Provincial Frozen Plasma/ Prothrombin Complex Concentrate Audit Report 2013

This report has been submitted on behalf of the Provincial Plasma Steering Committee:

Dr. Alan Tinmouth, The Ottawa Hospital - Chair
Dr. Jeannie Callum, Sunnybrook Health Sciences, Sponsor ORBCoN Central
Mr. Troy Thompson, ORBCoN Central
Dr. Peter Pinkerton, Consultant ORBCoN Central
Dr. Yulia Lin, Sunnybrook Health Sciences
Dr. Cyrus Chen Hsia, London Health Sciences
Ms. Kathleen Eckert, London Health Sciences
Dr. Donnie Arnold, Hamilton Health Sciences
Dr. Kathryn Webert, Canadian Blood Services
Ms. Doris Neurath, The Ottawa Hospital
Dr. Lois Shepherd, Kingston General Hospital
Mr. Marvin Jones, Sudbury General Hospital
Ms. Kathy Callaghan, Halton Healthcare Services
Ms. Laura Harrison, Trillium Health Partners-Credit Valley Hospital
Mr. Robert Romans, Canadian Blood Services
Ms. Nancy Heddle, McMaster Transfusion Research Program, Sponsor ORBCoN Southwest
Dr. Menaka Pai, Hamilton Health Sciences
Ms. Wendy Owens, ORBCoN Northern and Eastern
Ms. Debbie Lauzon, ORBCoN Central

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1.0 Executive Summary

Background and Purpose

- Use of Frozen Plasma (FP) in Ontario compared with other provinces is relatively low, but remains higher than in many other jurisdictions in Europe and elsewhere.
- Transfusion of FP has a constellation of adverse consequences, especially transfusion-related acute lung injury (TRALI) and transfusion associated circulatory overload (TACO) which is being recognized with increasing frequency.
- The costs of FP transfusions are substantial and savings could accrue from the elimination of inappropriate use:
    - Reduction in the costs of collecting, processing, distribution and administration of FP
    - Diversion of FP no longer transfused to the manufacturing of plasma derivatives (IVIG and albumin) thereby reducing dependence on more expensive purchased plasma
    - Reduction in the costs of managing complications of FP transfusion in hospital, in particular those cases requiring intensive care
- An audit of FP use in Ontario in 2008 showed considerable use of FP outside of published guidelines. The current (2013) audit was conducted to assess the effectiveness of measures recommended and implemented following the 2008 audit.
    - Creation and dissemination of Clinical Practice Recommendations for FP use in Ontario
    - Statement of conditions for which FP transfusion is not useful
    - Recommendations regarding dosage of FP
    - Use of vitamin K for reversal of warfarin effect
    - Dissemination of advice on the use of Prothrombin Complex Concentrates
    - Algorithm for medical laboratory technologist screening of FP orders
- Prothrombin Complex Concentrates (PCCs) were introduced in 2008 and have been widely used in Ontario with an associated decrease in FP use.
- The assessment of the appropriateness of PCC use in Ontario is timely.

Methods

Fifty-one (32%) of eligible hospitals, representing 60% of FP consumption in Ontario, participated. Each participating hospital collected data on FP transfusions and PCC infusions for 5 (not necessarily consecutive) days and submitted data using a web-based data tool designed for the purpose. Data on 329 FP orders and 113 PCC orders were received. Data on the indications for each transfusion order, including dose, were collected and the appropriateness of the clinical indication for each encounter was assessed according to criteria agreed in advance by a panel of 6 transfusion medicine physicians. Each encounter was classified into one of 3 categories – "appropriate", "inappropriate" or "indeterminate" (where there was insufficient evidence and/or clinical data to allow assignment to one of the other 2 categories). The data for FP and PCC will be separated in this report.

Principal Findings: Plasma

- Orders for FP were deemed "appropriate" in 42% of cases, "inappropriate" in 52% and "indeterminate" in 6%.
- The majority of the sources of orders within the hospitals were identified as intensive care units, medical wards, operating rooms and emergency departments, providing further guidance as to where best to focus future actions for change.
- Hospitals indicating they had "guidelines" for FP transfusion did not have significantly higher rates of appropriate transfusions and no significant decrease in inappropriate transfusions.
- The median dose of FP prescribed/administered was 2 units (equals 500mL) which is, for an adult, deemed less than the potentially effective amount (12-15 mL/kg or 4 units for a 70 kg patient).
- Only 19.7% of the transfusions for FP met the criteria for both an "appropriate" indication and a sufficient dose (≥3 units).
- 11.6% of FP is still being given for reversal of warfarin effect, either alone or in conjunction with PCCs.
- Of the 38 FP orders for reversal of warfarin effect, 79% (30/38) orders were from Community hospitals, while 21% (8/38) orders were from Teaching hospitals.
- No improvement is seen in FP use since the 2008 audit, beyond its partial replacement with PCCs.

Principal Findings: Prothrombin Complex Concentrates

- All audit participating hospitals indicated that they had guidelines for the use of PCCs; a requirement for their utilization.
- Orders for PCC were deemed "appropriate" in 70% of cases, "inappropriate" in 28% and "indeterminate" in 2%.
- Dosage of PCCs appeared more often than not, appropriate to the clinical situation.
- PCCs have not yet totally replaced FP for reversal of warfarin effect (11.6% of FP orders used for warfarin reversal despite safer and faster alternative therapy).
- The appropriateness and inappropriateness of use of FP and PCC in relation to the presence and absence of bleeding or surgical/invasive procedure and urgent warfarin reversal is compared (Table 8.5). The use of PCC is significantly less inappropriate than that of FP under these clinical circumstances (chi square test, $p<0.01$).

Observations/Recommendations

Observation	Recommendation
More than 50% of all FP transfusion episodes in audit were inappropriate including 26% of all FP transfusions given for INR <= 1.5.	1. Develop formal clinical practice recommendations for use of FP in Ontario which could then be adopted by all hospitals.

Studies indicate that provision of clinical practice guidelines and traditional knowledge translation measures have, at best, a limited capacity to improve clinical prescribing of FP. Inappropriate prescribing of FP continues to be widespread in Ontario.	2. Develop a Quality Improvement plan for FP transfusion in Ontario (to be incorporated into overall Quality Improvement plan for transfusion which has begun with red blood cell transfusions). Recommendations 3-5 could be included as part of QI initiative for FP transfusions.
	3. Develop a standardized, template order form for FP, which would include mandatory relevant pre-transfusion information to allow assessment of appropriateness of transfusion request. The form could be adopted by hospitals or the data elements from this form could be included in local transfusion forms. This would also be used in current and/or future development of Computerized Physician Order Entry for transfusions.
	4. All hospitals would be required to perform annual audit of FP utilization using standardized metrics.
No mechanism exists for inter-hospital comparison of use of FP transfusion, to allow hospitals to examine their use of FP in the context of the wider pattern of Provincial consumption of FP.	5. Results of annual audits from all hospitals should be reported to provincial body (e.g. BPCO or ORBCoN), and results would be distributed to all hospitals for peer comparison.
FP continues to be prescribed in situations better managed with PCC. PCC is being used for reversal of warfarin effect in the absence of bleeding or surgical intervention. PCC is also being used for coagulopathies other than urgent reversal of warfarin effect or vitamin K deficiency.	6. Specific criteria/algorithm for auditing FP transfusions specifically for Coumadin reversal by transfusion technologists be developed provincially and be implemented by local hospitals. The algorithm should include decision tree for referral of specific inappropriate FP/PCC requests to transfusion medicine physicians for review.
This audit provides information on the medical specialties/services most frequently prescribing FP and PCC.	7. Develop educational tools and resources that target the largest users of FP/PCC and those with highest inappropriate use. These tools can then be used by local transfusion medicine physicians to influence/change practice.

2.0 Background, Purpose and Recent Developments

In September-October 2008, ORBCoN undertook an audit of the clinical use of FP in Ontario hospitals. Using predetermined clinical practice guidelines developed by clinical hematologists/transfusion medicine specialists to assess appropriateness of prescribing practices, it was found that in 54.8% of FP transfusions an order was appropriate to the clinical findings, in 28.6% an order was inappropriate and in 16.6% the information available did not permit a determination of appropriateness or otherwise. Under-dosing was common with only 29% of FP transfusions both clinically appropriate and in an appropriate dose. Seventy-six hospitals representing 88% of FP consumption in Ontario participated (ORBCoN, Plasma Audit Report, 2009; Tinmouth et al., 2013).

Several recommendations for improvement were made. Clinical practice recommendations have been made available to Ontario hospitals including information on situations where FP is not useful (ORBCoN, Frozen Plasma Toolkit, 2010); these are broadly similar to the guidelines for FP use

published by various organizations over several decades (Appendix A). Advice on the use of four factor PCCs, which became available for clinical use in Canada in 2008, and vitamin K for reversal of warfarin effect has been provided (National Advisory Committee on Blood and Blood Products, 2008, 2011, 2014) and various efforts have been made to enhance awareness of potential adverse consequences of transfusion including FP. Information relevant to the appropriate clinical use of FP and PCCs is incorporated in the Resource Manual for Medical Directors of Transfusion Medicine (ORBCoN, 2013).

Purpose

The present (2013) audit has been undertaken to:

1. Assess the appropriateness of the clinical use of FP 5 years later to determine whether changes in practice are apparent.
2. Examine the appropriateness of the current clinical use of PCCs.
3. Recommend further measures to reduce inappropriate use of FP or PCCs.

Recent Developments

As background to the 2013 audit, recent information is briefly reviewed, including an overview of FP use in Ontario compared with other jurisdictions, preliminary information on the effect of PCCs on FP use, audits of appropriateness of FP transfusion in other countries, effectiveness of traditional educational approaches to conservation, newer more effective utilization control measures and updated information on serious adverse events.

(i) Comparative Data for FP consumption in Ontario and elsewhere

In general, FP consumption in Ontario as well as the rest of North America is higher *per capita* than in other countries (Fig. 2.1); sources of data are provided in Table 2.1. Ontario, of the larger Provinces, has one of the lower FP consumption rates (Fig. 2.1) and has shown a consistent year-over-year reduction in consumption over the last 6 years (Fig. 2.2). This is reflected in the steady reduction when the composite data for individual Ontario hospitals is examined (Fig. 2.3). However, wide variation is seen from hospital to hospital when FP consumption is measured against consumption of red blood cells (RBC) for transfusion as a denominator (Pinkerton, 2011). For example, Fig. 2.4 displays the data for FP/RBC ratios for each of the 16 university affiliated Ontario hospitals over the last 6 fiscal years (April 1 – March 31) (Canadian Blood Services Data Warehouse, CBS). Data for 44 community hospitals show lower FP/RBC consumption ratios than the university affiliated hospitals but also show considerable variation from hospital to hospital within the group. These data can be used by ORBCoN and individual hospital transfusion committees to monitor their FP consumption in (anonymous) comparison to peer-group institutions.

(ii) Impact of the introduction of PCCs on FP consumption

There has been a clear impact on FP consumption as a result of the introduction of PCCs into clinical practice. The reduction in FP consumption in Ontario in 2012-2013 compared with 2007-2008 is 47,718 units (Table 2.2). If it is assumed for the purposes of this exercise that 1,000 IU of PCC provides the equivalent replacement of coagulation factors as four 250mL units of FP, then the amount of FP equivalent to the 7.237 million IU of PCCs issued by CBS in 2012-2013 would be 28,984 units and the overall reduction in FP consumption in 2012-2013 compared with

2007-2008 would have been 18,770 units. Thus, there appears to be a reduction in FP consumption of about 19,000 units between these two fiscal years to be accounted for by factors other than the use of PCCs. A recent single academic centre audit of transfusion of FP and PCCs, found that a reduction of about 30% in FP use coincided with the introductions of PCCs consistent with the calculations of the wider effect in the province (Shih et al., 2014).

In an attempt to correlate PCC use more directly with reduction in hospital use of FP, the incremental decrease in FP consumption by individual hospitals between 2007-2008 and 2012-2013 was compared with the amount of PCC used in the same hospital in 2012-2013 (fig. 2.5). A significant correlation was found ($p<0.01$) supporting a direct effect of PCC use on FP consumption.

NOTE: A recent retrospective analysis of PCC treatment in the management of **intracranial hemorrhage** suggests that more complete reversal of warfarin effect is associated with more favourable outcomes (Karamatsu et al., 2015). Prospective studies are needed to fully assess the significance of this observation.

(iii) Summary of audits of FP transfusion in various jurisdictions

Since the first Ontario audit of FP use there have been further audits of clinical use of FP world-wide and these are listed in an updated version of Appendix B. These audits continue to show widespread inappropriate prescribing practices and some address the question of inadequate dosage. A recent study of over 72,000 FP transfusions from the United States shows a pattern of use in respect of attempted correction of a coagulation defect and dosage very similar to that seen in the ORBCoN audit of 2008 (Triulzi et al., 2014). Also, a recent audit in Ontario from a single academic medical centre confirms persistent inappropriate FP transfusion of about 45% (Shih et al., 2014).

(iv) Update on adverse events

Since the last audit in 2008, female FP donors (whether by whole blood donation or apheresis) who are at risk for causing Transfusion Associated Acute Lung Injury (TRALI) have been increasingly removed from donor populations. This precaution has been associated with a striking decline in the numbers of cases of TRALI reported to hemovigilance programs (Eder et al., 2010, Lin et al., 2012, Funk et al., 2012, Bolton-Maggs et al., 2013, Bolton-Maggs and Cohen, 2013).

By contrast, probably as a consequence of improved clinical recognition, there is an increasing rate of reporting of Transfusion Associated Circulatory Overload (TACO) (Robillard et al., 2008, Bolton-Maggs et al., 2013) and TACO was the most frequent cause of transfusion-associated mortality reported to the US Food and Drug Administration in 2013 (USFDA, accessed 2014). Menis et al. (2014) assessed 147,038 transfusion episodes in the elderly as reported to Medicare administration, resulting in the reporting of a total of 1340 episodes of TACO (62.4/10,000 transfusions); in the majority of episodes the component involved was either red cells (728) or was unidentified (305). FP was identified as the only component transfused in 49 cases at a rate of 66.2/100,000 transfusion episodes, and in a further 174 cases in combination with other components (118.3/100,000).

Passive reporting of TACO underestimates the frequency of this complication. In one hospital, over 8 years, 87 episodes of TACO were reported to the blood bank of which 20 (23%) were associated with FP transfusion. By contrast, a prospective surveillance study of 1 month's duration found 4 TACO episodes out of 84 recipients of FP transfusion, or 4.8% (Narick et al., 2012). A recent review of the medical records of 100 cases of TACO in 2 Toronto academic

medical centers identified 1 TACO event per 2,000 red cell platelet or plasma transfusions (Lieberman et al., 2013).

It is apparent that most databases underestimate the frequency of TACO and that the harder one looks, the more cases of TACO are identified. The economic impact of each episode has been estimated at about $14,000 per hospital visit, through increased length of stay and hospital costs (Magee and Zbrozek, 2013).

In addition to awareness of TACO and understanding of the predisposing medical conditions (Alam et al., 2013), the elimination of unnecessary or inappropriate transfusions, including those of FP, will reduce the hazard to individual recipients of this increasingly recognized complication, and diminish the "risk without benefit".

(v) Effect of traditional efforts to improve FP transfusion practice

Traditional approaches to improving practice such as educational measures, promotion of the use of guidelines, audit with feedback, and administrative interventions such as request forms incorporating information about appropriate indications have largely proved disappointing; a meta-analysis of 10 such attempts indicated a small reduction in inappropriate FP transfusions (Damiani et al., 2010) and a Canadian study found only "modestly improved" appropriate FP use after education audit and feedback and a modified request form requiring a clinical indication (Lauzier et al., 2007; Arnold et al., 2011). For these measures to be effective, intensive effort is required with persistent prolonged exposure of the practitioner to various educational measures (Morrison et al., 1989; Soumurai et al., 1993); the durability of changes in practice brought about may prove difficult to sustain without continuing reinforcement (Tobin et al., 2001). These approaches, to be effective, are likely to be beyond the resources of most institutions to support.

These studies indicate that provision of clinical practice guidelines and traditional knowledge translation strategies have, at best, a limited capacity to improve clinical prescribing of FP.

(vi) Recent reports of effective measures to control inappropriate FP transfusion

Several reports of more effective measures to eliminate inappropriate prescribing of FP have been published since the 2008 Ontario audit. The introduction of a computerized physician order entry (CPOE) system incorporating a required response to a list of indications for FP transfusion was associated with a reduction in orders deemed "inappropriate" from 42.9% before implementation to 27.9% after implementation (Yazer et al., 2013); nevertheless, this leaves a substantial residual proportion of apparently inappropriate orders. A detailed review of the current status of "decision support systems" provides a useful critical appraisal of their effectiveness (Hibbs et al., 2015).

Oversight of ordering practices for FP by physicians directly involved in transfusion medicine, while demanding, is apparently effective in reducing inappropriate FP transfusion. Three recent studies support this position. Triage of orders for FP not meeting guidelines by transfusion service personnel, with referral of non-compliant orders to an on-call transfusion medicine physician for discussion with the ordering physician to arrive at "mutually acceptable" decision, resulted in a 60% reduction in FP consumption and a decrease in the FP/RBC transfusion ratio from 0.48 to 0.22 (Sarode et al., 2010). A more recent study, using a similar approach, over 2 years resulted in 2 incremental decreases in FP consumption of 41.8% and 31.1% respectively (Politsmakher et al., 2013).

An analysis of the introduction of progressively effective measures to curb inappropriate use of FP over a 12 year period provides a measure of the comparative value of these measures. Over

the 12 years, 4 phases each of 3 years were examined. In phase 1, no particular steps were taken to screen orders; in phase 2 there was "education" and dissemination of practice guidelines without active oversight of orders for FP transfusion. Consumption of FP was similar when these two phases were compared in respect of FP per patient discharge, per 1000 patient days or FP/RBC ratio which varied from 22.2 to 29.7. In phase 3, requests not meeting guidelines were questioned by blood bank duty personnel, but were honoured if the ordering physician insisted on proceeding with FP transfusion. This resulted in reduction by about half in the three chosen indicators with the FP/RBC ratio dropping to 16.1 – 10.9. Finally, phase 4 was implemented in which non-compliant FP requests were referred to the transfusion medicine director before issue of product; This was associated with a further large reduction in the three consumption indicators, with the FP/RBC ratio falling to between 10.5 and 3.9 with the lowest figure occurring in the last year of study (Figs. 2.6, 2.7) (Tavares et al., 2011).

