Frozen Plasma Toolkit

Prepared by

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### Introduction

In 2008, an audit of Frozen Plasma was undertaken to establish the current ordering and utilization practices among Ontario physicians. Despite the publication of many recommended guidelines for the use of Frozen Plasma, a significant proportion of Frozen Plasma transfusions do not meet the criteria set forth in these guidelines. Of the 573 requests for Frozen Plasma, 54.8% were deemed appropriate, 28.6% inappropriate and 16.6% were indeterminate. Transfusion of Frozen Plasma has a constellation of adverse consequences, especially transfusion-related acute lung injury (TRALI) and transfusion associated circulatory overload (TACO).

The full report from the Ontario Provincial Frozen Plasma audit can be found on the Transfusion Ontario Web-site: [http://www.transfusionontario.org/media/docs/FP%20Audit%20Report_Final.pdf](http://www.transfusionontario.org/media/docs/FP%20Audit%20Report_Final.pdf)

In November 2009, the Ontario Frozen Plasma Recommendations working group was formed to develop a strategy to improve Frozen Plasma utilization in Ontario. The working group decided that the first priority was to develop evidence based Ontario recommendations for situations when the use of Frozen Plasma is appropriate and also to summarize the situations when the use of Frozen Plasma is not useful.

This toolkit is designed to provide hospital Transfusion Services with the tools required to optimize the use of Frozen Plasma.

The ORBCoN Frozen Plasma toolkit includes

1. The Ontario Clinical Practice Recommendations for the Use of Frozen Plasma
2. Ontario Frozen Plasma Recommendations-Supporting documentation
3. Algorithm for Screening Frozen Plasma Orders
5. Frozen Plasma Manual Data Collection Form
6. References

Also available on the ORBCoN website at [www.transfusionontario.org](http://www.transfusionontario.org) are two electronic resources:

1. Bloody Easy On-line Audit tool: an online audit tool available to all hospitals within Ontario
The Ontario Clinical Practice Recommendations for the Use of Frozen Plasma (FP)

Situations in which the transfusion of FP is reasonable:

<table>
<thead>
<tr>
<th>Clinical Indication</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Liver disease or DIC with INR above 1.5</td>
</tr>
<tr>
<td></td>
<td>Massive transfusion (expect more than 10 RBC units transfused in 24 hours) with INR above 1.5 (or rapidity of bleeding does not allow for MD to wait for results)</td>
</tr>
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<td></td>
<td>Reversal of warfarin or vitamin K deficiency only where intravenous vitamin K would not suffice and prothrombin complex concentrate (octaplex®) is unavailable</td>
</tr>
<tr>
<td></td>
<td>Inherited or acquired single factor deficiencies where specific factor concentrate is unavailable</td>
</tr>
<tr>
<td>Emergency surgery or major procedure (within 6 hours)</td>
<td>Reversal of warfarin or vitamin K deficiency only where intravenous vitamin K would not suffice and prothrombin complex concentrate (octaplex®) is unavailable</td>
</tr>
<tr>
<td>Surgery or major procedure</td>
<td>Liver disease or DIC with INR above 1.5</td>
</tr>
<tr>
<td></td>
<td>Inherited or acquired single factor deficiencies where specific factor concentrate is unavailable</td>
</tr>
<tr>
<td>Plasma exchange</td>
<td>Thrombotic thrombocytopenic purpura (TTP)</td>
</tr>
</tbody>
</table>

Situations in which transfusion of FP is NOT useful:

- INR 1.5 or less (including major or minor procedure/surgery)*
- Use of 1:1 (FP:RBC) replacement when patient is unlikely to require massive transfusion
- Coagulopathy in the absence of bleeding or need for emergency surgery
- Elective reversal of warfarin where time allows for warfarin cessation and/or use of vitamin K
- Reversal of anticoagulants other than warfarin (eg: heparin/LMWH, rivaroxaban)**
- Volume expansion or “nutrition support”

* Note: Patients with an increased INR do not have an increased risk of bleeding with minor procedures and there is no evidence that transfusing plasma will prevent or reduce bleeding.
** Note: FP has no effect in reversing or neutralizing heparins or thrombin inhibitors
Most Common Inappropriate Uses Of Frozen Plasma From Provincial Audit

Background

Frozen Plasma is a commonly used blood component. The primary indication for transfusing Frozen Plasma is the correction of coagulation factor deficiencies in patients who are bleeding and/or require an invasive procedure. Less commonly Frozen Plasma is used as the replacement fluid for plasmapheresis (usually Thrombotic Thrombocytopenic Purpura). In a recent provincial audit of Frozen Plasma utilization, 28.6% of the Frozen Plasma transfusions were deemed inappropriate. Other audits of Frozen Plasma use performed in the United Kingdom, Australia and the USA have shown similar or higher rates of inappropriate use.

