Perioperative platelet transfusion: recommendations of the Agence française de sécurité sanitaire des produits de santé (AFSSaPS) 2003

[Transfusion périopératoire de plaquettes : recommandations de l'Agence française de sécurité sanitaire des produits de santé (AFSSaPS) 2003]

Charles Marc Samama MD PhD,* Rachid Djoudi MD,† Thomas Lecompte MD PhD,‡
Nathalie Nathan-Denizot MD PhD,§ Jean-François Schved MD PhD,¶ and the AFSSAPS Expert Group

Purpose: To present the recommendations of the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSaPS; French Safety Agency for Health Products).

Methods: A panel of experts reviewed and graded the literature on platelet transfusions; recommendations were formulated.

Main findings: Threshold platelet counts (PC) for transfusions in the perioperative context have not been clearly defined and should be determined by the existence of hemorrhagic risk factors. In the case of commonly practiced invasive procedures, the recommendation is to transfuse in order to achieve $PC > 50,000 \mu L^{-1}$. In the absence of platelet dysfunction, regardless of the type of surgery, the standard hemorrhagic risk threshold for surgery is $50,000 \mu L^{-1}$. It has not been proven that the risk threshold is different according to the type of surgery. For neurosurgery and ophthalmologic surgery involving the posterior segment of the eye, a PC of $100,000 \mu L^{-1}$ is required. For axial regional anesthesia, a PC of $50,000 \mu L^{-1}$ is sufficient for spinal anesthesia; a PC of $80,000 \mu L^{-1}$ has been proposed for epidurals. During massive transfusion, prophylactic platelet infusion cannot be recommended beyond a loss of two blood volumes in less than 24 hr (Professional Consensus). As for the therapeutic transfusion of plasma and/or platelets, as much as possible, platelet deficit should be documented with test results (PC and fibrinogen) before transfusing. In the event of bleeding, platelet transfusion may precede plasma infusion. However, although this recommendation has been the subject of several professional consensus agreements, it is not based on any randomized studies.

Conclusion: Threshold PC for perioperative transfusions have not been clearly defined and most recommendations are the result of a professional consensus.

Objectif : Présenter les recommandations de l'Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSaPS).

Méthode : Un panel d'experts a revu et évalué la documentation sur les transfusions de plaquettes ; des recommandations ont été formulées.

Constatations principales : Le décompte plaquettaire seuil (DP) pour les transfusions périopératoires n'est pas clairement défini et doit être déterminé par l'existence de facteurs de risque hémorragique. Dans le cas de gestes invasifs pratiqués fréquemment, on recommande de transfuser pour atteindre un $DP > 50\,000 \mu L^{-1}$. En l'absence de dysfonction plaquettaire, peu importe le type de chirurgie, le seuil du risque hémorragique normal de la chirurgie est de $50\,000 \mu L^{-1}$. On n'a pas prouvé que le seuil de risque dépend du type de chirurgie. En neurochirurgie, et ophtalmologique touchant le segment postérieur de l'œil, il faut un DP de $100\,000 \mu L^{-1}$. En anesthésie régionale axiale, un DP de $50\,000 \mu L^{-1}$ est suffisant pour la rachianesthésie ; un DP de $80\,000 \mu L^{-1}$ a été proposé pour les péridurales. Pendant la transfusion massive, la perfusion prophylactique de plaquettes ne peut être recommandée au delà d'une perte de deux masses sanguines en moins de 24 h (Consensus professionnel). Comme pour la transfusion thérapeutique de plasma et/ou de plaquettes, autant que possible, le déficit de plaquettes doit être documenté avec les résultats de tests (DP et fibrinogène) avant de transfuser. En cas d'hémorragie, la transfusion de plaquettes peut précéder la transfusion de plasma. Cependant, même si cette recommandation a fait l'objet de certains accords du consensus professionnel, il n'est fondé sur aucune étude randomisée.

Conclusion : Le DP seuil pour les transfusions périopératoires n'a pas été clairement défini et la plupart des recommandations sont le résultat d'un consensus professionnel.

From the Département d'Anesthésie-Réanimation, Hôpital Avicenne,*Bobigny; Site transfusionnel Saint-Antoine,† EFS Ile-de-France, Paris; Service d'Hématologie Biologique, CHU de Nancy,‡ Nancy; Département d'Anesthésie-Réanimation Chirurgicale, Centre Hospitalier Universitaire Dupuytren,§ Limoges; Département d'Hématologie/Biologie, CHU Saint Eloi, Montpellier, France.