These studies point to the conclusion that some form of active stringent case by case peer review of physicians' ordering practices is required prior to issue of FP to effect changes in the clinical practice in FP transfusion, over and above promulgation of guidelines and traditional educational measures.

(vii) Benchmarking and Peer Comparison for FP Transfusion

There is at present in Ontario no mechanism for the hospital Medical Directors of Transfusion Medicine and the hospital Transfusion Committees to compare their use of FP (and other blood components and products) with any benchmark of desirable levels of consumption. A number of studies of attempts to monitor FP ordering practices provide some information on achievable targets for FP use in individual hospitals (see section 2 (vi) above); however, use of more comprehensive data for hospitals in general with a mechanism for feedback to allow assessment of individual hospitals' performance in the context of community practice as a whole does not appear to have been attempted. Databases exist in Ontario that allow assessment of FP use versus transfusion of red blood cells as a denominator (which correlates well with FP use versus active patient days) which could provide a basis for inter-hospital comparison to be used by hospital Transfusion Committees in their oversight and audit of their hospitals practices. Further, availability of denominator data on patient discharges or "patient days" in active treatment beds would provide a more objective comparison of FP transfusion events.

No mechanism exists for inter-hospital comparison of use of FP transfusion to allow hospitals to examine their use of FP in the context of the wider pattern of Provincial consumption of FP.

(viii) Therapeutic effectiveness of FP:

Over the last decade there has been increasing scepticism as to the clinical effectiveness of FP. Systematic reviews of RCTs of FP use have indicated a lack of evidence of significant benefit for the use of FP in a variety of clinical circumstances and bewailing the absence of high quality assessments of the risks and benefits of FP transfusion, both absolute and comparative (Stanworth et al., 2004; Roback et al., 2010; Tinmouth, 2012; Yang et al., 2012).

It has been known for many years that mild to moderate prolongation of the prothrombin time does not correlate with bleeding in association with liver biopsy (Ewe, 1981; McVay and Toy, 1990). Recent extensive reviews of hemostasis in liver disease (Lisman and Porte, 2010) points out that in liver disease not only are pro-coagulants reduced, so also are naturally occurring

anticoagulants accompanied by changes in fibrinolytic mechanisms. They postulate that there is an adjustment in hemostatic mechanisms balancing pro- and anticoagulant influences, and that such balance reduces the need for "correction" by transfusion of FP**.**

Segal and Dzik (2005) in an extensive review of the literature between 1966 and 2004 concerning the predictive value of elevated PT/INR for bleeding in association with an "invasive procedure" (bronchoscopy, central vein cannulation, femoral angiography, liver biopsy) found little evidence that pre-procedure elevation of the PT/INR was predictive of an increased risk of bleeding. They conclude that clinicians should not assume that mild-moderate elevation of the PT/INR represents an indication for pre-procedure transfusion of FP. Haas et al. (2011) concluded that the procedural risk of central venous catheter insertion did not increase with an INR up to 2.0. More recently, a small trial of the effectiveness of prophylactic FP transfusion in preventing bleeding in patients with INR 1.5-3.0, undergoing central venous catheterization, chest tube insertion, tracheostomy or abscess drainage, reported no disadvantage to patients not receiving prophylactic FP transfusion (Muller et al., 2015).

It appears that pre-procedure FP transfusions in diagnostic or therapeutic invasive procedures for mild-moderate increases in INR are not useful.

Small elevations of the PT/INR at the lower end of the scale represent relatively insignificant functional deficits in hemostatic capacity, since the pro-coagulant content of normal plasma contains an excessive reserve. An INR of 1.7 represents approximately 30% of normal coagulant capacity, sufficient for normal hemostasis (Dzik, 2007; Tinmouth, 2012). Also the lower the INR, the less impact FP will have in lowering it further (Stanworth et al., 2011b; Sezik et al., 2014). Repeated studies have shown that the transfusion of FP to patients with minor elevations of the INR results in either no or at most trivial reduction in the INR. Thus Holland and Brooks (2006) found minimally elevated INRs (<1.6) showed no reduction from FP transfusion. Abdel-Wahab and Dzik (2006) estimated the INR before and after 324 transfusion episodes in patients with pre-transfusion INR 1.1 – 1.85 and found a median decrease in INR of only 0.07 and failure fully to correct the INR in 99% of transfusions. In a large multi-center ICU audit, Stanworth et al. (2011b) found that patients with an INR of <1.6 showed essentially no correction of the INR and for those between 1.6 and 2.5 correction was minimal (median 0.4).

It appears that FP transfusion in the presence of mild-moderate increases in INR produce no or only trivial decreases unlikely to be of clinical significance.

Comment: In spite of the ***lack*** of evidence that bleeding is increased in patients with minor elevations of INR undergoing invasive procedures, and the evidence that transfusion of FP to patients with minor elevations of INR fails to produce any or, at most, trivial, correction of the INR or any apparent reduction in bleeding in such patients, futile transfusion of FP continues.
The original Canadian Medical Association Guidelines for FP transfusion recommended an INR "cut-off" value of 2.0. More recently, the Canadian Society for Transfusion Medicine has recommended a "cut-off" of 1.8 for the INR in its memorandum on "Choosing Wisely" (CSTM, 2014).

Perhaps it is time for a reconsideration of the Ontario Recommendations for FP Transfusion, including but not confined to the "trigger" INR threshold.

Figures

Figure 2.1. FP Consumption in Various Countries and Provinces (Units per Million Population).

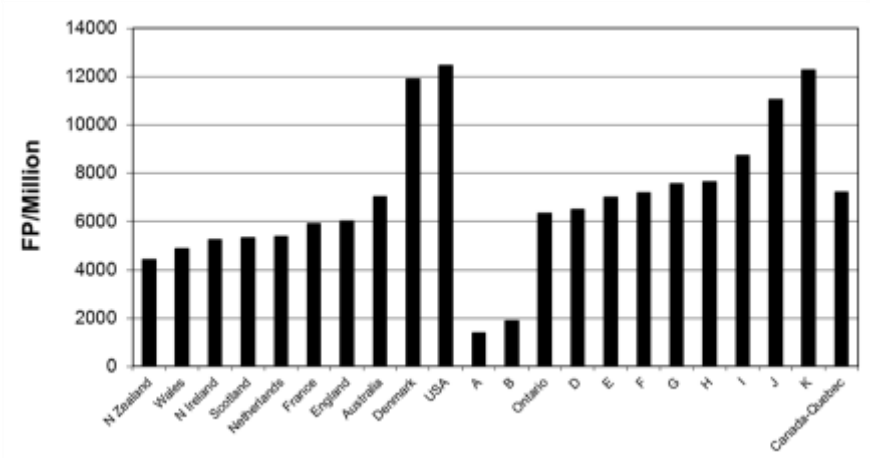


Figure 2.2. Changes in FP consumption per 1,000 population in 8 Provinces from 2007-08 to 2012-13.

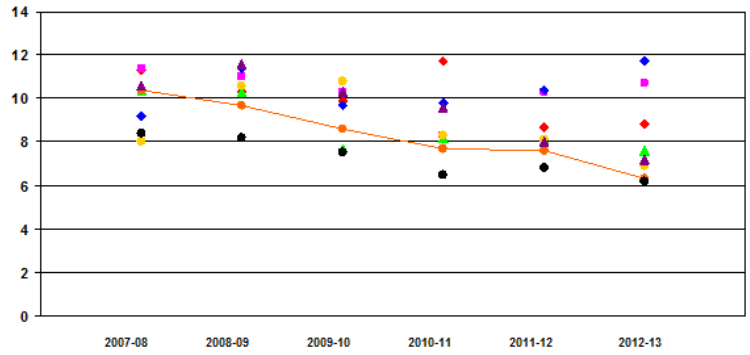


Figure 2.3. Median and Inter-quartile Range for FP Units Issued per 100 Red Cell Units Issued to 60 Ontario Hospitals Annually from 2007-08 to 2012-13.

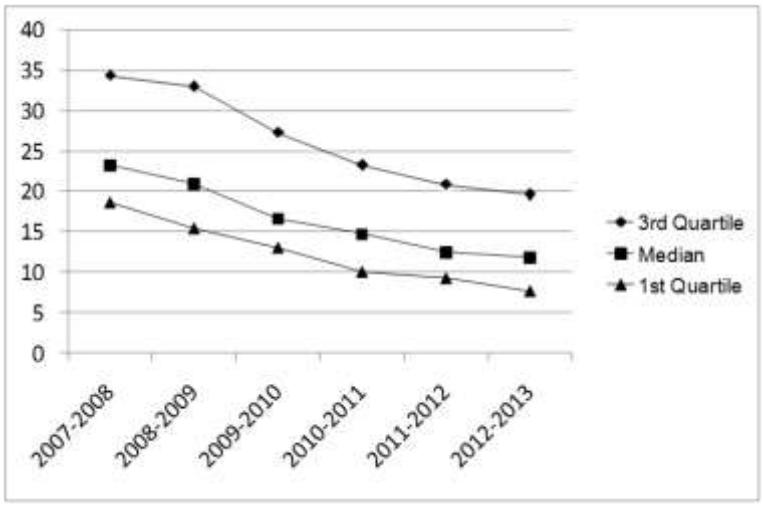


Figure 2.4. FP RBC Consumption Ratios (FP/100RBC) for Six Years for 16 University Affiliated Hospitals.

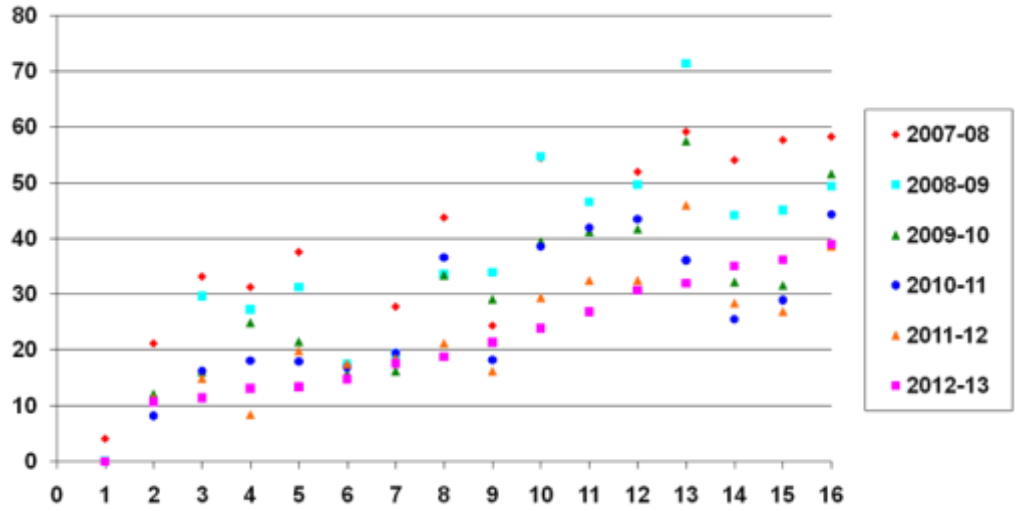


Figure 2.5. Decrease in FP use by individual hospitals (2007-08 vs. 2012-13) shows a significant inverse relationship to use of PCCs in 2012-13.

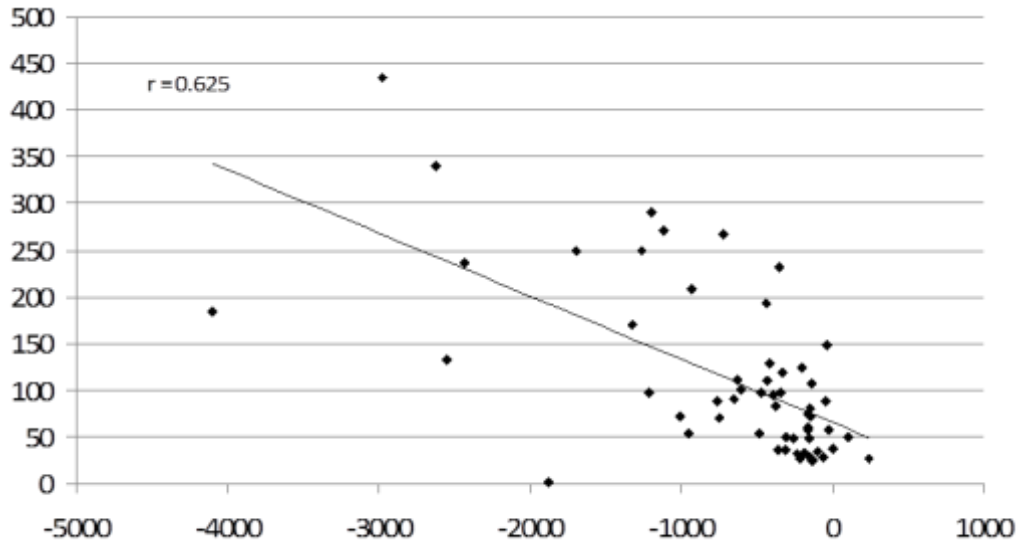


Figure 2.6. Effect of Conservation Measures on FP Consumption per 1000 Patient Discharges (FP/1000Dis) and per 1000 Patient Days (FP/1000PD).

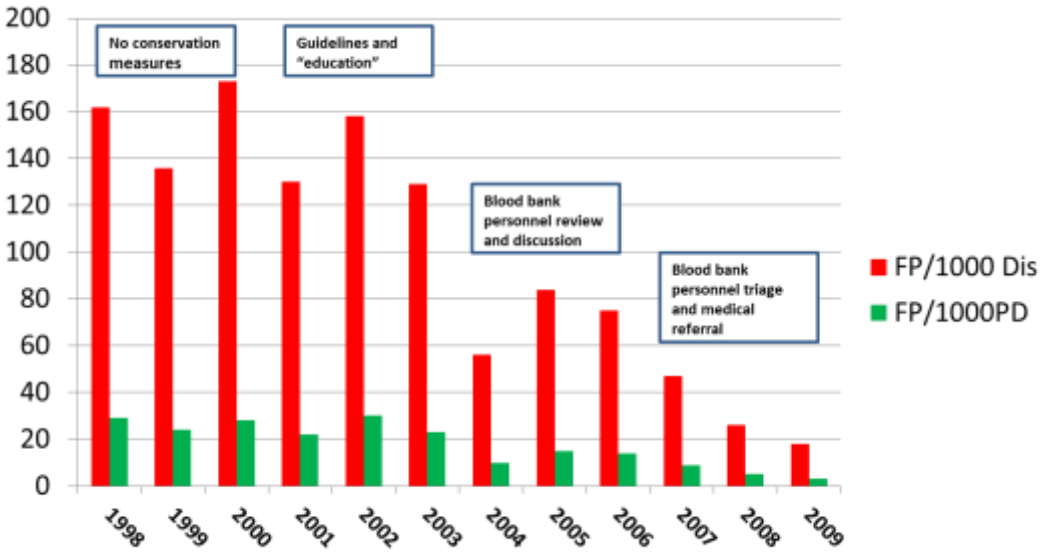
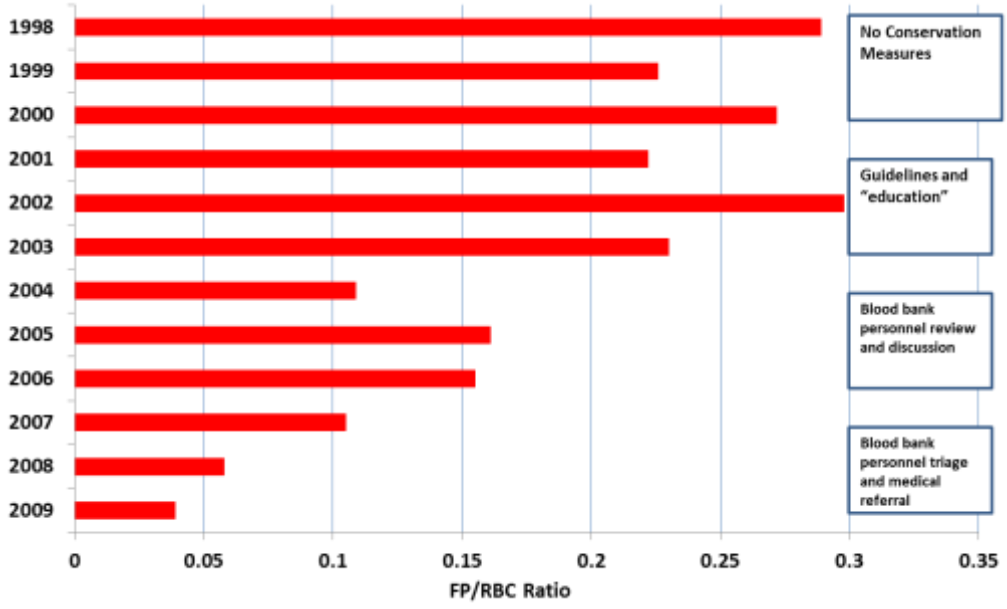


Figure 2.7. Effect of various measures to promote appropriate use of FP. Changes in FP/RBC consumption ratios.



Tables

Table 2.1. Comparison of Issues of FP per 100 Red Cell Units Issued with FP Units Issued per Million Population for Various Countries.