Following the results of the provincial audit, a working group has developed a summary of recommendations for Frozen Plasma utilization. These recommendations were based on a review of existing national guidelines and incorporate the introduction of octaplex, a prothrombin complex concentrate that is indicated for the urgent reversal of warfarin, in Canada.

The recommendations are intended to serve as an aid to improve Frozen Plasma utilization at individual hospitals, particularly if there are currently no guidelines in place. In the provincial audit, hospitals with guidelines for Frozen Plasma transfusions had lower rates of inappropriate utilization. Implementation of these recommendations at individual hospitals, especially if used in conjunction with the algorithm, may help identify inappropriate transfusion orders and improve transfusion practice.

Most common inappropriate uses of Frozen Plasma

1. **Treatment for mild abnormalities of coagulation test results that are not associated with an increased risk of bleeding**
   - All guidelines universally indicate that Frozen Plasma should only be given for an INR above 1.5. The levels of individual coagulation factor levels are adequate for hemostasis when the INR is below this level. Even INR results above this level likely do not represent a clinically important coagulation factor deficiency. A recent systematic review demonstrated that there was no increase in bleeding complications associated with invasive procedures (e.g., central vein catheterization, liver biopsy, etc) among patients with an elevated INR as compared to patients with normal test results.

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• Additionally, recent observational studies have shown that Frozen Plasma transfusions do not result in a clinically significant reduction in the INR unless the INR is above 1.8.\textsuperscript{7,8}

2. **Correction of abnormal coagulation test results in the absence of either bleeding or an emergency surgery**

• Frozen Plasma is not indicated if the patient is not bleeding or does not require an emergency invasive procedure or surgery. The effect of Frozen Plasma is transient (lasts hours) as the half life of the transfused coagulation factors is as short as 4-5 hours.

3. **Elective reversal of warfarin**

• If the coagulopathy is due to warfarin then giving vitamin K or simply withholding the warfarin is appropriate when urgent INR reversal is not required (i.e no active bleeding and no need for emergency procedures). Vitamin K should be given orally or intravenously, but not subcutaneously due to variable absorption. Please refer to guidelines that specifically address the reversal of warfarin.\textsuperscript{9,10}

4. **Emergency reversal of warfarin when octaplex® is available**

• For emergency reversal of warfarin, octaplex® is more effective than Frozen Plasma in correcting the INR. In most cases, vitamin K should be given in conjunction with octaplex® or Frozen Plasma, as the effect of both products is transient. Please refer to guidelines that specifically address the reversal of warfarin\textsuperscript{9,10}, and the use of octaplex®\textsuperscript{11}.

5. **Reversal of anticoagulants other than warfarin**

• Frozen Plasma is not effective in reversing heparin or newer anticoagulants such as direct thrombin inhibitors.

• Frozen Plasma contains anti-thrombin which could increase the anticoagulant effect of heparin.

• For unfractionated heparin, protamine can be used to neutralize heparin.

\textsuperscript{7} Abdel-Wahab OI, Healy B, Dzik WH. Effect of fresh-frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. Transfusion 2006; 46(8):1279-1285.

\textsuperscript{8} Holland LL, Brooks JP. Toward rational fresh frozen plasma transfusion: The effect of plasma transfusion on coagulation test results. Am J Clin Pathol 2006; 126(1):133-139


\textsuperscript{11} National Advisory Committee on Blood Products Recommendations for the use of octaplex®. [http://www.nacblood.ca/guidelines/downloads/recommendations-for-use-of-octaplex.pdf].
Algorithm for Screening Frozen Plasma Orders

* Each Facility will need to establish a policy for management of plasma orders that do not meet the recommendations
The Ontario Provincial Frozen Plasma Audit conducted in 2008 demonstrated that while 55% of the orders for Frozen Plasma were deemed appropriate, the remaining 45% of the requests for Frozen Plasma during the audit period were either inappropriate or indeterminate. This algorithm was designed for use by ordering physicians, Transfusion Medicine medical directors and technologists to prospectively or retrospectively review/audit orders for Frozen Plasma to support the implementation of the Ontario Frozen Plasma Recommendations developed by the Provincial Frozen Plasma Recommendations working group in 2010.