Address correspondence to: Pr. Charles Marc Samama, Département d'Anesthésie-Réanimation, Hôpital Avicenne, 125, route de Stalingrad, 93009 Bobigny cedex, France. Phone: +33-1-48955591; Fax: +33-1-48955589; E-mail: cmsamama@invivo.edu

Accepted for publication October 10, 2004.

IN 2003, the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSaPS; French Safety Agency for Health Products) issued new recommendations on platelet transfusion to update the previous recommendations issued in 1997. A large working group was constituted, composed of several experts originating from different medical fields (anesthesiology, intensive care, transfusion medicine, hematology, immunology, pediatrics). The literature was screened extensively, using several databases (Medline, Embase, etc) and after one year of intensive work and several meetings, an extensive review of the subject and the related recommendations became available. The texts were reviewed by a multidisciplinary reading committee whose comments were implemented in the final version. Recommendations were classified (grade) according to the evidence level of the studies supporting them (Table I). Finally, the texts were validated by the "Comité de validation des recommandations et Références médicales de l'AFSSaPS." Members of these three groups are listed in Appendix 1.

We have chosen to extract the perioperative section of these recommendations for the information of clinical anesthesiologists.

The original, integral version of the recommendations on platelet transfusions can be found on the website of the Agence Française de Sécurité Sanitaire des Produits de Santé: AFSSaPS (French Safety Agency for Health Products): <http://www.agmed.sante.gouv.fr/htm/5/rbp/indrpb.htm>

Perioperative platelet transfusions: recommendations

Threshold platelet counts (PC) for perioperative transfusions have not been clearly defined and should be determined by the existence of hemorrhagic risk factors:

- The existence and severity of spontaneous bleeding syndrome or bleeding caused by a minor trauma.
- A history of bleeding or transfusions during previous minor surgery or invasive procedures.

- Associated hemostatic abnormality, particularly in the case of disseminated intravascular coagulation.
- Changes in platelet function induced by drugs or associated diseases: blood diseases (monoclonal gammopathy, myelodysplasia), kidney disease.
- Hypothermia, anemia, splenomegaly.
- Persistent shock, infection.
- Hypertension.

Regardless of the hemorrhagic risk assessment:

- The procedure should always be performed by an experienced practitioner.
- The rapid availability of blood products should be ensured.
- Hemorrhagic risk factors should be corrected.

It is recommended, particularly for surgery, that non-specific methods of reduction of bleeding be used, i.e., (Professional Consensus):

- First choose the method that provides the best surgical control of hemostasis.
- Maintain normothermia.¹
- Limit hemodilution.²⁻⁴
- Ensure the early detection of a hemorrhagic syndrome requiring complementary surgical hemostasis.⁵
- Limit therapies interfering with hemostasis (anticoagulants, antiplatelet agents...) to strict indications.⁶

Platelet transfusion before an invasive procedure or surgery in the event of thrombocytopenia

Invasive procedure

For common invasive procedures (transparietal liver biopsy, lumbar puncture, transbronchial endoscopic biopsy, gastrointestinal endoscopy with biopsy, placement of catheter, etc.) performed in thrombocytopenic patients, the recommendation is to transfuse platelets to achieve a PC > 50,000· μL^{-1} (Grade C).^{7,8} Post-transfusion PC should be monitored prior to the procedure. It is not necessary to systematically check the bleeding time.^{9,10}

TABLE I Levels of evidence and grades of recommendations

<i>Level of evidence</i>		<i>Grade of recommendation</i>
Level I:	Large randomized trials with clear-cut results (and low risk of error) Metaanalyses of randomised trials Decision analysis based on well conducted studies	Grade A:
Level II:	Small randomized trials with uncertain results Well conducted non-randomized studies Cohort studies	Grade B:
Level III:	Case-control series	Grade C:
Level IV:	Comparative studies with major bias, Retrospective studies, historical controls, case series, epidemiological studies	

Surgery

In the absence of platelet dysfunction, regardless of the type of surgery, there is no hemorrhagic risk associated with thrombocytopenia alone for $PC > 50,000 \cdot \mu L^{-1}$. The risk is low for PC between 50,000 to $100,000 \cdot \mu L^{-1}$. The standard threshold for hemorrhagic risk for surgery is therefore $50,000 \cdot \mu L^{-1}$, including cardiac surgery with cardiopulmonary bypass (Professional Consensus).¹¹⁻¹⁵