Jurisdiction	Population In Millions	Reference	RBC Issued or Transfused	Frozen Plasma Issued or Transfused	Reference	FP/100 RBC	FP per Million Population (Rank order)	Year of Data
Scotland	5.222	www.ons.gov.uk	191,037	27,799	www.shotuk.org	14.6	5,323 (4)	2011
France	62.628	www.oecd.org	2,339,834	317,658	www.ihn-org.com	15.9	5,920 (6)	2009
New Zealand	4.405	www.oecd.org	119,950	19,487	www.nzblood.co.nz	16.2	4,424 (1)	2011-2
Netherlands	16.656	www.oecd.org	544,324	89,631	www.sanquin.nl	16.5	5,381 (5)	2011
Wales	3.064	www.ons.gov.uk	87,831	14,396	www.shotuk.org	17.0	4,875 (2)	2011
England	52.234	www.ons.gov.uk	1,829,951	314,178	www.shotuk.org	17.2	6,014 (7)	2011
North Ireland	1,814	www.ons.gov.uk	53,318	9,503	www.shotuk.org	17.8	5,239 (3)	2011
Sweden	9.378	www.oecd.org	488,275	89,063	www.haemovigilans.se	18.2	9,497 (12)	2010
Australia	22.618	www.oecd.org	801,295	159,024	www.donateblood.com.au	19.8	7,030 (9)	2011-2
Ontario	13.505	www.canada.gc.ca	409,001	85,609	Canadian Blood Services	20.9	6,339 (8)	2012-3
Denmark	5,548	www.oecd.org	294,449	66,345	www.laegemiddelstyrelsen.dk	22.5	11,895 (13)	2011
Canada excluding Quebec	25.574	www.canada.gc.ca	819,130	184,932	www.blood.ca	22.6	7,231 (10)	2011-2
Quebec	7,903	www.canada.gc.ca	246,363	62,287	www.hemaquebec.qc.ca	25.3	7,879 (11)	2011-2
USA	311.592	www.census.gov	13,785,000	3,882,000	Whitaker and Henry [20].	28.2	12,459 (14)	2011

Table 2.2. Annual Issues of FP and PCCs to Ontario Hospitals over Six Fiscal Years (2007-08 to 2012-13).

Year	Issues of FP (units of 250mL)	Issues of PCC (thousands of units)	FP equivalent units for PCC issues (units of 250 mL)	FP + PCC FP equivalents (units of 250 mL)
2007-2008	133,327	0	0	133,327
2008-2009	125,101	620.7	2,482	127,583
2009-2010	112,462	3,231.0	12,924	125,386
2010-2011	101,891	5,399.5	21,598	123,489
2011-2012	101,373	6,686.0	26,744	128,117
2012-2013	85,609	7,237.0	28,948	114,557

3.0 Design and Methodology

A prospective audit was undertaken of the clinical indications and laboratory data for all transfusion episodes of FP and PCCs occurring in participating Ontario hospitals for any five days, not necessarily consecutive, between November 18th and December 13th of 2013. The days chosen for audit were left to the discretion of the hospital in order to maximize the number of participating hospitals and enable each site to balance workload and staffing. The data were collected using a web-based audit tool developed for this audit (created in collaboration with Lixar IT Inc.). Each site was pre-coded by their MAK code, which is assigned by Canadian Blood Services for any site receiving blood and blood components. Access was restricted to the hospital by user ID and password. Data variables for collection were chosen by a subgroup of the Plasma Steering Committee.

The data elements collected included:

- Hospital site
- Patient care area
- Date of transfusion
- Patient age (year of birth) and sex
- Number of plasma units ordered and transfused
- Number of PCC vials ordered and infused
- Ordering physician specialty
- Indication for transfusion/infusion
- Pre and post coagulation testing results

4.0 Validation Procedures

Verification and validation procedures took place during the data collection period and at the end of the final data entry period. As part of the verification process, all the data were reviewed for any duplicate entries or any discrepant entries. 21 hospitals were contacted regarding forty (40) questionable/problematic entries. 36/40 questionable entries were confirmed by the participating sites. 4 orders were corrected; approximately ten (10) percent of the manual entry sheets were obtained from a random sample of participating hospitals and compared to the web-based data for consistency to confirm a match between the two entries. There was a 98% (43/44) agreement rate between the manual entry sheets and the web-based data with all discrepancies found in the random sample being rectified.
It is concluded that discrepancies in the database in general were sufficiently rare that they would not materially affect the analysis and /or conclusions.

Reporting Results to Participating Hospitals

The details for each hospital's individual patient/transfusion data together with the interpretation as "Appropriate", "Inappropriate" or "Indeterminate" for each case are contained in Appendix C. The hospital identities are coded for confidentiality reasons. When this report is issued and copies sent to hospitals, individual participating institutions will be informed of their code so that they may review the interpretation of the data they submitted but will not be able to identify the source of any other institution's data.

5.0 Determination of Appropriate/Inappropriate ratings for Frozen Plasma transfusions

The criteria for assessing the appropriateness of each plasma and PCC order were developed by 6 volunteer Hematologists (see table 5.1). These criteria were based on published plasma guidelines, but the specific criteria for appropriateness were liberal to avoid overestimating the number of inappropriate transfusions especially given the limited clinical and laboratory data that were collected as part of the audit. The indeterminate rating was used when there was insufficient evidence from the literature to judge appropriateness or insufficient clinical data were provided. Appropriate, inappropriate and indeterminate transfusions were sub classified by clinical indication.

Each order was reviewed and independently rated by two Hematologists. For any discrepancies in either the rating of appropriate, inappropriate or indeterminate, or the sub classification, the final rating was reached by consensus.

Table 5.1. Criteria developed for classification of orders for FP transfusions and PCC infusions as "appropriate", "inappropriate" or "indeterminate".

Code	Plasma Indication Criteria
	Appropriate
A1	• Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants • Urgent surgery or invasive procedure • Pre- or post- transfusion INR >1.5 and/or PTT > 1.5x upper limit of normal
A2	• Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants • Bleeding • Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal
A3	• "Massive transfusion" • Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no laboratory coagulation data available at the time of product issue
A4	• Apheresis/plasma exchange or TTP • Regardless of coagulation status
A5	• Peri-surgical bleeding not due to any anticoagulant medication • Minor bleeding • Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal
A6	• Peri-surgical bleeding not due to any anticoagulant medication • Major bleeding • Pre- or post-transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no coagulation data available
A7	• Congenital coagulation factor deficiency other than Factor II, VII, VIII, IX, X, XIII • Bleeding and or surgery/procedure • No factor concentrates available
A8	• Reversal of coagulation defect due to warfarin or vitamin K deficiency • Bleeding or urgent surgery or invasive procedure • Contraindication to PCCs (e.g. history of heparin induced thrombocytopenia)
	Inappropriate
I1	• Reversal of coagulation defect due to warfarin or vitamin K deficiency • Absence of bleeding and/or no urgent surgery/procedure

I2	• Reversal of coagulation defect due to warfarin or vitamin K deficiency • Bleeding or surgery or invasive procedure • No contraindication to PCC
I3	• INR ≤ 1.5 and PTT ≤ 1.5x upper limit of normal pre- transfusion • Irrespective of bleeding status or procedure status
I4	• Heparin reversal (regardless of INR)
15	• Reversal of other anticoagulants (Dabigatran/Pradaxa, Rivaroxiban, Apixaban, etc)
I6	• Volume replacement
I7	• Reversal of coagulation defect other than coumadin/warfarin or vitamin K or heparin • Pre or post transfusion INR ≥1.5 and/or PTT ≥1.5x upper limit of normal • No bleeding or surgery/procedure
	Indeterminate
M1	• No laboratory coagulation data pre- or post- transfusion
M2	• No laboratory coagulation data pre- transfusion (with normal coags post-procedure)

Code	PCC Indication Criteria
	Appropriate
PCC-A1	• Reversal of warfarin or vitamin K deficiency • Bleeding • Pre- or post-transfusion INR >1.5
PCC-A2	• Reversal of warfarin or vitamin K deficiency • Urgent surgery or invasive procedure (within 6 hours) • Pre- or post-transfusion INR >1.5
PCC-A3	• Congenital deficiency of Factors II, VII, IX, or X • Bleeding, surgery or invasive procedure
	Inappropriate
PCC-I1	• Reversal of coagulopathy other than warfarin, vitamin K deficiency or congenital deficiency of factors II, VII, IX, or X • Regardless of bleeding status or surgical/procedure
PCC-I2	• Reversal of warfarin, vitamin K deficiency • Absence of bleeding • Non-urgent surgery or invasive procedure (>6 hours)
PCC-I3	• Reversal of congenital factor deficiency other than factors II, VII, IX, or X
	Indeterminate
PCC-M1	• Reversal of other anticoagulants, Fondaparinux, Dabigatran, Rivaroxaban, Apixaban) • Bleeding and/or surgery/procedure

6.0 Frozen Plasma Utilization Results

Participating hospitals

Fifty-one of 158 eligible hospitals (32%) participated in the Provincial audit. (Minimal plasma and PCC usage and increased workload involved in taking part were common reasons for non-participation). The participating hospitals represent 60% of the FP transfused in the province. The hospital sites were classified into three different types of institutions: 3 small hospitals (< 100 beds),

37 community hospitals (> 100 beds) and 11 teaching hospitals (sites affiliated with an academic centre). The data collected primarily reflect plasma and PCC used by the adult population. Among the participating hospitals, 49 sites had requests for FP and PCC and 2 Small community sites had no requests for FP and PCC during the audit period. The data from the 1 remaining Small community (<100 beds) hospital will be combined into the Community hospital category. There were a total of 329 orders for FP and 113 orders for PCC. The total number of plasma units transfused was 969 and cryosupernant plasma was 88 units. The breakdown for the types of units transfused or otherwise disposed of is provided in Table 6.1 which incorporates aggregate data for all participating hospitals. 7 orders for FP were for use in Apheresis/Plasma Exchange procedures and these orders were deemed appropriate and taken out of the dataset for further analysis. The ordering and transfusion of units of FP for the 38 community and teaching hospitals in detailed in Table 6.2

Table 6.1. Units of various plasma products ordered, transfused during the audit period.

*Total number of reported FP orders	329 (7 apheresis/plasma exchange)
Total number of FP units ordered	969 (14 units apheresis)
Total number of FP units transfused	922 (14 units apheresis)
Total number of Cryosupernatant unis ordered	88
Total number of Cryosupernatant transfused	88
FP (250 mL) units transfused	724
Apheresis (250 mL) transfused	2
Apheresis (500 mL) transfused	98

Table 6.2. Distribution of ordering and transfusion of units of FP by hospital classification (excluding apheresis/plasma exchange).

	All (n=49 sites)	Community Hospitals (n=38)	Teaching Hospitals (n=11)
Total # FP orders	322	189	133
# of units ordered	955	538	417
Median # units ordered (min-max)	2 (1-18)	2 (1-16)	2 (1-18)
# of units transfused	908	514	394
Median # units transfused (min-max)	2 (1-18)	2 (1-15)	2 (1-18)

Table 6.3 presents the data defining the clinical services from which orders for FP originated. Critical care: medicine, internal medicine and general surgery each represented greater than 10% of the total number of orders for all FP orders. Differences in ordering specialty for FP use were seen between Community and Teaching hospital classifications. Internal medicine and general surgery represented the largest users of FP in the Community hospital setting while critical care and anesthesia represented the largest users of FP in the Teaching hospital setting.

The specialty of the physician ordering FP and the location of the patient for whom FP was prescribed are given in Tables 6.4 and 6.5 respectively.

Table 6.3. Physician ordering specialty for plasma orders by hospital classification.

Specialty ordering plasma	Total # (%)	Community # (%)	Teaching # (%)
Critical care medicine	72 (22.4)	22 (11.6)	50 (37.6)
Internal Medicine	54 (16.8)	48 (25.4)	6 (4.5)
Surgery, General	38 (11.8)	27 (14.3)	11 (8.3)
Anesthesia	26 (8.1)	10 (5.3)	16 (12.0)
Emergency	20 (6.2)	15 (7.9)	5 (3.8)
Surgery, Cardiovascular	18 (5.6)	6 (3.2)	12 (9.0)
Critical care, cardiac	17 (5.3)	8 (4.2)	9 (6.8)
Other	14 (4.3)	13 (6.9)	1 (0.8)
Gastroenterology	8 (2.5)	7 (3.7)	1 (0.8)
General Practice/Family Medicine	8 (2.5)	6 (3.2)	2 (1.5)
Unknown	8 (2.5)	6 (3.2)	2 (1.5)
Cardiology	6 (1.9)	4 (2.1)	2 (1.5)
Oncology	5 (1.6)	4 (2.1)	1 (0.8)
Pediatrics, General	4 (1.2)	1 (0.5)	3 (2.3)
Obstetrics & Gynecology	4 (1.2)	2 (1.1)	2 (1.5)
Nephrology	4 (1.2)	3 (1.6)	1 (0.8)
Surgery, Orthopedic	4 (1.2)	2 (1.1)	2 (1.5)
Surgery, Other	3 (0.9)	2 (1.1)	1 (0.8)
Surgery, Neurosurgery	3 (0.9)	0 (0.0)	3 (2.3)
Hematology	2 (0.6)	1 (0.5)	1 (0.8)
Neurology	1 (0.3)	1 (0.5)	0 (0.0)
Respirology	1 (0.3)	1 (0.5)	0 (0.0)
Neonatology	1 (0.3)	0 (0.0)	1 (0.8)
Radiology	1 (0.3)	0 (0.0)	1 (0.8)
Total	322	189	133

Table 6.4 shows the location within the hospitals to which FP was issued and where transfusion of FP was assumed to have taken place. The Intensive Critical Care Units and Medical Ward transfused 36.0% and 17.4% respectively of all the FP units transfused. The next most frequent areas for FP transfusion were the operating room and the emergency department.

Table 6.4. Hospital location to which FP was issued for transfusion by hospital classification.

FP Issued to	Total # (%)	Community # (%)	Teaching # (%)
Intensive Critical Care Unit	116(36.0)	64(33.9)	52(39.1)

Medical Ward	56(17.4)	44(23.3)	12(9.0)
Operating Room	52(16.1)	20(10.6)	32(24.1)
Emergency Room	28(8.7)	21(11.1)	7(5.3)
Cardiovascular ICU	25(7.8)	10(5.3)	15(11.3)
Surgical Ward	21(6.5)	15(7.9)	6(4.5)
Other	9(2.8)	8(4.2)	1(0.8)
Dialysis	5(1.6)	2(1.1)	3(2.3)
Outpatient Clinic	2(0.6)	1(0.5)	1(0.8)
Coronary Care Unit	2(0.6)	1(0.5)	1(0.8)
Neonatal ICU	2(0.6)	0(0.0)	2(1.5)
Unknown	2(0.6)	2(1.1)	0(0.0)
Recovery Room	1(0.3)	1(0.5)	0(0.0)
Diagnostic Imaging	1(0.3)	0(0.0)	1(0.8)
Total	322	189	133

175/322 (54.3%) of the total FP orders were for patients with a coagulopathy. In Community and Teaching hospital classifications coagulopathy accounted for 87 (46.0%) and 88 (66.2%) respectively (Table 6.5)

Table 6.5. Does the patient have a coagulopathy?

Coagulopathy	Total # (%)	Community # (%)	Teaching # (%)
Yes	**175 (54.3)**	**87 (46.0)**	**88 (66.2)**
Liver disease	53 (30.3)	40 (46.0)	13 (14.8)
Massive transfusion	46 (26.3)	7 (8.0)	39 (44.3)
Unknown	34 (19.4)	21 (24.1)	13 (14.8)
Sepsis	25 (14.3)	12 (13.8)	13 (14.8)
DIC	10 (5.7)	2 (2.3)	8 (9.1)
Trauma	6 (3.4)	4 (4.6)	2 (2.3)
Vit K deficiency	1 (0.6)	1 (1.1)	0 (0.0)
No	**98 (30.4)**	**70 (37.0)**	**28 (21.0)**
Unknown	**49 (15.2)**	**32 (17.0)**	**17 (12.8)**

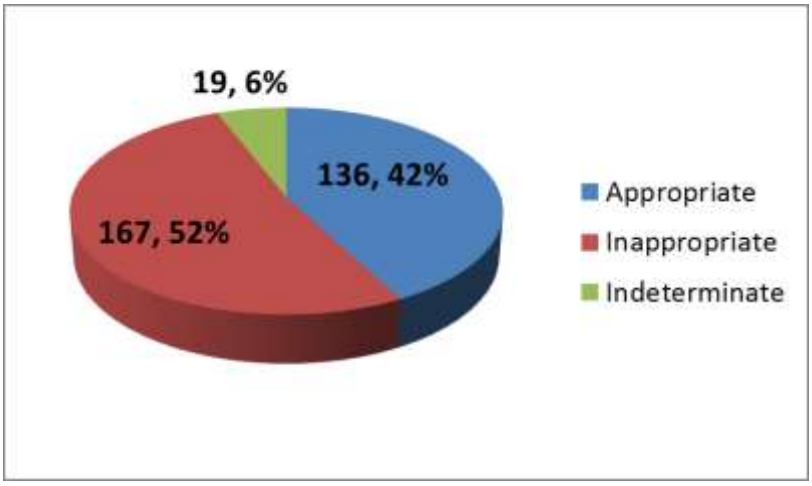
The nature of interventions leading to FP transfusion in preparation for the intervention is detailed in Table 6.6.

Table 6.6. Procedure/Indication for FP.

Procedure/Indication	Total # (%)	Community # (%)	Teaching # (%)
Surgery	108	49	59
Unknown	45	30	15
Other	32	17	15
Image guided therapy	7	1	6
Scope	6	1	5
Central line placement	2	2	0
Liver biopsy	2	1	1
Thoracentesis	1	1	0

Appropriateness of Frozen Plasma transfusions

Figure 6.1. Of the 322 (excluding FP orders for apheresis) orders for FP, 136 (42.0%) were classified as appropriate while 167 (52.0%) were deemed inappropriate and 19 (6.0%) were indeterminate.



The frequency of the various reasons for orders of FP that were deemed "appropriate", "inappropriate" or "indeterminate" are given in Table 6.8 in which the proportion of the different categories defined in Table 1 are listed in descending order.

Table 6.8. Summary of frequency of reasons transfusion orders for FP were deemed "appropriate", "inappropriate" or "indeterminate".

