulations,* CRC, SOR/2013-178 (2015). Current to 2021-09-11.