There is no proof that the risk threshold is different according to the type of surgery. Nonetheless, for neurosurgery and ophthalmologic surgery involving the posterior segment of the eye, a PC of $100,000 \cdot \mu L^{-1}$ is required.¹⁶

For axial regional anesthesia:

a PC of $50,000 \cdot \mu L^{-1}$ is deemed sufficient for spinal anesthesia.

a PC of $80,000 \cdot \mu L^{-1}$ has been proposed for epidurals, but other hemorrhagic risk factors must be taken into account, particularly those cited previously, as well as the progressive nature of the thrombocytopenia.¹⁷⁻²¹

Aside from cases of massive transfusion, platelet transfusion is considered useful in cardiac surgery and major liver surgery (particularly liver transplantation and portocaval shunt).

In cardiac surgery, therapeutic platelet transfusion is justified if the $PC < 50,000 \cdot \mu L^{-1}$ (Professional Consensus). Platelet transfusion is justified in the event of microvascular bleeding associated with $PC < 100,000 \cdot \mu L^{-1}$ (Grade B evidence).

In liver surgery, particularly transplantation, therapeutic platelet transfusion is justified if the PC is $50,000 \cdot \mu L^{-1}$ (Grade C). Correction of other factors that foster bleeding such as hypovolemia, hypothermia and anemia is imperative and is an integral part of the platelet transfusion process.

In obstetrics, there is no indication for platelet transfusion in the case of gestational thrombocytopenia²² in late pregnancy (also known as idiopathic thrombocytopenic purpura (Professional Consensus).

In the event of thrombocytopenia associated with hemolysis, elevated liver enzymes, and low platelets syndrome (HELLP) or preeclampsia, platelet transfusion is recommended immediately before a Cesarean section for a PC of less than $50,000 \cdot \mu L^{-1}$ and immediately before vaginal delivery for a $PC < 30,000 \cdot \mu L^{-1}$ (Professional Consensus).

In autoimmune thrombocytopenic purpura, transfused platelets are very rapidly destroyed, as are the patient's own platelets. Therefore, there is no indication for platelet transfusion, aside from life-threatening hemorrhagic emergencies (Professional

Consensus). In this case, they should be combined with intravenously administered immunoglobulin and high doses of corticosteroids.

Platelet transfusion during an invasive procedure or surgery in the event of thrombopathy

Hematologic thrombopathy

Constitutional or acquired thrombopathy should be managed by specialists for an in-depth investigation. There is no proof that any specific test (particularly the bleeding time) can predict hemorrhagic risk in these patients.

Drug-induced thrombopathy

Drug-induced thrombopathies are the most frequent cause of acquired thrombopathy.²³⁻³⁰ The main drugs involved are platelet function inhibitors and nonsteroidal anti-inflammatory drugs, which have an effect on platelet function^A (depending on the drug and the dosage).

Drugs involved⁶

The hemorrhagic risks by type of surgery are presented in Appendix 2.

Prophylaxis

Prophylactic platelet transfusion before an invasive procedure, when platelet inhibitor therapy has not been discontinued in a timely manner, is not recommended (Professional Consensus).

Role of transfusion

There are no clinical studies validating the benefits of platelet transfusion in reducing the risk of bleeding (prophylactic administration) or in limiting bleeding when it occurs (therapeutic administration) in patients with drug induced thrombopathy. However, this is the only therapeutic option that can be envisaged in the event of severe hemorrhage (Professional Consensus).

Platelet transfusion in the event of massive transfusion

Several definitions for massive transfusion have been proposed:^{5,31-35}

- Replacement of the loss of more than one blood volume in less than 24 hr.
- Replacement of the loss of more than 50% of blood volume in less than three hours.
- Blood loss of more than $150 \text{ mL} \cdot \text{min}^{-1}$.

^A See experts' conference organized at the initiative of the Société française d'anesthésie et de réanimation (SFAR; the French Society of Anesthesiology and Intensive Care) on "Antiplatelet agents in the perioperative period", available at www.sfar.org.