Code	# of orders (%)	Code Description
Appropriate		
A2	86 (26.1)	Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants Bleeding

		Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal
A3	29 (8.8)	"Massive transfusion" Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no laboratory coagulation data available at the time of product issue
A1	20 (6.1)	Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants Urgent surgery or invasive procedure Pre- or post- transfusion INR >1.5 and/or PTT > 1.5x upper limit of normal
A4	7(2.1)	Apheresis/plasma exchange or TTP Regardless of coagulation status
A6	1(0.3)	Peri-surgical bleeding not due to any anticoagulant medication Major bleeding Pre- or post-transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no coagulation data available
A5	0 (0.0)	Peri-surgical bleeding not due to any anticoagulant medication Minor bleeding Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal.
Inappropriate		
I3	76 (23.1)	INR ≤ 1.5 and PTT ≤ 1.5x upper limit of normal pre- transfusion Irrespective of bleeding status or procedure status
I2	38 (11.6)	Reversal of coagulation defect due to warfarin or vitamin K deficiency Bleeding or surgery or invasive procedure No contraindication to PCC
I7	21 (6.4)	Reversal of coagulation defect other than coumadin/warfarin or vitamin K or heparin Pre or post transfusion INR ≥1.5 and/or PTT ≥1.5x upper limit of normal No bleeding or surgery/procedure
I4	18 (5.5)	Heparin reversal (regardless of INR)
I5	8 (2.4)	Reversal of other anticoagulants (Dabigatran/Pradaxa, Rivaroxiban, Apixaban, etc)
I1	6 (1.8)	Reversal of coagulation defect due to warfarin or vitamin K deficiency, Absence of bleeding and/or no urgent surgery/procedure
Indeterminate		
M1	11 (3.3)	No laboratory coagulation data pre- or post- transfusion
M2	8 (2.4)	No laboratory coagulation data pre- transfusion (with normal coags post-procedure)

Breakdown of I3, I2 and I7 Inappropriate Categories by Hospital Classification (#/% of orders by inappropriate classification)

Code	Total # of orders (%)	Community # of orders (%)	Teaching # of orders (%)
I3	76 (23.1)	36 (47.4)	40 (52.6)
I2	38 (11.6)	30 (79.0)	8 (21.0)
I7	21 (6.4)	17 (81.0)	4 (19.0)

Appropriateness of orders for transfusion of Frozen Plasma by hospital class

Table 6.9. The proportion of FP orders deemed "appropriate", "inappropriate" or "indeterminate" by hospital class, number and percentage.

Hospital classification	Appropriate (%)	Inappropriate (%)	Indeterminate (%)	
Community	73 (38.6)	103 (54.5)	13 (6.9)	189
Teaching	63 (47.4)	64 (48.1)	6 (4.5)	133
Total	136 (42.2)	167 (51.9)	19 (5.9)	322

Effect of the presence of "guidelines" on appropriateness of transfusion of Frozen Plasma

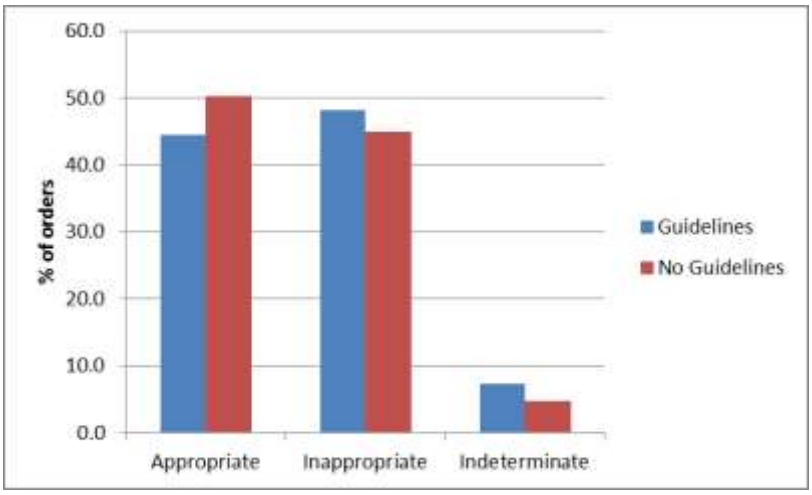
There was not a significant difference between the number of appropriate (44.4% vs. 50.3%) and inappropriate transfusions (48.1% vs. 44.9%) in hospitals with "guidelines" for the appropriate use of FP as compared to those hospitals that did not have "guidelines". The audit tool posed the simple question "Does your facility have institutional guidelines for the use of frozen plasma?" (Table 6.10, Figure 6.2).
There were 27 hospitals reporting the existence of "guidelines" and 22 hospitals did not have such "guidelines" for the use of FP.

Table 6.10. Significance of differences in proportion of orders deemed "appropriate", "inappropriate" or "indeterminate" in hospitals with and without "guidelines" for transfusion of FP.

Orders	Guidelines (%) (n=27)	No Guidelines (%) (n=22)
Appropriate	60 (44.4)	94 (50.3)
Inappropriate	65 (48.1)	84 (44.9)
Indeterminate	10 (7.4)	9 (4.8)

**All p values >0.2 (not significant)*

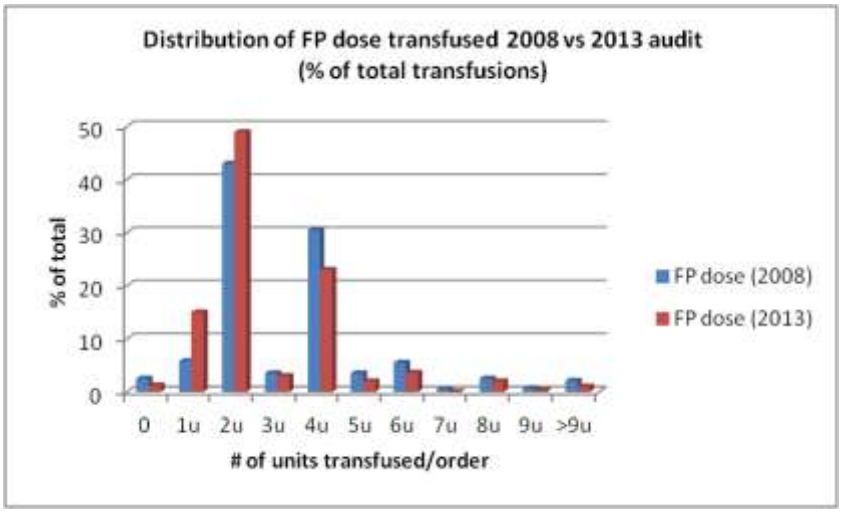
Figure 6.2. Differences in proportion of orders deemed "appropriate", "inappropriate" and "indeterminate" in hospitals with and without guidelines for transfusion of FP. Establishment of guidelines was not associated with a significant difference between the frequencies of appropriate and inappropriate ordering of FP for transfusion.



Dose of Frozen Plasma transfusions

The most common dose of FP transfused (2013 audit) was 2 units (49.0% of transfusions) and the next most common dose was 4 units (23.5% of transfusions)-excluding apheresis/plasma exchange (Figure 6.3). For an average 70 kg patient, the 2 unit dose represents a dose of about 7 ml/kg which is below the recommended dose of 10-15 mls/kg. Assuming a 70 kg patient weight, the 10-15 ml/kg recommended dose is equivalent to 3-4 250mL units.
When data on the appropriateness of the order for FP and for adequacy of dosage are combined, only 19.7% of the orders for FP met the criteria for an appropriate indication and the recommended dose range.

Figure 6.3. Distribution of doses of plasma transfused as reported by audit participants 2008 and 2013 audit (1 "unit" is equivalent to 250 mL of random donor plasma).

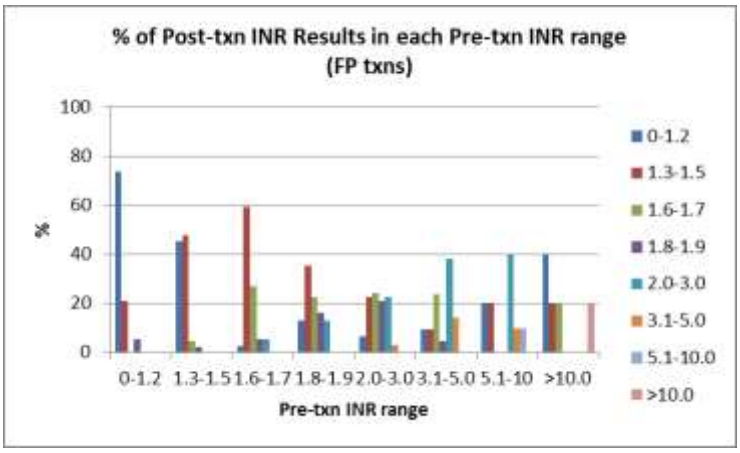


Coagulation Testing Results for Frozen Plasma Orders

Pre and post transfusion coagulation testing results were collected during the audit. 84/322 (26.1%) of FP orders had a pre-transfusion INR <1.6 with 22/322 (6.8%) having no pre-transfusion INR results.

The Effect of Frozen Plasma on INR results

Figure 6.4. Pre and Post Transfusion INR results for all FP transfusion.



The effect of FP to reduce INR values <1.5 is limited. For FP transfusions with a pre- transfusion INR of 1.6-1.7, only 38% of transfusions resulted in an INR <1.5. For FP transfusions with a pre-transfusion INR of 2.0-3.0 and 3.1-5.0, the percentage of post-transfusion INR results <1.5 was 29% and 19% respectively.

7.0 Prothrombin Complex Concentrate (PCC) Audit Results

Units of PCC ordered and infused included in this audit and ordering by hospital classification are presented in Tables 7.1 and 7.2.

Table 7.1. Vials of PCC ordered and infused during the audit period.

Total number of reported orders	113
Total number of vials ordered	410
Total number of vials infused	402
Average number of vials ordered (min-max)	4 (1-6)
Average number of vials infused (min-max)	4 (1-6)

Table 7.2. Distribution of ordering and infusion of PCC vials by hospital classification.

	All	Community Hospitals (n=37)	Teaching Hospitals (n=11)
Total # PCC orders	113	90	23
# of units ordered	410	318	92
Median # units ordered (min-max)	4 (1-6)	4 (1-6)	4 (1-6)
# of units infused	402	310	92
Median # units infused (min-max)	4 (1-6)	4 (1-6)	4 (1-6)

Table 7.3. Criteria developed for classification of orders for PCC infusions as "appropriate", "inappropriate" or "indeterminate".

Criteria Code	PCC Indication
Appropriate	
PCC-A1	Reversal of warfarin or vitamin K deficiency Bleeding Pre- or post-transfusion INR >1.5
PCC-A2	Reversal of warfarin or vitamin K deficiency Urgent surgery or invasive procedure (within 6 hours) Pre- or post-transfusion INR >1.5
PCC-A3	Congenital deficiency of Factors II, VII, IX, or X Bleeding, surgery or invasive procedure
Inappropriate	
PCC-I1	Reversal of coagulopathy other than warfarin, vitamin K deficiency or congenital deficiency of factors II, VII, IX, or X Regardless of bleeding status or surgical/procedure
PCC-I2	Reversal of warfarin, vitamin K deficiency Absence of bleeding Non-urgent surgery or invasive procedure (>6 hours)
PCC-I3	Reversal of congenital factor deficiency other than factors II, VII, IX, or X
Indeterminate	
PCC-M1	Reversal of other anticoagulants, Fondaparinux, Dabigatran, Rivaroxaban, Apixaban) Bleeding and/or surgery/procedure

The specialty designation of the physician ordering PCC and the patient location for community and teaching hospitals and all hospitals are presented in 7.4 and 7.5.

Table 7.4. Physician ordering specialty for PCC orders by hospital classification.

Specialty ordering	Total (%)	Community (%)	Teaching (%)
Emergency	44 (38.9)	35 (37.5)	9 (39.1)
Internal Medicine	16 (14.2)	16 (18.2)	0 (0.0)
Surgery: Orthopedic	12 (10.6)	11 (12.5)	1 (4.3)
Pediatrics: General	7 (6.2)	7 (8.0)	0 (0.0)
Critical care: medicine	5 (4.4)	5 (5.7)	0 (0.0)
Anesthesia	4 (3.5)	2 (2.3)	2 (8.7)
Cardiology	4 (3.5)	3 (3.4)	1 (4.3)
General Practice/Family Medicine	4 (3.5)	4 (4.5)	0 (0.0)
Oncology	3 (2.7)	0 (0.0)	3 (13.0)
Gastroenterology	3 (2.7)	0 (0.0)	3 (13.0)
Obstetrics & Gynecology	2 (1.8)	2 (2.3)	0 (0.0)
Hematology	2 (1.8)	0 (0.0)	2 (8.7)
Surgery: Cardiovascular	2 (1.8)	2 (2.3)	0 (0.0)
Critical care: cardiac	1 (0.9)	1 (1.1)	0 (0.0)
Neurology	1 (0.9)	0 (0.0)	1 (4.3)
Surgery: General	1 (0.9)	1 (1.1)	0 (0.0)
Surgery: Other	1 (0.9)	1 (1.1)	0 (0.0)
Unknown	1 (0.9)	0 (0.0)	1 (4.3)
Total	**113**	**90**	**23**

Table 7.5. Location PCC issued to by hospital classification.

PCC Issued to	Total # (%)	Community # (%)	Teaching # (%)
Emergency Room	57 (50.4)	46 (51.1)	11 (47.8)
Medical Ward	19 (16.8)	16 (17.8)	3 (13.0)
Intensive Critical Care Unit	14 (12.4)	13 (14.4)	1 (4.3)
Surgical Ward	10 (8.8)	6 (6.7)	4 (17.4)
Operating Room	5 (4.4)	3 (3.3)	2 (8.7)
Unknown	4 (3.5)	2 (2.2)	2 (8.7)
Coronary Care Unit	2 (1.8)	2 (2.2)	0 (0.0)
Recovery Room	1 (0.9)	1 (1.1)	0 (0.0)
Cardiovascular ICU	1 (0.9)	1 (1.1)	0 (0.0)
Total	**113**	**90**	**23**

Prothrombin Complex Concentrates- Patient on Anticoagulants

Figure 7.1.

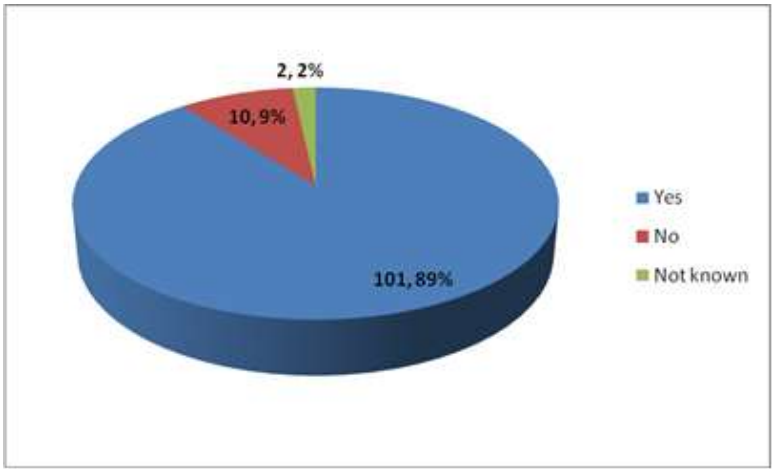


Figure 7.1 Anticoagulant use accounted for 101/113 (89%) of the orders for PCCs. 95% of the PCC use for anticoagulant reversal was for patients on warfarin/coumadin.

Type of Anticoagulants

The types of anticoagulants for which PCC was prescribed for reversal of anticoagulant effect are listed in Table 7.6.

Table 7.6. PCC utilization for Anticoagulant reversal.

Procedure/Other Indication	Total # (%)	Community # (%)	Teaching # (%)
Warfarin (Coumadin)	98 (95.1)	78 (96.3)	20 (91.0)
Dabigatran (Pradaxa)	2 (1.9)	1 (1.2)	1 (4.5)
Rivaroxaban (Xarelto)	2 (1.9)	2 (2.5)	0 (0.0)
LMWH	1 (1.0)	0 (0.0)	1 (4.5)
Total	**103***	**81**	**22**

*1 PCC order war/rivar; 1 PCC order war/dabig

Procedure/Other Indication for Prothrombin Complex Concentrates

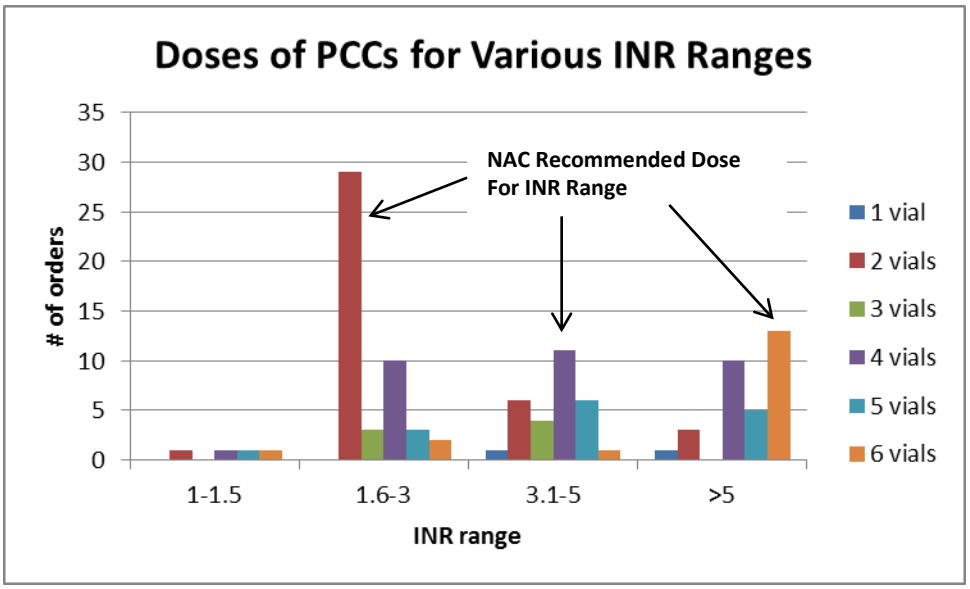
Table 7.7.

Procedure/Other Indication	Total # (%)	Community # (%)	Teaching # (%)
Unknown	23 (37.1)	20 (40.8)	3 (23.1)
Surgery	18 (29.0)	15 (30.6)	3 (23.1)
Other	18 (29.0)	12 (24.5)	6 (46.2)
Central line placement	2 (3.2)	1(2.0)	1 (7.7)
Image guided therapy	1 (1.6)	1(2.0)	0 (0.0)
Total	62	49	13

Dose of Prothrombin Complex Concentrates

The NAC recommended dose for PCC use was based upon the INR results and not body weight as data on weight were not collected in the data collection tool. Using the INR results to assess the appropriateness of dosage, 53/112 (47.3%) of the PCC orders (with Pre-INR results) were reported as having the recommended dose.