Implementation of guidelines should include feedback on performance either to individual physicians or the system in general. Auditing Frozen Plasma use is one mechanism that can be used to collect and analyze utilization patterns.

Caveats to the use of the Frozen Plasma algorithm:

1. The algorithm does not address the use of Frozen Plasma for plasmapheresis. It is assumed that plasmapheresis would be undertaken following the consultation of a Hematologist since it is a treatment that occurs in centres that specialize in managing a relatively small and unique patient population.

2. The algorithm does not provide information related to appropriate dosing for Frozen Plasma or vitamin K. The results of the Ontario Provincial Frozen Plasma Audit indicate that there appears to be a trend toward “under-dosing” for Frozen Plasma requests.

Recommended dosing:

- **Plasma**: 10 – 15mL/kg or 3 units for a small adult, 4 units for a large adult.

- **Vitamin K**: Dose and route depends on specific clinical circumstances. Please refer to specific guidelines for warfarin reversal.

3. Each institution should establish processes for the management of transfusion requests that fall outside evidence based guidelines. Each Transfusion Committee will need to decide how these orders will be managed. The boxes indicating “contact ordering physician” are meant as a guide only and can be customized with site specific instructions. The process will also vary depending upon whether the algorithm is being used prospectively or retrospectively.

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Frozen Plasma Manual Data Collection Form

*For onsite use only*—please enter all records electronically into *Blood Easy Audits.*

1. Order number: ____________

2. Patient age: ____ years/months

3. Transfusion date: ____________

4. Patient sex:  □ Male  □ Female

5. Number of units ordered: ____ (1-20)

6. How many units were transfused:
   - FP/FFP ______
   - Apheresis 250mL ______
   - Apheresis 500mL ______
   - Cryo-poor plasma ______

7. Specialty of physician ordering Frozen Plasma:

<table>
<thead>
<tr>
<th>□ Anaesthesia</th>
<th>□ Emergency</th>
<th>□ Infectious Diseases</th>
<th>□ Obstetrics &amp; Gynecology</th>
<th>□ Rheumatology</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Cardiology</td>
<td>□ Gastroenterology</td>
<td>□ Internal Medicine</td>
<td>□ Oncology</td>
<td>□ Surgery: Cardiovascular</td>
</tr>
<tr>
<td>□ Critical care: cardiac</td>
<td>□ General Practice/Family Medicine</td>
<td>□ Neonatology</td>
<td>□ Pediatrics</td>
<td>□ Surgery: General</td>
</tr>
<tr>
<td>□ Critical care: Medicine</td>
<td>□ Hematology</td>
<td>□ Nephrology</td>
<td>□ Radiology</td>
<td>□ Surgery: Neurosurgery</td>
</tr>
<tr>
<td>□ Dermatology</td>
<td>□ Immunology</td>
<td>□ Neurology</td>
<td>□ Respirology</td>
<td>□ Surgery: Orthopedic</td>
</tr>
<tr>
<td>□ Unknown</td>
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</tr>
<tr>
<td>□ Other</td>
<td>Please specify:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
8. Frozen Plasma issued to:

| ☐ Apheresis | ☐ Diagnostic Imaging | ☐ Endoscopy | ☐ Neonatal ICU | ☐ Recovery Room |
| ☐ Cardiovascular ICU | ☐ Dialysis | ☐ Intensive Critical Care Unit | ☐ Operating Room | ☐ Surgical Ward |
| ☐ Coronary Care Unit | ☐ Emergency Room | ☐ Medical Ward | ☐ Outpatient Clinic | ☐ Unknown |
| ☐ Other | Please specify: |

9. Was a Pre-transfusion INR ordered?

- ☐ Yes- Results Available (see a)
- ☐ Yes- Results Pending
- ☐ No

  a) What was INR result?
     - ☐ 0.5-1.0  ☐ 2.1-5.0
     - ☐ 1.1-1.5  ☐ 5.1-10.0
     - ☐ 1.6-2.0  ☐ >10.0