TABLE II Proposals to help with therapeutic decision making

		<i>Presence of clinical bleeding</i>	
		<i>Yes</i>	<i>No</i>
Presence of abnormal laboratory tests*	Yes	Transfusion of platelets and FFP based on test results (starting with (e.g., platelet concentrates)**	Transfusion based related to the procedure on risks neurosurgery and PC < 100,000- μL^{-1})
	No	Look for a cause other than a hemostatic abnormality Assess the extent of transfusions and eventually transfuse platelets and FFP if loss exceeds one blood volume (starting with platelets)** Monitor laboratory tests.	No indication for transfusion
	Unknown	Transfusion based on the probable type of hemostatic disorder	No indication for transfusion Repeat laboratory tests

*Platelets < 50,000- μL^{-1} , fibrinogen < 0.5 to 0.8 g- L^{-1} , prothrombin time and/or activated partial thromboplastin time > 1.5 to 1.8 times control. **Platelet transfusion could precede plasma infusion. Although this recommendation has been made by several professional consensus statements, it is not based on any randomized trials. FFP = fresh frozen plasma.

Treatment priorities are:

- Restore blood volume to maintain tissue perfusion and oxygenation.
- Control hemostasis by treating the cause of bleeding and by correcting the coagulopathy with an appropriate choice of blood products.

Prophylactic platelet transfusions based on volume replaced

Prophylactic infusion of platelets is not recommended beyond the replacement of two blood volumes in less than 24 hr (Professional Consensus).

It is important to consider the individual clinical situation and reasons for bleeding. It is likely but not certain that the preventive administration of platelets is not useful if the patient is not bleeding.

Fresh frozen plasma (FFP) should be transfused at the same time as platelets.

Therapeutic platelet transfusion

Abnormal bleeding is bleeding that is unexpected and does not respond either to compression or to electrocoagulation. Although clinical assessment remains an important element in the decision making process, alone is not a sufficient indication for transfusion.

Transfusion of FFP or platelets

As much as possible, it is desirable to document platelet deficits with test results (PC and fibrinogen) before transfusing.

It is also desirable to closely monitor PC and fibrinogen and to begin with platelet concentrates

(Professional Consensus). A number of authors suggest using point of care coagulation monitors for surgical bleeding.³⁶

Other elements involved in increased hemostatic problems during massive transfusion

Hypothermia interferes with hemostasis. It is imperative that all available techniques be used to warm the patient as well as the infusion and transfusion products.^{1,37,38} A drop in hematocrit increases the risk of bleeding, particularly in the presence of thrombocytopenia. Infusion of packed red blood cells should not be delayed.²⁻⁴ Hemostatic problems observed during massive transfusion are increased by shock. Optimization of the patient's hemodynamic status is an essential objective.³⁹ If a multiple trauma victim with multiple transfusions has a head injury, perioperative hemostasis should be controlled even further (earlier infusion of plasma, platelets).

Table II summarizes the available information and proposes a therapeutic transfusion protocol based on the presence/absence of clinical bleeding and the results of laboratory tests.

References

- 1 Reed RL II, Johnston TD, Hudson JD, Fischer RP. The disparity between hypothermic coagulopathy and clotting studies. *J Trauma* 1992; 33: 465-70.
- 2 Escolar G, Garrido M, Mazzara R, Castillo R, Ordinas A. Experimental basis for the use of red cell transfusion in the management of anemic-thrombocytopenic patients. *Transfusion* 1988; 28: 406-11.