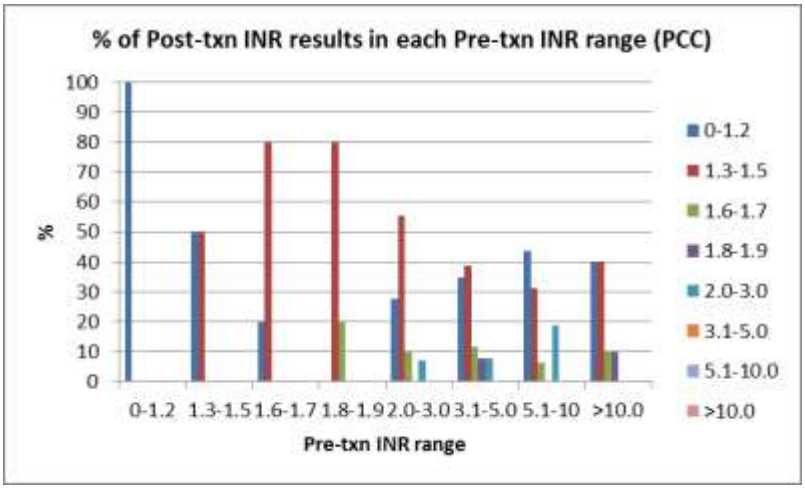
Figure 7.2.



Coagulation Testing results for Prothrombin Complex Concentrate Orders

The majority of PCC orders, 108/113 (95.6%) were for pre-transfusion INR results of >1.5.

Figure 7.3. Pre and Post Transfusion INR results for PCC infusions.



For pre-transfusion INR results of 1.6-1.7, all patients infused PCC had a post-transfusion INR of 1.5 or below. For higher pre-transfusion INR results, the percentage of post-transfusion INRs below 1.5 was between 70-80%.

Appropriateness of Prothrombin Complex Concentrate Orders

Figure 7.4. Of the 113 orders for PCC, 79 (70.0%) were classified as appropriate while 32 orders (28%) were inappropriate and 2 orders (2.0%) were indeterminate.

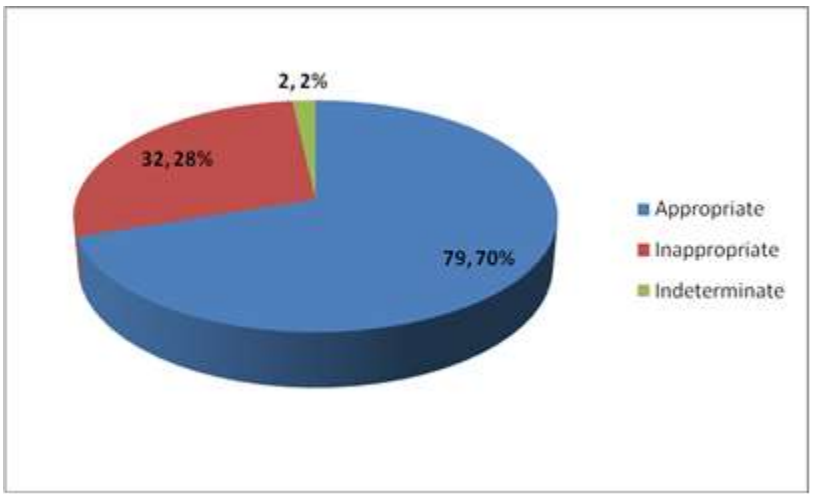


Table 7.8. Summary of frequency of reasons transfusion orders for PCCs were deemed "appropriate", "inappropriate" or "indeterminate".

Criteria Code	# of orders (%)	Code Description
Appropriate		
PCC-A1	62 (55.9)	Reversal of warfarin or vitamin K deficiency Bleeding Pre- or post-transfusion INR >1.5
PCC-A2	18 (15.3)	Reversal of warfarin or vitamin K deficiency Urgent surgery or invasive procedure (within 6 hours) Pre- or post-transfusion INR >1.5
PCC-A3	0 (0.0)	Congenital deficiency of Factors II, VII, IX, or X Bleeding, surgery or invasive procedure
Inappropriate		
PCC-I2	18 (15.3)	Reversal of warfarin, vitamin K deficiency Absence of bleeding Non-urgent surgery or invasive procedure (>6 hours)
PCC-I1	11 (9.9)	Reversal of coagulopathy other than warfarin, vitamin K deficiency or congenital deficiency of factors II, VII, IX, or X Regardless of bleeding status or surgical/procedure
PCC-I3*	2 (1.8)	Reversal of warfarin, vitamin K deficiency INR <1.5 Absence of bleeding
Indeterminate		

PCC-M1	2 (1.8)	Reversal of other anticoagulants, Fondaparinux, Dabigatran, Rivaroxaban, Apixaban) Bleeding and/or surgery/procedure

*PCCI3 category added to adjudication criteria after adjudication process.

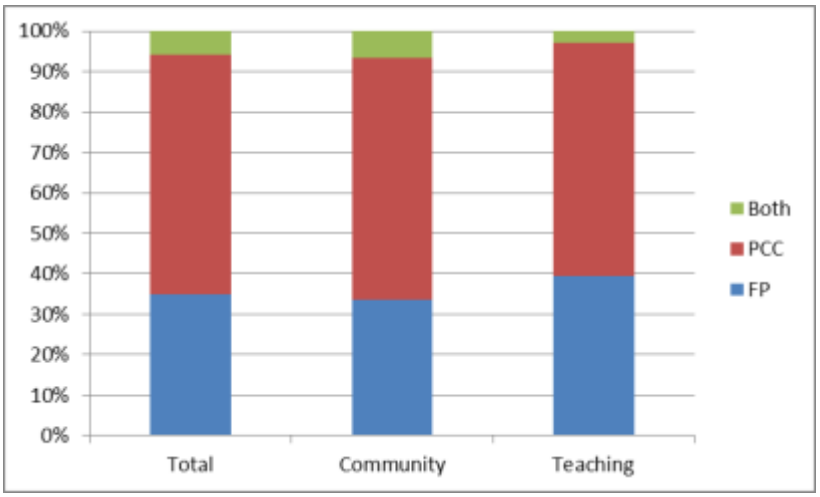
Anticoagulant Reversal Table (Warfarin) by Hospital Classification

This audit revealed continuing use of FP for reversal of warfarin effect, both as the only treatment (53 orders) and in conjunction with orders for PCC (9 orders). See also Fig. 7.5 below.

Table 7.9.

	Total # (%)	**Community # (%)**	**Teaching # (%)**
Plasma order	53 (34.9)	40 (33.6)	13 (39.4)
PCC order	90 (59.2)	71 (59.7)	19 (57.6)
Both ordered	9 (5.9)	8 (6.7)	1 (3.0)

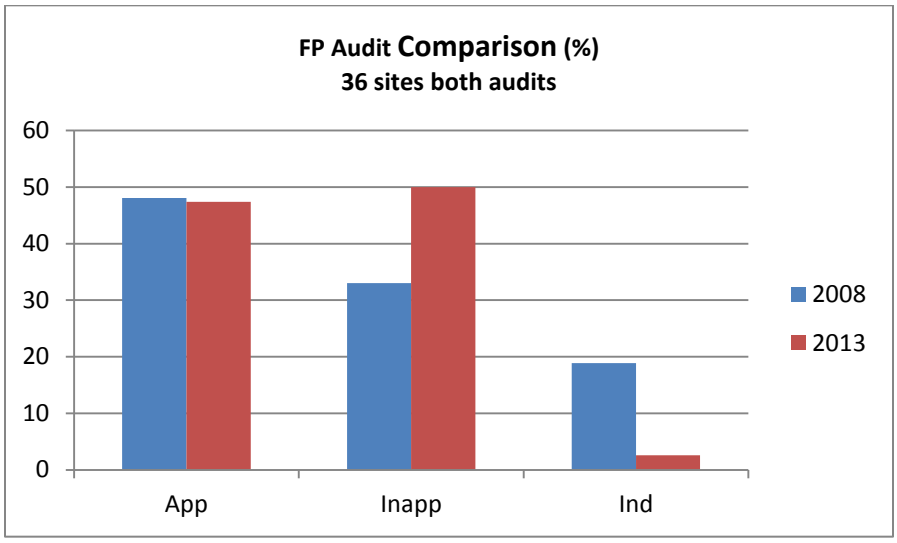
Figure 7.5. Anticoagulant Reversal (Warfarin) by Hospital Classification.



8.0 Comparison of 2008 and 2013 Frozen Plasma Audit Results

There were 36 hospital sites that participated in both the 2008 and the 2013 audits for FP utilization. Appropriate FP orders for the 2008 and the 2013 FP audit were 48.1% and 47.4% respectively. Inappropriate FP orders were 33.0% (2008) and 50% (2013). Indeterminate FP orders were 18.9% (2008) and 2.6% (2013).

Figure 8.1. Appropriate/Inappropriate/Indeterminate Comparison for sites that participated in 2008 and 2013 audits.



Comparison of Appropriate, Inappropriate and Indeterminate Status for 2008 and 2013 Frozen Plasma orders (2008 and 2013 audits)

Table 8.2.

Appropriate	2013 Audit # orders (%)	2008 Audit # orders (%)
Coagulopathy other than coumadin or vitamin K deficiency Bleeding Pre- or post-transfusion INR >1.5	88 (26.7)	176 (30.8)
Coagulopathy other than coumadin or vitamin K deficiency Urgent intervention or surgery Pre- or post-transfusion INR>1.5	20 (6.1)	43 (7.5)
Reversal of coumadin/warfarin or vitamin K deficiency Bleeding or surgery or invasive procedure Pre- or post-transfusion INR>1.5*****	38 (11.6)	37 (6.4)
"Massive transfusion" Pre- or post-transfusion INR>1.5	29 (8.8)	35 (6.1)
Apheresis/plasma exchange or TTP Regardless of coagulation status	7 (2.1)	23 (4.0)

***Indicates category changed to Inappropriate from Appropriate use of FP in 2013 audit as this is now an indication for the use of PCCs.**

Inappropriate	2013 Audit # orders (%)	2008 Audit # orders (%)
INR≤1.5 pre-transfusion and normal post-procedure INR Irrespective of bleeding status or procedure status	76 (23.1)	97 (16.9)
Reversal of coagulation defect due to warfarin or	6 (1.8)	41 (7.2)

vitamin K deficiency Absence of bleeding and/or no urgent surgery/procedure		
Reversal of coagulation defect other than coumadin/warfarin or heparin Pre- or post-transfusion INR>1.5 No bleeding or surgery/procedure	20 (6.1)	15 (2.6)
Heparin reversal (Regardless of INR)	18 (5.5)	10 (1.7)
Reversal of other anticoagulants (Dabigatran/Pradaxa, Rivaroxiban, Apixaban, etc.)	8 (2.4)	0 (0.0)
Volume replacement	0 (0.0)	1 (0.2)

Indeterminate	2013 Audit # orders (%)	2008 Audit # orders (%)
No laboratory coagulation pre- or post-transfusion	11 (3.3)	27 (4.7)
No laboratory coagulation pre- or post-transfusion (with normal coags post-procedure)	8 (2.4)	17 (3.0)
Abnormal coagulation pre- or post-transfusion Bleeding unknown	0 (0.0)	31 (5.4)
Abnormal coagulation- diagnosis unknown Not bleeding Procedure unknown	0 (0.0)	12 (2.1)
"Massive transfusion" Pre- or post-transfusion INR≤1.5 or no laboratory coagulation data available	0 (0.0)	8 (1.4)

Pre-INR results ≤1.5 by Hospital Classification

Table 8.3.

Hospital Classification	2013 Audit # orders (%)	2008 Audit # orders (%)
Community	39/189 (20.6)	80/300 (26.7)
Teaching	45/133 (33.8)	80/273 (29.3)

Pre-INR results ≤1.5 by Physician Specialty

Table 8.4. # of orders/% of orders for FP for INR ≤1.5 by physician specialty.

Physician Specialty	# of FP orders INR ≤1.5	Total # of FP orders	% of total FP orders INR≤1.5
Neurology	1	1	100.0
Respirology	1	1	100.0
Radiology	1	1	100.0
Surgery: Other	2	3	66.7

Surgery: Neurosurgery	2	3	66.7
Critical care: cardiac	9	17	52.9
Unknown	4	8	50.0
Other	6	14	42.9
Surgery: General	12	38	31.6
Anesthesia	8	26	30.8
Gastroenterology	2	8	25.0
General Practice/Family Medicine	2	8	25.0
Nephrology	1	4	25.0
Obstetrics & Gynecology	1	4	25.0
Pediatrics: General	1	4	25.0
Internal Medicine	12	54	22.2
Oncology	1	5	20.0
Cardiology	1	6	16.7
Critical care: medicine	12	72	16.7
Surgery: Cardiovascular	3	18	16.7
Emergency	2	20	10.0
Hematology	0	2	0.0
Surgery: Orthopedic	0	4	0.0
Neonatology	0	1	0.0

The Use of Frozen Plasma and Prothrombin Complex Concentrates in relation to Bleeding/Procedure Status

Table 8.5.

Product	Code	Number (%)	Clinical Circumstance	Interpretation
Frozen Plasma	A2	86 (26.1)	Bleeding	Appropriate
	A1	20 (6.1)	Surgery/Procedure	Appropriate
	A6	1 (0.03)	Major peri-surgical bleeding	Appropriate
	I2	38 (11.6)	Bleeding/Procedure on Warfarin	Inappropriate
	I7	21 (6.4)	No Bleeding/Procedure	Inappropriate
Prothrombin Complex Concentrates	A1	62 (55.9)	Bleeding	Appropriate
	A2	18 (15.3)	Surgery/Procedure	Appropriate
	I2	18 (15.3)	No Bleeding or Urgent Procedure INR>1.5	Inappropriate

	I3	2 (1.8)	No Bleeding or Urgent Procedure INR ≤1.5	Inappropriate

The appropriateness and inappropriateness of use of FP and PCC in relation to the presence and absence of bleeding or surgical/invasive procedure and urgent warfarin reversal is compared. The use of PCC is significantly less inappropriate than that of FP under these clinical circumstances (chi square test, $p<0.01$).

Limitations of audit data

- Only 51/158 hospitals participated in the 2013 compared to 73 sites in the previous 2008 audit.
- Minor and major bleeding was not distinguished; any type of bleeding was categorized together.
- Weight data were not collected as this information is often very difficult to obtain consistently at the hospital sites.
- Limited sample size as only 5 days of FP/PCC data was collected during the audit.

9.0 Comments and Recommendations

The comments on the present (2013) audit are made partly on the results of the audit themselves, partly in the context of the new information in the literature outlined in Section 2 above and partly in comparison with the 2008 audit (www.transfusionontario.org).

Comments in general:

1. There has been a steady decrease in the consumption of FP in Ontario year over year since the last audit. On a *per capita* basis Ontario has the lowest consumption of all the large provinces. In spite of this, consumption here remains higher than in several European and other jurisdictions for which data are available.

2. About 60% of the decline in consumption in Ontario can probably be ascribed to the progressive introduction and uptake of PCCs.

3. There continues to be widespread, worldwide, inappropriate prescribing of FP as evidenced by numerous audits in various countries (see Appendix B for details). A recent extensive study of over 72,000 FP transfusions in the United States, conducted under the auspices of the National Heart, Lung and Blood Institute (Triulzi et al., 2014), reports patterns of FP use very similar to those seen in Ontario in the previous and current audits. We are not alone!

4. There is increasing evidence being reported in the literature to confirm the lack of efficacy of FP in reversing mild to moderate elevations in INR. Repeated systematic reviews have confirmed and emphasized the lack of evidence to support the use of FP

transfusion for correction of mild to moderate elevations in the results of standard laboratory tests of disordered coagulation.

5. Clinical evidence of lack of efficacy in influencing bleeding in patients with mild to moderate coagulopathy who are undergoing minor invasive procedures is beginning to emerge. The value of FP in protecting against hemorrhage in connection with liver biopsy in the presence of the coagulopathy of liver disease has long been questioned.

6. The literature suggests that conventional educational interventions have generally proved ineffectual, or the effects have been ill-sustained, in reducing inappropriate prescribing of FP. Measures to bring about pre-transfusion screening of FP orders for clinical appropriateness have met with mixed success which is mainly dependent on the vigour with which they are applied and overseen. These include the use of blood component request forms containing clinically relevant order criteria to be identified, computer-based physician order entry with decision criteria and guidance included, active pre-transfusion order review for appropriateness with blood bank technical review and questioning of non-conforming requests, and, lastly, professional peer review of non-conforming requests. Of these, the last appears to be the most effective but the most difficult to implement.

7. The incidence of Transfusion Associated Acute Lung Injury (TRALI), while a serious complication, is declining in frequency as a consequence of elimination of female derived plasma components from inventory. On the other hand, Transfusion Associated Circulatory Overload (TACO) is becoming increasingly identified as a hazard of transfusion including FP, and it should be recognized that the large volumes of FP required to influence significantly coagulation factor deficiencies present a particular problem in this regard.

8. FP continues to be used for the reversal of warfarin effect even when PCCs are available. 11.6% of FP orders were deemed inappropriate for this reason (Code- I2). This figure is close to that found (12.7%) in a recent single centre audit of FP and PCC use in Ontario (Shih et al., 2014).

Comments on the present (2013) audit:

1. There is no evidence of improvement in clinical practice in the prescribing and transfusion of FP since the previous audit in 2008, apart from the reduction in FP use resulting from the availability of PCC (See item below).

2. There is no clear evidence of improvement in FP transfusion in any particular clinical specialty or clinical service.

3. In this survey there is no evidence that the availability of clinical practice guidelines influences transfusion of FP.

4. The principal reasons for deeming transfusion of FP inappropriate were:
    - INR <= 1.5
    - Reversal of warfarin effect when PCC are available and not contraindicated

- Coagulation defect other than warfarin effect/vitamin K deficiency and INR > 1.5 with no bleeding or intervention

5. The median dosage of FP ordered was 2 units (500 mL), as in the previous audit, considered inadequate in an adult. In only 19.7% of FP transfusion episodes was there an adequate dose administered for an appropriate indication, compared with 29% in the 2008 audit.