10. Was a Pre-transfusion aPTT ordered?

- ☐ Yes- Results Available (see a)
- ☐ Yes- Results Pending
- ☐ No

  a) What was aPTT result?
     - ☐ Within Normal Range
     - ☐ 1-2 x limit of normal range
     - ☐ > 2 x limit of normal range
11. Was a Post-transfusion INR ordered? (within 6 hours)
   □ Yes- Results Available (see a)
   □ Yes- Results Pending
   □ No
      a) What was INR Result?
         □ 0.5-1.0   □ 2.1-5.0
         □ 1.1-1.5   □ 5.1-10.0
         □ 1.6-2.0   □ >10.0

12. Was a Post-transfusion aPTT ordered? (within 6 hours)
   □ Yes- Results Available (see a)
   □ Yes- Results Pending
   □ No
      a) What was aPTT result?
         □ Within Normal Range
         □ 1-2 x limit of normal range
         □ > 2 x limit of normal range

13. Clinical indication:
    □ Bleeding*    □ Minor Bleeding**    □ No Bleeding    □ Unknown

*  Bleeding defined as hemorrhage sufficient to require at least one RBC within 24 hours OR intracranial or spinal bleeding OR haemoglobin drop to <80 g/L
** Minor bleeding defined as all other situations not meeting above definition of “Bleeding”
14. Procedure / Clinical indication:

<table>
<thead>
<tr>
<th>Procedure / Clinical indication</th>
<th>Anticoagulant Reversal</th>
<th>Coumadin</th>
<th>Heparin</th>
<th>Warfarin</th>
<th>Other Please specify:</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central line placement</td>
<td></td>
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<tr>
<td>Coagulopathy</td>
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<tr>
<td>(liver disease, DIC, etc)</td>
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<tr>
<td>Exchange Transfusion</td>
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<td>Fine Needle aspirate</td>
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<td>Image guided therapy</td>
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<td>Kidney biopsy</td>
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<tr>
<td>Liver biopsy</td>
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<td>Massive transfusion</td>
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<tr>
<td>Paracentesis</td>
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<td>Plasma exchange</td>
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<tr>
<td>(therapeutic apheresis)</td>
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<tr>
<td>Plasma Protein deficiency</td>
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<td>Please specify:</td>
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<tr>
<td>Surgery</td>
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<td>Thoracentesis</td>
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<tr>
<td>Unknown</td>
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<tr>
<td>Volume Expansion</td>
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<tr>
<td>Other</td>
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<td>Please specify:</td>
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</tr>
</tbody>
</table>

15. Was an adverse transfusion reaction (ATR) reported within 6 hours?
   □ Yes (see a & b)
   □ No

   a) What symptoms of the ATR were reported? (Select all that apply)
   □ Fever                  □ Chills
   □ Tachycardia            □ Dyspnea
   □ Hypotension            □ Hives, Urticaria
   □ Other Please specify: _____________________________
b) What was the ATR diagnosis? (Select only one)

- Febrile non-hemolytic
- TRALI (Transfusion related acute lung injury)
- Allergic reaction
- TACO (Transfusion associated circulatory overload)
- Acute hemolytic reaction
- Other Please specify: __________________________

16. Does your facility have guidelines for the use of Frozen Plasma?

- Yes (see a)
- No

   a) Was this order refused because it did not meet your institution’s guidelines?

- Yes
- No

17. Does your ordering process include a requirement for providing clinical/laboratory information to justify Frozen Plasma transfusion?

- Yes
- No

18. Were any of the units in this order thawed and not transfused?

- Yes (see a)
- No

   a) What was the final disposition?

   - Used for another patient _________________________
   - Discarded- not used within 24 hrs of thawing _________________________
   - Discarded- broke in the waterbath _________________________
Guidelines:


Systematic Reviews:

1. Segal JB, Dzik WH. *Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review.* Transfusion 2005; 45(9):1413-1425.


Effectiveness:


**Adverse Effects:**


5. **Serious Hazards of Transfusion (SHOT) Annual Report.** 2009. www.shot-uk.org

**Audits:**


2. Luk C, Eckert KM, Barr RM, Chin-Yee IH. **Prospective audit of the use of fresh frozen plasma based on Canadian Medical Association Guidelines.** CMAJ 2002; 166: 1539-1540.

Publications:


Acknowledgments

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We would also like to acknowledge Dr. Ben Saxon, former Medical Director of the Toronto Centre- Canadian Blood Services, for his vision and enthusiasm in generating the idea for this audit.