6. There was only one report of an adverse reaction to FP transfusion, an allergic reaction.

7. The use of PCC in this audit appears to conform more closely with clinical practice guidelines although considerable room for improvement remains.
    - In about 70% of PCC transfusions the indication was appropriate and more often than not the dose transfused appeared appropriate (it is not possible with the data available to be more precise as many or most doses are determined for individual patients on the basis of body weight, data not collected for this audit).
    - About 30% of PCC transfusions were deemed inappropriate, mostly for reversal of warfarin effect in the absence of bleeding or intervention.
    - In 9 cases, patients received both FP and PCC for reversal of warfarin effect.

8. The effectiveness of FP transfusions in reducing the post-transfusion INR to 1.5 or less was significantly worse than that observed with PCCs.

Lessons from this audit:

1. Numerous transfusions of FP continue to be inappropriate based on clinical practice guidelines (52% in this audit) and in an inadequate dose (also more than half in this audit), and in less than 1 in 5 was the dose both adequate and the clinical indication appropriate. The reasons for inappropriate transfusion of FP are essentially unchanged since 5 years ago.
   It is apparent that the provision of clinical practice recommendations alone, educational measures taken, following the previous audit have failed to impact practice, except, perhaps, for the (incomplete) uptake of treatment of warfarin effect with PCC.
   Knowledge transfer measures included promulgation of guidelines based on those widely accepted in the literature, a decision assisting algorithm, and a clear statement of conditions for which FP transfusion is not useful; guidance has also been provided through ORBCoN's Resource Manual for Medical Directors of Transfusion Medicine.
   Review of the literature in the light of these audit findings confirms that passive educational measures generally have little or no effect in improving ordering practices in a culture where prescribing habits are deeply ingrained. Even active ongoing educational approaches prove difficult to sustain and recidivism is common when active measures are discontinued.
   Reports appearing in the literature since the last audit have indicated that computerized physician order-entry capabilities incorporating decision assistance through built-in criteria of appropriateness can produce a reduction in inappropriate orders, but over-ride

capacity may reduce the effectiveness. This approach is expensive and difficult to implement except as part of a larger IT capability.
Recent reports suggest that prospective screening of orders using hospital guidelines and review of non-conforming requests by Transfusion Medicine physicians can be more effective in reducing inappropriate FP use.
Review by non-medical staff without capacity for appropriate physician review tends to founder as it is difficult sufficiently to empower non-medical staff.

2. There is developing evidence that FP transfusion makes no material difference to INR and to clinical outcomes when the INR is only mildly prolonged, up to 1.7 or 1.8. In this audit, there are many inappropriate transfusions at INRs of 1.5 or less. There are also FP transfusions at INRs of 1.6-1.7 where the reduction in post-transfusion INR is variable. The original Canadian Medical Association guidelines proposed a cut-off at an INR of 2.0 [for liver disease], and recently the Canadian Society for Transfusion Medicine in its document on "Choosing Wisely" recommends that FP transfusion be regarded as not indicated with an INR of less than 1.8. This audit confirms that the use of FP transfusion within this equivocal range and below 1.6 is common and without clear clinical value.

3. The use of PCCs in this audit shows better conformance to clinical practice guidelines both in respect of indication and dose. However there is still incomplete replacement of FP for indications that are appropriate for PCC and situations in which both treatments are used together. PCCs are also sometimes used in clinical situations for which they are inappropriate. Reasons for the apparently better performance in using PCCs are not immediately clear but may represent the introduction of a new treatment with the advantages of novel guidelines for use, the analogy to a new drug, and the absence of an ingrained historical culture of accepted uses. Nevertheless, there are still sufficient shortcomings to require some remedial action.

Observations/Recommendations:

Observation	Recommendation
More than 50% of all FP transfusion episodes in the audit were inappropriate including 26% of all FP transfusions given for INR <= 1.5	1. Develop formal clinical practice recommendations for use of FP in Ontario which could then be adopted by all hospitals.
Studies indicate that provision of clinical practice guidelines and traditional knowledge translation measures have, at best, a limited capacity to improve clinical prescribing of FP. (Item 2(v)). Inappropriate prescribing of FP continues to be widespread in Ontario (Table 6.8).	2. Develop a Quality Improvement plan for FP transfusion in Ontario (to be incorporated into overall Quality Improvement plan for transfusion which has begun with red blood cell transfusions). Recommendations 3-5 could be included as part of QI initiative for FP transfusions.
	3. Develop a standardized, template order form for FP, which would include mandatory relevant pre-transfusion information to allow assessment of appropriateness of transfusion request. The form could be adopted by hospitals or the data elements from this form could be included in local transfusion forms. This would also be used in current and/or future development of Computerized Physician Order Entry for transfusions.

	4. All hospitals would be required to perform annual audit of FP audits using standardized metrics.
No mechanism exists for inter-hospital comparison of use of FP transfusion, to allow hospitals to examine their use of FP in the context of the wider pattern of Provincial consumption of FP (Item 2(vi)).	5. Results of annual audits from all hospitals should be reported to provincial body (e.g. BPCO or ORBCON), and results would be distributed to all hospitals for peer comparison.
FP continues to be prescribed in situations better managed with PCC (Table 6.8). PCC is being used for reversal of warfarin effect in the absence of bleeding or surgical intervention (Table 7.8). PCC is also being used for coagulopathies other than urgent reversal of warfarin effect or vitamin K deficiency.	6. Specific criteria/algorithm for auditing FP transfusions specifically for Coumadin reversal by transfusion technologists be developed provincially and be implemented by local hospitals. The algorithm should include decision tree for referral of specific inappropriate FP requests to transfusion medicine physicians for review.
This audit provides information on the medical specialties/services most frequently prescribing FP and PCC (Tables 6.3 and 6.4)	7. Develop educational tools and resources that target the largest users of FP and those with highest inappropriate use. These tools can then be used by local transfusion medicine physicians to influence/change practice.

10.0 Acknowledgements

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The Provincial Plasma Audit Steering Committee

Appendices

Appendix A: Summary of Published Guidelines for the Use of Fresh Frozen Plasma

Guideline	Single factor deficiency	Multiple factor deficiency	Reversal of warfarin effect	Liver disease	Surgical bleeding, massive transfusion	Volume replacement
British Committee for Standards in Haematology[29, 30]	No safe fractionated product available	Multiple factor deficiencies with severe bleeding +/- DIC	Only in presence of severe bleeding. Partial effect only	Doubtful value. Monitor coagulation for effectiveness	If, and amount, guided by timely tests of coagulation	Not indicated
College of American Pathologists[31]	No safe fractionated or single factor product available	Active bleeding. PT 1.5x mid-point normal range, PTT 1.5x top of normal range	Active bleeding or urgent surgery	No specific recommendation	Active bleeding or before invasive procedure + laboratory evidence of coagulopathy	Contra-indicated
Canadian Medical Association[32]	Concentrates preferred	Active bleeding or urgent surgery with significant increase in PT, INR or PTT	Severe bleeding or urgent surgery. Pro-thrombin complex preferred.	Actual bleeding. PT, INR, PTT elevated. Not indicated for pre-procedure prophylaxis if INR=<2.0	Severe bleeding in presence if possible of laboratory evidence of coagulopathy	Not indicated
Australian Natl. Health and Med. Res. Council[33]	Specific factors if available	Active bleeding	Life-threatening bleeding	May be appropriate with active bleeding and evidence of coagulopathy.	Bleeding with coagulopathy	Not indicated
American Society of Anesthesiol-ogists[34]	Only if specific concentrates are not available	Microvascular bleeding. PT or PTT >1.5x normal	Urgent reversal	No comment	Active bleeding when timely laboratory tests are not available	Contra-indicated

Appendix B: FP audit findings in other jurisdictions (Highlighted represents Canadian audits).

Reference	Country	Guideline	Inappropriate	Indeterminate	Dose adequacy
Brien et al. 1989	Canada	Local*	10%	-	-
Mozes et al. 1989]	Israel	Local	84%	-	-
Barnette et al. 1990	USA	Local	53%	-	-
Thomson et al. 1991	UK	NIH 1985	60%	19%	-
Metz et al. 1995	Australia	Local	31%	-	-
Cheng et al. 1996	Hong Kong	BCSH 1992	71%	-	-
Marconi et al. 1996	Italy	Local	27%	-	-
Tuckfield et al. 1997	Australia	Local	15%	-	-
Jones et al. 1998	UK	BCSH 1992	37%	-	-
Hameedullah et al. 2000	Pakistan	BCSH 1992	45.1%	40.2%	-
Prabitha et al. 2001	Malaysia	CAP 1994	69%	-	-
Luk et al. 2002	Canada	Canadian 1997	45%	-	-
Schofield et al. 2003	Australia	Australian 2001	37%	-	-
Pentti et al. 2003	Finland	Local	52%	-	-
Chng et al. 2003	Singapore	CAP 1994	73%	Not quantified	50.3% inadequate
Kakkar et al. 2003	India	BCSH 1992	60%	-	-
Hui et al. 2004	Australia	Australian 2001	8%	20%	-
Yeh et al. 2006	Taiwan	BCSH 2004	70.4%	-	-
Moiz et al. 2006	Pakistan	BCSH 1992	21.3%	-	-
Atkinson 2006	UK	BCSH 2004	32%	-	-
Lauzier et al. 2007	Canada	Canadian 1997	47.6%	-	-

Makroo et al. 2007	India	CAP 1994	30.2%	Not quantified	-
Shariff et al. 2007	Pakistan	BCSH 1992	33.9%	-	-
Liambruno et al. 2007	Italy	BCSH 2004	24.5%	4.7%	-
Moylan et al. 2008	Australia	Australian 2001	14%	17%	-
Iorio et al. 2008	Italy	Local	68.5%	-	25.6% inadequate
Arewa 2009	Nigeria	Local	36%	-	-
Pervaiz et al. 2009	India	CAP 1994	81%	-	-
Haslindamani et al. 2010	Malaysia	CAP 1994	41.5%	Included in 41.5%	-
Shingara et al. 2010	India	Australian 2001	39.4%	-	Included in 39.4%
ANZICS Clinical Trials Group 2010	Australia and New Zealand	Australian 2001]	29%	-	-
Stanworth et al. 2011	UK	Local	"Frequent"	3%	40% inadequate
Pahuja et al. 2012	India	Local	78.2%	-	-
Pybus et al. 2012	UK	BCSH 2004	89%	-	48% inadequate
Tinmouth et al. 2013	Canada	Local	28.6%	16.6%	29% adequate and appropriate
Shih et al.	Canada	Local	44.9%	-	-

Appendix C: Site Specific Data

Site 1

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-389	0	1	No Bleeding	Yes	Other	Dialysis	2.0 - 3.0		A1	Appropriate
2013-390	6	0	Major Bleeding	No			10+		PCCA1	Appropriate
2013-391	0	2	Minor Bleeding	Yes	Other	Splenectomy	1.3 - 1.5	1.3 - 1.5	I4	Inappropriate
2013-392	0	4	Unknown	Yes	Surgery		5.1 - 10	2.0 - 3.0	I4	Inappropriate
2013-393	0	1	No Bleeding	No			3.1 - 5.0	3.1 - 5.0	I4	Inappropriate

Site 2

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-031	0	4	No Bleeding	Yes	Central line placement		3.1 - 5.0	1.6 - 1.7	I5	Inappropriate
2013-041	0	3	Major Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-042	0	6	Unknown	No			1.6 - 1.7	1.6 - 1.7	A2	Appropriate
2013-088	0	4	Minor Bleeding	Yes	Unknown		1.8 - 1.9	1.6 - 1.7	A2	Appropriate

Site 3

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-170	0	2	Major Bleeding	Yes	Surgery			0 - 1.2	M2	Indeterminate
2013-172	0	2	Unknown	No				1.3 - 1.5	I7	Inappropriate
2013-173	0	2	Major Bleeding	Yes	Surgery				M1	Indeterminate
2013-174	0	1	Minor Bleeding	No			0 - 1.2		I3	Inappropriate
2013-175	5	0	Major Bleeding	No			3.1 - 5.0	0 - 1.2	PCCA1	Appropriate

Site 4

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-335	0	2	Major Bleeding	No			0 - 1.2		I3	Inappropriate
2013-336	0	1	Major Bleeding	No					M1	Indeterminate
2013-337	0	1	Major Bleeding	No					M1	Indeterminate
2013-338	0	3	Major Bleeding	No					M1	Indeterminate

Site 5

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-439	0	2	Major Bleeding	No			1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-440	0	5	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	I2	Inappropriate
2014-441	0	2	No Bleeding	Yes	Other	permanent catheter insertion	2.0 - 3.0	2.0 - 3.0	A1	Appropriate
2014-444	0	2	Major Bleeding	No			0 - 1.2	0 - 1.2	I3	Inappropriate
2014-445	4	0	Major Bleeding	Yes	Surgery		1.3 - 1.5	1.3 - 1.5	PCCI1	Inappropriate
2014-445	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2014-450	0	1	Minor Bleeding	No					M1	Indeterminate
2014-452	0	4	Major Bleeding	No			2.0 - 3.0		I4	Inappropriate
2014-453	4	0	Major Bleeding	No			10+	0 - 1.2	PCCI2	Inappropriate
2014-453	0	4	Major Bleeding	No			10+	0 - 1.2	A2	Appropriate

2014-456	4	0	Major Bleeding	No			10+	0 - 1.2	PCCI2	Inappropriate
2014-456	0	6	Major Bleeding	No			10+	0 - 1.2	A2	Appropriate

Site 6

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-265	3	0	Minor Bleeding	Yes	Unknown		3.1 - 5.0	0 - 1.2	PCCA2	Appropriate
2013-268	6	0	Major Bleeding	Yes	Scope	endoscopy	5.1 - 10		PCCA1	Appropriate
2013-271	0	9	Major Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-276	3	0	No Bleeding	No			3.1 - 5.0	1.6 - 1.7	PCCI2	Inappropriate
2013-277	2	0	No Bleeding	Yes	Surgery		1.3 - 1.5		PCCI1	Inappropriate

Site 7

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-477	4	0	Major Bleeding	Yes	Other	drain large hematoma	2.0 - 3.0	0 - 1.2	PCCA1	Appropriate
2014-478	3	0	No Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	PCCA2	Appropriate
2014-479	0	4	Major Bleeding	Yes	Unknown		2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2014-480	0	4	Unknown	No			1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-481	0	2	No Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate

Site 8

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-347	0	6	Major Bleeding	No			3.1 - 5.0	1.6 - 1.7	I4	Inappropriate
2013-348	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	1.8 - 1.9	I3	Inappropriate
2013-349	0	1	Major Bleeding	Yes	Surgery		1.8 - 1.9	1.6 - 1.7	A2	Appropriate
2013-350	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	2.0 - 3.0	A2	Appropriate
2013-351	0	2	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	A2	Appropriate
2013-352	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.6 - 1.7	A2	Appropriate
2013-353	0	4	Unknown	No			1.8 - 1.9	1.3 - 1.5	I7	Inappropriate
2013-354	0	2	No Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-355	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-356	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-357	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	1.3 - 1.5	I3	Inappropriate
2013-358	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-359	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-360	0	1	Minor Bleeding	Yes	Scope	SCOPE	1.8 - 1.9	2.0 - 3.0	A1	Appropriate
2013-361	0	2	Minor Bleeding	Yes	Scope	SCOPE	2.0 - 3.0	2.0 - 3.0	A1	Appropriate
2013-362	0	4	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.6 - 1.7	A2	Appropriate
2013-363	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	2.0 - 3.0	A3	Appropriate
2013-364	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	A3	Appropriate
2013-365	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	1.8 - 1.9	A3	Appropriate
2013-366	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.8 - 1.9	A1	Appropriate
2013-367	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	I4	Inappropriate
2013-368	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	1.8 - 1.9	I3	Inappropriate

2013-369	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-370	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I5	Inappropriate
2013-371	0	4	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.8 - 1.9	I2	Inappropriate
2013-372	4	0	Major Bleeding	Yes	Surgery		1.8 - 1.9	1.3 - 1.5	PCCA1	Appropriate
2013-373	0	1	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-374	0	4	Major Bleeding	No					M1	Indeterminate

Site 9

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-333	0	4	No Bleeding	No			1.3 - 1.5		I3	Inappropriate
2013-334	4	0	Major Bleeding	No			5.1 - 10	0 - 1.2	PCCA1	Appropriate
2013-339	0	4	Major Bleeding	No			0 - 1.2	0 - 1.2	I3	Inappropriate
2013-340	6	0	Major Bleeding	Yes	Scope	Endoscopy	2.0 - 3.0	0 - 1.2	PCCA1	Appropriate
2013-341	5	0	No Bleeding	Yes	Surgery		3.1 - 5.0	0 - 1.2	PCCI1	Inappropriate
2013-342	3	0	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	PCCA1	Appropriate
2013-343	0	4	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-344	5	0	Major Bleeding	Yes	Unknown		3.1 - 5.0	0 - 1.2	PCCA1	Appropriate

Site 10

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-292	0	2	Major Bleeding	Yes	Scope	Endoscopy	1.3 - 1.5	0 - 1.2	I3	Inappropriate

Site 11

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-175	1	0	Major Bleeding	Yes	Scope	Endoscopy	3.1 - 5.0	1.8 - 1.9	PCCA1	Appropriate
2013-176	0	1	Major Bleeding	Yes	Surgery	Tracheotomy	0 - 1.2		I3	Inappropriate
2013-177	0	2	Major Bleeding	Yes	Image guided therapy	Interventional Radiology guided CTA	2.0 - 3.0	1.8 - 1.9	A3	Appropriate
2013-178	0	2	Major Bleeding	Yes	Image guided therapy	Interventional Radiology guided CTA	2.0 - 3.0	1.8 - 1.9	A3	Appropriate
2013-179	0	2	Major Bleeding	Yes	Image guided therapy	Interventional Radiology guided CTA	2.0 - 3.0	1.8 - 1.9	A3	Appropriate
2013-180	0	2	Major Bleeding	Yes	Other	Post Procedure	1.8 - 1.9	1.6 - 1.7	A3	Appropriate
2013-181	0	6	Major Bleeding	Yes	Other	Post Procedure	1.8 - 1.9	1.3 - 1.5	A3	Appropriate
2013-182	0	2	Major Bleeding	Yes	Other	Post Procedure	1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-183	0	1	Major Bleeding	Yes	Scope	Scope	1.8 - 1.9	1.8 - 1.9	A3	Appropriate
2013-186	0	1	Major Bleeding	Yes	Scope	Scope	1.8 - 1.9	2.0 - 3.0	A3	Appropriate
2013-188	0	2	Major Bleeding	Yes	Other	Scope	2.0 - 3.0	1.8 - 1.9	A3	Appropriate
2013-189	0	2	Major Bleeding	Yes	Other	Scope	1.8 - 1.9	1.8 - 1.9	A3	Appropriate
2013-190	0	4	Major Bleeding	Yes	Unknown		2.0 - 3.0	2.0 - 3.0	A3	Appropriate
2013-191	0	4	Major Bleeding	Yes	Unknown		1.8 - 1.9	1.3 - 1.5	A2	Appropriate
2013-197	0	1	Major Bleeding	Yes	Unknown		2.0 - 3.0	3.1 - 5.0	A3	Appropriate
2013-198	0	2	Major Bleeding	Yes	Unknown		2.0 - 3.0	2.0 - 3.0	A3	Appropriate
2013-199	0	4	Major Bleeding	Yes	Unknown		2.0 - 3.0	1.6 - 1.7	A3	Appropriate

2013-200	5	0	No Bleeding	Yes	Scope	Bronchoscopy	5.1 - 10	1.3 - 1.5	PCCA2	Appropriate
2013-201	0	1	Major Bleeding	Yes	Unknown		0 - 1.2		I3	Inappropriate
2013-202	0	1	Major Bleeding	Yes	Unknown		0 - 1.2		I3	Inappropriate

Site 12

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-170 Changed to 2013-171	4	0	Major Bleeding	No			3.1 - 5.0	1.3 - 1.5	PCCA1	Appropriate
2013-183	3	0	No Bleeding	No			3.1 - 5.0		PCCI2	Inappropriate
2013-185	0	4	Minor Bleeding	Yes	Unknown		1.6 - 1.7	1.3 - 1.5	A2	Appropriate

Site 13

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-250	0	2	Minor Bleeding	No			1.6 - 1.7	1.8 - 1.9	I4	Inappropriate
2013-253	0	2	Unknown	Yes	Surgery		2.0 - 3.0	2.0 - 3.0	I2	Inappropriate
2013-255	0	4	Unknown	No			3.1 - 5.0	2.0 - 3.0	I7	Inappropriate
2013-257	5	0	Unknown	Yes	Surgery		3.1 - 5.0	1.3 - 1.5	PCCA2	Appropriate
2013-259	2	0	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	PCCA1	Appropriate
2013-260	0	2	Unknown	Yes	Surgery		2.0 - 3.0	2.0 - 3.0	I5	Inappropriate
2013-262	4	0	Unknown	Yes	Surgery		3.1 - 5.0	0 - 1.2	PCCA2	Appropriate
2013-263	4	0	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate
2013-264	0	2	Minor Bleeding	No			1.8 - 1.9	1.3 - 1.5	A2	Appropriate
2013-265	6	0	Minor Bleeding	No			5.1 - 10	0 - 1.2	PCCA1	Appropriate

Site 14

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-057	0	2	No Bleeding	Yes	Surgery		3.1 - 5.0	2.0 - 3.0	A1	Appropriate
2013-058	0	2	Major Bleeding	Yes	Surgery		3.1 - 5.0	2.0 - 3.0	A2	Appropriate
2013-059	0	18	Major Bleeding	Yes	Surgery		2.0 - 3.0	2.0 - 3.0	A3	Appropriate
2013-060	0	2	No Bleeding	Yes	Other	Renal Dialysis	0 - 1.2		I3	Inappropriate
2013-061	0	0	No Bleeding	Yes	Surgery		0 - 1.2		I3	Inappropriate
2013-062	0	4	Major Bleeding	No			2.0 - 3.0		A3	Appropriate
2013-063	0	8	Major Bleeding	Yes	Surgery			0 - 1.2	M2	Indeterminate
2013-064	0	2	No Bleeding	Yes	Other	Renal Dialysis	0 - 1.2		I3	Inappropriate
2013-065	0	4	Major Bleeding	Yes	Surgery			1.8 - 1.9	A2	Appropriate
2013-066	0	4	Major Bleeding	Yes	Surgery			1.3 - 1.5	M2	Indeterminate
2013-067	0	6	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-068	0	8	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A3	Appropriate
2013-069	0	2	No Bleeding	Yes	Other	Renal Dialysis	1.8 - 1.9		I4	Inappropriate

Site 15

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-375	2	0	Major Bleeding	Yes	Unknown		2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate
2013-376	2	0	Major Bleeding	No			1.8 - 1.9	1.3 - 1.5	PCCA1	Appropriate
2013-377	2	0	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	PCCA1	Appropriate
2013-378	0	2	Major Bleeding	No			1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-379	0	4	Major Bleeding	No			0 - 1.2	1.3 - 1.5	I3	Inappropriate
2013-380	0	2	Major Bleeding	Yes	Other	Open Reduction Internal Fixation fractured femur	1.8 - 1.9		I2	Inappropriate
2013-382	0	2	No Bleeding	No			3.1 - 5.0		I7	Inappropriate
2013-383	0	2	No Bleeding	No			3.1 - 5.0		I7	Inappropriate
2013-384	0	2	No Bleeding	No					M1	Indeterminate
2013-385	0	1	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	I2	Inappropriate
2013-386	0	2	Major Bleeding	No			5.1 - 10		I2	Inappropriate
2013-387	0	2	Major Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-388	2	0	Major Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate

Site 16

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-070	0	2	No Bleeding	No			3.1 - 5.0	2.0 - 3.0	I7	Inappropriate
2013-071	0	4	No Bleeding	Yes	Liver biopsy		1.6 - 1.7		A1	Appropriate
2013-072	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-073	0	4	Minor Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	I2	Inappropriate
2013-074	0	4	Minor Bleeding	Yes	Surgery		1.8 - 1.9	0 - 1.2	I2	Inappropriate
2013-075	0	2	Minor Bleeding	Yes	Surgery			0 - 1.2	I4	Inappropriate
2013-076	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	I4	Inappropriate
2013-077	0	2	No Bleeding	Yes	Surgery		1.8 - 1.9	1.3 - 1.5	A1	Appropriate
2013-105	0	2	No Bleeding	No					M1	Indeterminate
2013-106	0	8	Major Bleeding	Yes	Unknown		1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-107	0	2	Minor Bleeding	No			2.0 - 3.0	0 - 1.2	A2	Appropriate
2013-108	0	1	No Bleeding	Yes	Unknown		1.3 - 1.5		I5	Inappropriate
2013-109	4	0	No Bleeding	Yes	Central line placement		3.1 - 5.0	1.3 - 1.5	PCCA2	Appropriate
2013-110	0	10	Major Bleeding	Yes	Surgery		1.6 - 1.7	0 - 1.2	I4	Inappropriate
2013-111	0	2	Minor Bleeding	No			3.1 - 5.0	1.8 - 1.9	I4	Inappropriate
2013-112	4	0	Major Bleeding	No			10+	0 - 1.2	PCCA1	Appropriate
2013-113	0	4	Major Bleeding	No			10+	10+	A2	Appropriate

Site 17

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-046	5	0	Minor Bleeding	Yes	Unknown		10+	1.3 - 1.5	PCCA1	Appropriate
2013-047	0	2	No Bleeding	Yes	Other	iliac angioplasty	1.6 - 1.7	1.6 - 1.7	A1	Appropriate
2013-048	0	4	Major Bleeding	No			2.0 - 3.0	2.0 - 3.0	A2	Appropriate

2013-049	0	4	No Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	I2	Inappropriate
2013-050	4	0	Minor Bleeding	Yes	Surgery		1.6 - 1.7		PCCA2	Appropriate
2013-078	0	4	Major Bleeding	Yes	Surgery		0 - 1.2	1.3 - 1.5	I3	Inappropriate
2013-084	0	2	Major Bleeding	Yes	Other	endoscopy	1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-086	0	2	Major Bleeding	No			1.8 - 1.9	1.8 - 1.9	A3	Appropriate
2013-087	0	6	Major Bleeding	No			1.8 - 1.9	1.3 - 1.5	A3	Appropriate
2013-097	0	2	No Bleeding	No			3.1 - 5.0	2.0 - 3.0	I4	Inappropriate
2013-098	0	2	Minor Bleeding	Yes	Other	bronchoscopy	1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-099	0	6	Major Bleeding	Yes	Image guided therapy		1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-100	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5		I3	Inappropriate
2013-101	0	2	No Bleeding	Yes	Surgery		5.1 - 10	2.0 - 3.0	I2	Inappropriate
2013-103	0	2	Minor Bleeding	Yes	Other	endoscopy	3.1 - 5.0		I2	Inappropriate
2013-104	0	6	Major Bleeding	No			1.8 - 1.9	1.3 - 1.5	A3	Appropriate
2013-114	0	2	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-115	0	1	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-116	0	2	Major Bleeding	Yes	Image guided therapy		0 - 1.2	0 - 1.2	I3	Inappropriate

Site 18

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-140	6	0	Major Bleeding	No			5.1 - 10	0 - 1.2	PCCA1	Appropriate
2013-141	4	0	Major Bleeding	No			10+	1.8 - 1.9	PCCA1	Appropriate
2013-142	5	0	Major Bleeding	No			10+	0 - 1.2	PCCA1	Appropriate
2013-143	5	0	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	PCCM1	Indeterminate
2013-144	0	0	No Bleeding	Yes	Surgery	Appendectomy	2.0 - 3.0	1.3 - 1.5	PCCA2	Appropriate
2013-144	0	2	No Bleeding	Yes	Other	Appendectomy	2.0 - 3.0	1.3 - 1.5	I2	Inappropriate
2013-145	0	6	Major Bleeding	No			1.6 - 1.7		I4	Inappropriate

Site 19

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-249	0	5	No Bleeding	No			1.6 - 1.7	1.3 - 1.5	I7	Inappropriate
2013-252	0	5	No Bleeding	Yes	Liver biopsy		1.3 - 1.5		I3	Inappropriate
2013-266	2	0	No Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCI1	Inappropriate
2013-267	0	4	No Bleeding	Yes	Surgery				M1	Indeterminate
2013-272	4	0	No Bleeding	No			3.1 - 5.0	1.3 - 1.5	PCCI2	Inappropriate

Site 20

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-468	0	4	Major Bleeding	Yes	Other	Laparotomy for control of bleeding	2.0 - 3.0	1.3 - 1.5	A2	Appropriate
2014-469	0	1	Major Bleeding	No			2.0 - 3.0	1.3 - 1.5	A2	Appropriate
2014-470	2	0	No Bleeding	Yes	Other	CT-guided core biopsy	1.6 - 1.7	0 - 1.2	PCCA2	Appropriate
2014-471	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-472	6	0	Major Bleeding	No			5.1 - 10	0 - 1.2	PCCA1	Appropriate

2014-473	2	0	Major Bleeding	Yes	Scope	Gastroscopy	3.1 - 5.0	0 - 1.2	PCCA1	Appropriate
2014-474	0	2	Major Bleeding	Yes	Surgery			0 - 1.2	M2	Indeterminate
2014-475	0	2	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2014-476	2	0	Minor Bleeding	Yes	Unknown		2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate

Site 21

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-003	0	2	No Bleeding	Yes	Other	Peritoneal Dialysis	1.8 - 1.9		I2	Inappropriate
2013-004	0	4	Major Bleeding	Yes	Other	Necrotizing Fasciitis	2.0 - 3.0	1.6 - 1.7	I4	Inappropriate
2013-005	0	2	Major Bleeding	Yes	Other	Necrotizing Fasciitis	1.6 - 1.7		A2	Appropriate
2013-027	0	2	Major Bleeding	Yes	Surgery		3.1 - 5.0		A2	Appropriate
2013-028	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-043	0	4	Major Bleeding	Yes	Surgery				M1	Indeterminate
2013-044	0	4	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-045	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-091	0	2	Major Bleeding	No			1.3 - 1.5		I3	Inappropriate

Site 22

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-029	0	2	Minor Bleeding	Yes	Surgery		3.1 - 5.0		I1	Inappropriate
2013-030	0	1	Minor Bleeding	No			1.3 - 1.5		I3	Inappropriate
2013-032	0	2	Major Bleeding	No			3.1 - 5.0		A2	Appropriate
2013-033	0	2	Major Bleeding	No			2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2013-034	0	2	Major Bleeding	No			2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2013-035	0	4	Major Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-036	0	4	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	A2	Appropriate

Site 23

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-002	0	2	Unknown	No			1.6 - 1.7	1.6 - 1.7	I7	Inappropriate
2013-037	0	3	No Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	A1	Appropriate
2013-089	0	2	No Bleeding	No			2.0 - 3.0		I1	Inappropriate
2013-090	0	2	No Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate

Site 24

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-431	0	2	Major Bleeding	No			5.1 - 10	1.3 - 1.5	A2	Appropriate
2014-432	0	2	Major Bleeding	Yes	Unknown		2.0 - 3.0	0 - 1.2	A2	Appropriate
2014-433	4	0	Major Bleeding	Yes	Unknown		3.1 - 5.0	1.3 - 1.5	PCCA1	Appropriate
2014-434	0	1	No Bleeding	Yes	Unknown		2.0 - 3.0		A1	Appropriate
2014-435	0	1	Major Bleeding	Yes	Unknown		1.6 - 1.7		A2	Appropriate
2014-436	2	0	Major Bleeding	Yes	Unknown		5.1 - 10		PCCA1	Appropriate
2014-437	6	0	No Bleeding	Yes	Unknown		3.1 - 5.0	0 - 1.2	PCCI2	Inappropriate

2014-438	3	0	No Bleeding	Yes	Unknown		3.1 - 5.0	1.3 - 1.5	PCCA2	Appropriate

Site 25

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-246	0	1	Major Bleeding	No			0 - 1.2		I3	Inappropriate

Site 26

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-192	0	4	Major Bleeding	Yes	Central line placement		2.0 - 3.0	1.6 - 1.7	A2	Appropriate
2013-193	0	2	Major Bleeding	No			1.8 - 1.9		A2	Appropriate
2013-194	0	1	Major Bleeding	No			5.1 - 10		A2	Appropriate
2013-195	2	0	Major Bleeding	No			1.8 - 1.9	1.6 - 1.7	PCCI1	Inappropriate
2013-196	2	0	Major Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate

Site 27

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-345	6	0	Major Bleeding	Yes	Unknown		5.1 - 10	0 - 1.2	PCCA1	Appropriate
2013-345	0	2	Major Bleeding	Yes	Unknown		5.1 - 10	0 - 1.2	A2	Appropriate
2013-346	4	0	Minor Bleeding	Yes	Unknown		2.0 - 3.0	2.0 - 3.0	PCCA1	Appropriate

Site 28

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-222	4	0	Unknown	No			10+	1.3 - 1.5	PCCI2	Inappropriate
2013-224	0	2	Unknown	No			1.6 - 1.7	1.6 - 1.7	I7	Inappropriate
2013-225	0	2	Unknown	No			1.6 - 1.7	1.6 - 1.7	I7	Inappropriate
2013-226	0	2	Unknown	No			1.3 - 1.5	1.6 - 1.7	I3	Inappropriate
2013-227	2	0	Unknown	No			1.6 - 1.7		PCCI1	Inappropriate
2013-228	2	0	Unknown	No			1.6 - 1.7		PCCI1	Inappropriate

Site 29

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-421	6	0	Major Bleeding	No			5.1 - 10		PCCM1	Indeterminate
2014-422	0	2	Major Bleeding	Yes	Other	esophagogastroduodenoscopy	1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2014-423	0	2	Major Bleeding	Yes	Surgery		0 - 1.2		I3	Inappropriate
2014-424	6	0	No Bleeding	Yes	Unknown		5.1 - 10	0 - 1.2	PCCI2	Inappropriate
2014-424	0	1	No Bleeding	Yes	Unknown		5.1 - 10	0 - 1.2	I1	Inappropriate
2014-425	2	0	No Bleeding	Yes	Surgery		2.0 - 3.0	0 - 1.2	PCCA2	Appropriate
2014-426	2	0	Minor Bleeding	Yes	Other	packing of nose	2.0 - 3.0	1.3 - 1.5	PCCA1	Appropriate
2014-427	0	8	Major Bleeding	Yes	Unknown		2.0 - 3.0	1.3 - 1.5	A2	Appropriate

Site 30

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-419	0	5	Minor Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	A2	Appropriate
2014-420	0	3	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate

2014-428	0	2	No Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A1	Appropriate

Site 31

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-414	0	4	Minor Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2014-415	0	2	Minor Bleeding	No			1.3 - 1.5		I3	Inappropriate
2014-416	2	0	Major Bleeding	No			3.1 - 5.0	1.6 - 1.7	PCCA1	Appropriate
2014-416	0	2	Major Bleeding	No			3.1 - 5.0	1.6 - 1.7	A2	Appropriate
2014-417	0	4	Major Bleeding	No			2.0 - 3.0		A2	Appropriate
2014-418	0	2	No Bleeding	Yes	Surgery		2.0 - 3.0	1.8 - 1.9	I7	Inappropriate

Site 32

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-409	0	2	Major Bleeding	No			2.0 - 3.0	2.0 - 3.0	A2	Appropriate
2014-410	2	0	No Bleeding	No			1.6 - 1.7	1.3 - 1.5	PCCI2	Inappropriate
2014-411	0	1	Major Bleeding	Yes	Unknown		3.1 - 5.0	2.0 - 3.0	I2	Inappropriate
2014-412	2	0	Unknown	No			5.1 - 10		PCCA1	Inappropriate
2014-412	0	3	Unknown	No			5.1 - 10		I7	Inappropriate
2014-413	0	4	Major Bleeding	No			3.1 - 5.0	0 - 1.2	I2	Inappropriate

Site 33

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-083	0	2	Major Bleeding	No			1.6 - 1.7	1.6 - 1.7	A2	Appropriate
2013-084	0	2	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-229	0	2	Minor Bleeding	No			5.1 - 10	3.1 - 5.0	A2	Appropriate
2013-230	0	4	Minor Bleeding	No			3.1 - 5.0	2.0 - 3.0	A2	Appropriate
2013-231	0	2	Minor Bleeding	No			3.1 - 5.0		A2	Appropriate
2013-232	0	2	Minor Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-233	0	4	Major Bleeding	No			5.1 - 10	2.0 - 3.0	A2	Appropriate
2013-234	0	2	Major Bleeding	No			3.1 - 5.0		I2	Inappropriate

Site 34

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-038	2	0	Minor Bleeding	Yes	Surgery		1.6 - 1.7		PCCA1	Appropriate
2013-039	0	1	Minor Bleeding	Yes	Unknown		3.1 - 5.0	0 - 1.2	I2	Inappropriate
2013-040	0	0	Major Bleeding	Yes	Unknown		0 - 1.2		I3	Inappropriate
2013-132	0	2	Minor Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-133	0	1	Minor Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-136	0	3	No Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-137	0	1	No Bleeding	No			5.1 - 10	5.1 - 10	I1	Inappropriate
2013-138	0	1	No Bleeding	Yes	Unknown		1.6 - 1.7		A2	Appropriate
2013-139	0	4	Major Bleeding	Yes	Unknown		1.3 - 1.5	1.3 - 1.5	I5	Inappropriate

Site 35

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-079	0	2	Major Bleeding	No			3.1 - 5.0	3.1 - 5.0	A2	Appropriate
2013-080	0	2	No Bleeding	Yes	Surgery		1.8 - 1.9	1.3 - 1.5	I1	Inappropriate
2013-081	0	2	No Bleeding	Yes	Surgery		1.8 - 1.9	1.6 - 1.7	A1	Appropriate
2013-208	0	3	Minor Bleeding	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-209	0	2	Minor Bleeding	No			1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-210	0	2	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2013-211	2	0	No Bleeding	No			2.0 - 3.0		PCCI2	Inappropriate
2013-213	4	0	Major Bleeding	No			3.1 - 5.0	1.3 - 1.5	PCCA1	Appropriate
2013-214	2	0	No Bleeding	No			1.8 - 1.9	1.3 - 1.5	PCCI2	Inappropriate
2013-217	2	0	No Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	PCCA2	Appropriate
2013-218	4	0	No Bleeding	Yes	Surgery		5.1 - 10	2.0 - 3.0	PCCA2	App
2013-219	2	0	No Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	PCCA2	App
2013-221	4	0	Major Bleeding	No			3.1 - 5.0	1.3 - 1.5	PCCA1	App

Site 36

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-145	0	2	Major Bleeding	No			2.0 - 3.0	2.0 - 3.0	I2	Inappropriate
2013-147	0	1	Unknown	Yes	Unknown		3.1 - 5.0		I2	Inappropriate
2013-148	0	2	No Bleeding	Yes	Other	Ventral hernia repair	2.0 - 3.0	1.3 - 1.5	I2	Inappropriate
2013-149	0	8	Major Bleeding	Yes	Other	endoscope bending	2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2013-159	0	1	Minor Bleeding	Yes	Scope	gastroscopy	2.0 - 3.0	1.6 - 1.7	I2	Inappropriate
2013-160	4	0	Major Bleeding	Yes	Surgery	dissected aorta	3.1 - 5.0	1.8 - 1.9	PCCA1	App
2013-161	0	4	No Bleeding	No			1.6 - 1.7	1.3 - 1.5	I7	Inappropriate
2013-203	0	4	Major Bleeding	No			1.8 - 1.9		I2	Inappropriate
2013-204	0	2	Unknown	Yes	Other	ICD change, SOB	5.1 - 10		I2	Inappropriate

Site 37

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-402	4	0	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	PCCA1	App
2014-402	0	4	Major Bleeding	No			2.0 - 3.0	1.6 - 1.7	I2	Inappropriate
2014-403	0	4	No Bleeding	No				2.0 - 3.0	I7	Inappropriate
2014-404	0	2	No Bleeding	No			0 - 1.2	0 - 1.2	I3	Inappropriate
2014-405	0	1	No Bleeding	No			1.8 - 1.9	1.6 - 1.7	I7	Inappropriate
2014-406	0	6	No Bleeding	No			2.0 - 3.0	1.3 - 1.5	I7	Inappropriate
2014-407	0	2	No Bleeding	No			1.6 - 1.7	1.3 - 1.5	I7	Inappropriate
2014-408	2	0	Minor Bleeding	No			2.0 - 3.0	0 - 1.2	PCCI1	Inapp

Site 38

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-150	0	1	Unknown	No			1.3 - 1.5	1.3 - 1.5	I7	Inappropriate
2013-151	0	0	Major Bleeding	Yes	Surgery		1.3 - 1.5		I3	Inappropriate
2013-152	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-153	0	1	Unknown	No			1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-154	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-155	0	2	No Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	A1	Appropriate
2013-156	0	4	No Bleeding	Yes	Other	scope	2.0 - 3.0	1.8 - 1.9	A1	Appropriate
2013-157	0	2	Minor Bleeding	Yes	Other	tracheostomy	1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-158	0	4	Major Bleeding	Yes	Surgery			0 - 1.2	M2	Indeterminate

Site 39

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-129	4	0	Major Bleeding	Yes	Unknown		3.1 - 5.0		PCCA1	App
2013-130	0	1	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-131	0	2	No Bleeding	Yes	Unknown		2.0 - 3.0	3.1 - 5.0	I7	Inappropriate
2013-134	0	2	Major Bleeding	Yes	Surgery		2.0 - 3.0	0 - 1.2	I5	Inappropriate
2013-135	0	2	Major Bleeding	Yes	Surgery		3.1 - 5.0	1.3 - 1.5	I2	Inappropriate

Site 40

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-001	0	0	Minor Bleeding	No			1.6 - 1.7	1.3 - 1.5	PCCI2	Inapp

Site 41

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-205	5	0	Major Bleeding	Yes	Surgery		3.1 - 5.0	1.3 - 1.5	PCCA1	App
2013-206	0	12	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	A3	Appropriate
2013-207	4	0	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	PCCI1	Inapp
2013-208	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	1.6 - 1.7	A2	Appropriate
2013-213	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.6 - 1.7	A2	Appropriate
2013-215	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-219	0	2	Major Bleeding	Yes	Surgery			1.3 - 1.5	M2	Indeterminate
2013-221	0	2	Unknown	Yes	Surgery			1.3 - 1.5	M2	Indeterminate
2013-247	0	2	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	I2	Inappropriate
2013-248	0	2	Major Bleeding	No			1.6 - 1.7	1.3 - 1.5	I4	Inappropriate
2013-249	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	2.0 - 3.0	A3	Appropriate
2013-250	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	2.0 - 3.0	A3	Appropriate
2013-253	0	2	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	A3	Appropriate
2013-254	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.6 - 1.7	A3	Appropriate
2013-256	0	2	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A3	Appropriate
2013-262	1	0	Major Bleeding	Yes	Unknown		5.1 - 10	2.0 - 3.0	PCCA1	App

2013-269	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5		I3	Inappropriate
2013-274	0	1	Major Bleeding	Yes	Unknown		1.6 - 1.7		A2	Appropriate
2013-275	0	4	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A3	Appropriate

Site 42

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-282	2	0	Minor Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCI2	Inapp
2013-283	6	0	No Bleeding	No			0 - 1.2	0 - 1.2	PCCI	Inapp
2013-285	6	0	No Bleeding	No			5.1 - 10	1.6 - 1.7	PCCI2	Inapp
2013-286	2	0	No Bleeding	Yes	Surgery	TRACHEOSTOMY, LARYNGEAL BIOPSY	2.0 - 3.0	0 - 1.2	PCCI1	Inapp
2013-287	6	0	Major Bleeding	No			5.1 - 10	1.3 - 1.5	PCCA1	App
2013-288	2	0	Major Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCA1	App
2013-296	0	1	Major Bleeding	No			2.0 - 3.0	2.0 - 3.0	A2	Appropriate
2013-300	0	4	Major Bleeding	No			1.8 - 1.9	1.3 - 1.5	A2	Appropriate
2013-301	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	1.8 - 1.9	A2	Appropriate
2013-303	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-304	0	2	Major Bleeding	Yes	Surgery		1.8 - 1.9	0 - 1.2	A2	Appropriate
2013-310	0	3	Major Bleeding	Yes	Unknown		2.0 - 3.0	1.6 - 1.7	A2	Appropriate
2013-311	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-314	0	6	Major Bleeding	Yes	Unknown		3.1 - 5.0	1.6 - 1.7	A2	Appropriate
2013-316	0	1	Major Bleeding	Yes	Unknown		1.8 - 1.9	1.6 - 1.7	A2	Appropriate
2013-322	0	1	Major Bleeding	No			2.0 - 3.0	1.3 - 1.5	A2	Appropriate
2013-323	0	4	Major Bleeding	Yes	Surgery		0 - 1.2	1.3 - 1.5	A2	Appropriate
2013-325	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-331	0	4	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.3 - 1.5	A2	Appropriate
2013-332	0	4	Major Bleeding	Yes	Surgery		1.6 - 1.7	1.6 - 1.7	A2	Appropriate

Site 43

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-116	0	1	Minor Bleeding	No			2.0 - 3.0		A2	Appropriate
2013-119	0	4	Unknown	Yes	Image guided therapy		5.1 - 10	1.3 - 1.5	I2	Inappropriate
2013-120	0	2	Minor Bleeding	Yes	Surgery		1.6 - 1.7		A1	Appropriate
2013-121	0	2	Major Bleeding	Yes	Surgery		0 - 1.2		I3	Inappropriate
2013-122	0	1	Minor Bleeding	No			2.0 - 3.0		I7	Inappropriate
2013-123	0	8	Major Bleeding	No			2.0 - 3.0	1.8 - 1.9	A2	Appropriate
2013-124	6	0	Major Bleeding	No			10+	1.3 - 1.5	PCCA1	App
2013-124	0	2	Major Bleeding	No			10+	1.3 - 1.5	I2	Inappropriate
2013-125	0	2	Minor Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I4	Inappropriate
2013-126	0	2	Minor Bleeding	Yes	Surgery		1.3 - 1.5	1.3 - 1.5	I3	Inappropriate
2013-127	0	4	Minor Bleeding	No			5.1 - 10	2.0 - 3.0	A2	Appropriate
2013-128	0	4	Minor Bleeding	Yes	Unknown		1.6 - 1.7		I5	Inappropriate

Site 44

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-237	0	2	Major Bleeding	Yes	Surgery		0 - 1.2	0 - 1.2	I3	Inappropriate
2013-238	0	2	Major Bleeding	Yes	Surgery		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2013-239	2	0	Minor Bleeding	Yes	Unknown		3.1 - 5.0	1.3 - 1.5	PCCA1	App
2013-240	2	0	No Bleeding	Yes	Central line placement		3.1 - 5.0	2.0 - 3.0	PCCA2	App
2013-241	4	0	Minor Bleeding	No			5.1 - 10	1.3 - 1.5	PCCA1	App
2013-241	4	0	Minor Bleeding	No			5.1 - 10	1.3 - 1.5	PCCA1	App
2013-243	2	0	No Bleeding	Yes	Surgery		2.0 - 3.0	0 - 1.2	PCCA2	App
2013-244	2	0	Major Bleeding	No			3.1 - 5.0		PCCA1	App
2013-245	0	1	Minor Bleeding	Yes	Surgery		2.0 - 3.0		I2	Inappropriate
2013-278	4	0	No Bleeding	No			10+	1.3 - 1.5	PCCI2	Inapp
2013-279	0	4	No Bleeding	Yes	Surgery		3.1 - 5.0	1.6 - 1.7	A1	Appropriate
2013-280	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	1.3 - 1.5	A2	Appropriate

Site 45

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2014-441	5	0	No Bleeding	Yes	Scope	bronchoscopy	1.3 - 1.5	0 - 1.2	PCCI	Inapp
2014-443	5	0	Major Bleeding	Yes	Unknown		10+	1.6 - 1.7	PCCA1	App
2014-444	0	1	No Bleeding	Yes	Unknown		1.3 - 1.5		I3	Inappropriate
2014-446	6	0	Major Bleeding	Yes	Unknown		2.0 - 3.0		PCCA1	App
2014-447	3	0	Major Bleeding	Yes	Surgery	craniotomy for evacuation of hematoma right temporal intracranial hemorrhage	2.0 - 3.0	0 - 1.2	PCCA1	App
2014-448	0	15	Major Bleeding	Yes	Unknown		3.1 - 5.0	3.1 - 5.0	A2	Appropriate
2014-451	0	4	Major Bleeding	Yes	Surgery		2.0 - 3.0	2.0 - 3.0	A2	Appropriate
2014-452	0	4	Major Bleeding	Yes	Surgery		1.3 - 1.5	1.6 - 1.7	A6	Appropriate
2014-454	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-456	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-457	0	2	Major Bleeding	Yes	Unknown		1.3 - 1.5	0 - 1.2	I3	Inappropriate
2014-459	4	0	Major Bleeding	Yes	Unknown		3.1 - 5.0	1.6 - 1.7	PCCA1	App
2014-460	5	0	Major Bleeding	Yes	Unknown		1.8 - 1.9	1.3 - 1.5	PCCA1	App
2014-460	0	1	Major Bleeding	Yes	Unknown		1.8 - 1.9	1.3 - 1.5	I2	Inappropriate
2014-461	0	2	No Bleeding	Yes	Unknown		10+	1.8 - 1.9	I2	Inappropriate
2014-462	0	8	Major Bleeding	Yes	Surgery		1.8 - 1.9	0 - 1.2	A2	Appropriate
2014-463	0	5	No Bleeding	Yes	Unknown		1.6 - 1.7		A1	Appropriate
2014-464	5	0	Minor Bleeding	Yes	Unknown		5.1 - 10		PCCA1	App
2014-465	0	2	No Bleeding	Yes	Unknown		1.6 - 1.7		I5	Inappropriate
2014-466	2	0	No Bleeding	Yes	Surgery	bowel resection	1.6 - 1.7	1.3 - 1.5	PCCA2	App
2014-467	0	2	Minor Bleeding	Yes	Unknown		2.0 - 3.0		I2	Inappropriate

Site 46

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-393	5	0	Major Bleeding	Yes	Scope	upper endoscopy	2.0 - 3.0	1.3 - 1.5	PCCA1	App
2013-394	0	0	Major Bleeding	Yes	Image guided therapy		5.1 - 10	2.0 - 3.0	I2	Inappropriate
2013-394	2	0	Major Bleeding	Yes	Image guided therapy		5.1 - 10	2.0 - 3.0	PCCA1	App
2013-396	0	2	Minor Bleeding	Yes	Other	Dialysis - BP low, followed by RACE team	2.0 - 3.0		A1	Appropriate
2013-397	0	4	Major Bleeding	Yes	Unknown		3.1 - 5.0	1.3 - 1.5	I2	Inappropriate
2013-398	0	3	Major Bleeding	Yes	Other	ELECTIVE SURGERY	1.8 - 1.9	0 - 1.2	A2	Appropriate
2013-399	0	2	Major Bleeding	Yes	Other	LAP ILEOSTOMY	1.6 - 1.7	1.3 - 1.5	A1	Appropriate
2013-400	0	2	No Bleeding	No			1.8 - 1.9		I4	Inappropriate
2013-401	4	0	No Bleeding	No					PCCI2	Inapp

Site 47

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-162	2	0	Minor Bleeding	Yes	Other	Possible Angioembolization	2.0 - 3.0	1.3 - 1.5	PCCA1	App
2013-163	0	4	Major Bleeding	No			1.8 - 1.9		A2	Appropriate
2013-164	0	2	Major Bleeding	No					M1	Indeterminate
2013-165	0	1	No Bleeding	Yes	Surgery	Splenectomy		0 - 1.2	M2	Indeterminate
2013-166	2	0	No Bleeding	No			2.0 - 3.0	1.3 - 1.5	PCCI2	Inapp
2013-167	0	2	No Bleeding	No			3.1 - 5.0		I1	Inappropriate
2013-168	0	2	Minor Bleeding	Yes	Other	Endoscopy	2.0 - 3.0	2.0 - 3.0	A2	Appropriate
2013-169	0	2	Major Bleeding	Yes	Other	Gastroscopy	1.8 - 1.9	1.3 - 1.5	A2	Appropriate

Site 48

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-051	2	0	Minor Bleeding	Yes	Unknown		2.0 - 3.0	2.0 - 3.0	PCCI1	Inapp
2013-051	0	2	Minor Bleeding	Yes	Unknown		2.0 - 3.0	2.0 - 3.0	I7	Inappropriate
2013-052	2	0	Minor Bleeding	Yes	Scope	Bronchoscopy	3.1 - 5.0	0 - 1.2	PCCA1	App
2013-053	6	0	No Bleeding	No			5.1 - 10	0 - 1.2	PCCI2	Inapp
2013-054	0	4	Major Bleeding	No			1.3 - 1.5		I3	Inappropriate
2013-055	5	0	Major Bleeding	Yes	Unknown		3.1 - 5.0	2.0 - 3.0	PCCA1	App
2013-056	6	0	Major Bleeding	Yes	Unknown		5.1 - 10	1.3 - 1.5	PCCA1	App

Site 49

Order #	# PCC Vials Infused	Total Plasma tx'd	Bleeding status	Was procedure/other indication?	Procedure	Procedure (other)	Pre-INR	Post-INR	Consensus	A/I/Ind
2013-006	0	2	Major Bleeding	No			10+		I2	Inappropriate
2013-022	4	0	Major Bleeding	Yes	Other	cerebral bleed	3.1 - 5.0	0 - 1.2	PCCA1	App
2013-023	0	2	Unknown	Yes	Surgery		1.8 - 1.9		I2	Inappropriate
2013-024	4	0	No Bleeding	Yes	Surgery		2.0 - 3.0	0 - 1.2	PCCA2	App
2013-024	0	6	No Bleeding	Yes	Surgery		2.0 - 3.0	0 - 1.2	I2	Inappropriate
2013-025	0	4	Minor Bleeding	Yes	Other	CT abdo/pelvis	2.0 - 3.0		I2	Inappropriate
2013-026	0	2	Minor Bleeding	Yes	Thoracentesis		3.1 - 5.0	2.0 - 3.0	I2	Inappropriate

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