- 3 Santos MT, Valles J, Marcus AJ, et al. Enhancement of platelet reactivity and modulation of eicosanoid production by intact erythrocytes. A new approach to platelet activation and recruitment. *J Clin Invest* 1991; 87: 571–80.
- 4 Ouaknine-Orlando B, Samama CM, Riou B, et al. Role of the hematocrit in a rabbit model of arterial thrombosis and bleeding. *Anesthesiology* 1999; 90: 1454–61.
- 5 Stainsby D, MacLennan S, Hamilton PJ. Management of massive blood loss: a template guide. *Br J Anaesth* 2000; 85: 487–91.
- 6 Samama CM, Bastien O, Forestier F, et al. Antiplatelet agents in the perioperative period: expert recommendations of the French Society of Anesthesiology and Intensive Care (SFAR) 2001 – summary statement. *Can J Anesth* 2002; 49(Suppl): S26–35.
- 7 Cadranet JF, Rufat P, Degos F. Practices of transcutaneous liver biopsies in France. Results of a retrospective nationwide study (French). *Gastroenterol Clin Biol* 2001; 25: 77–80.
- 8 Weiss SM, Hert RC, Gianola FJ, Clark JG, Crawford SW. Complications of fiberoptic bronchoscopy in thrombocytopenic patients. *Chest* 1993; 104: 1025–8.
- 9 Rodgers RP, Levin J. A critical reappraisal of bleeding time. *Semin Thromb Hemost* 1990; 16: 1–10.
- 10 O'Kelly SW, Lawes EG, Luntley JB. Bleeding time: is it a useful clinical tool? *Br J Anaesth* 1992; 68: 313–5.
- 11 College of American Pathologists. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets. Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. *JAMA* 1994; 271: 777–81.
- 12 Rebull P. Trigger for platelet transfusion. *Vox Sang* 2000; 78(Suppl 2): 179–82.
- 13 Consensus conference. Platelet transfusion therapy. *JAMA* 1987; 257: 1777–80.
- 14 Murphy ME, Brozovic B, Murphy W, Ouwehand W, Waters AH. Guidelines for platelet transfusions. British Committee for Standards in Haematology, Working Party of the Blood Transfusion Task Force. *Transfus Med* 1992; 2: 311–8.
- 15 Contreras M. Final statement from the consensus conference on platelet transfusion. *Transfusion* 1998; 38: 796–7.
- 16 Hay A, Olsen KR, Nicholson DH. Bleeding complications in thrombocytopenic patients undergoing ophthalmic surgery. *Am J Ophthalmol* 1990; 109: 482–3.
- 17 Rolbin SH, Abbott D, Mutschlow E, Papsin F, Lie LM, Freedman J. Epidural anesthesia in pregnant patients with low platelet counts. *Obstet Gynecol* 1988; 71: 918–20.
- 18 Edelson RN, Chernik NL, Posner JB. Spinal subdural hematomas complicating lumbar puncture. *Arch Neurol* 1974; 31: 134–7.
- 19 Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm(³). *Anesth Analg* 1997; 85: 385–8.
- 20 Hew-Wing P, Rolbin SH, Hew E, Amato D. Epidural anaesthesia and thrombocytopenia. *Anaesthesia* 1989; 44: 775–7.
- 21 Vandermeulen EP, Van Aken H, Vermeylen J. Anticoagulants and spinal-epidural anaesthesia. *Anesth Analg* 1994; 79: 1165–77.
- 22 Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6715 deliveries. *Am J Obstet Gynecol* 1990; 162: 731–4.
- 23 Lecompte T. Inhibiteurs du fonctionnement plaquettaire et chirurgie. In: Samama CM, de Moerloose P, Hardy JF, Sié P, Steib A (Eds). *Hémorragies et Thromboses Périopératoires en Anesthésie-Réanimation: Approches Pratiques - Groupe d'Intérêt en Hémostase Périopératoire (GIHP)*. Paris: Masson; 2000: 77–87.
- 24 Schafer AI. Effects of nonsteroidal anti-inflammatory therapy on platelets. *Am J Med* 1999; 106: 25S–36S.
- 25 van Hecken A, Schwartz JI, Depré M, et al. Comparative inhibitory activity of rofecoxib, meloxicam, diclofenac, ibuprofen, and naproxen on cox-2 versus cox-1 in healthy volunteers. *J Clin Pharmacol* 2000; 40: 1109–20.
- 26 Patrono C. Antiplatelet strategies. *Eur Heart J* 2002; 4: A42–7.
- 27 FitzGerald GA, Patrono C. The coxibs, selective inhibitors of cyclooxygenase-2. *N Engl J Med* 2001; 345: 433–42.
- 28 Collaborative overview of randomised trials of antiplatelet therapy - II: Maintenance of vascular graft or arterial patency by antiplatelet therapy. Antiplatelet Trialists' Collaboration. *BMJ* 1994; 308: 159–68.
- 29 Topol EJ, Byzova TV, Plow EF. Platelet GPIIb-IIIa blockers. *Lancet* 1999; 353: 227–31.
- 30 Gammie JS, Zenati M, Kormos RL, et al. Abciximab and excessive bleeding in patients undergoing emergency cardiac operations. *Ann Thorac Surg* 1998; 65: 465–9.
- 31 Hiippala S. Replacement of massive blood loss. *Vox Sang* 1998; 74 (Suppl 2): 399–407.
- 32 Hiippala ST, Myllylä GJ, Vahtera EM. Hemostatic factors and replacement of major blood loss with plasma-poor red cell concentrates. *Anesth Analg* 1995; 81: 360–5.
- 33 Harvey MP, Greenfield TP, Sugrue ME, Rosenfeld D. Massive blood transfusion in a tertiary referral hospital. Clinical outcomes and haemostatic complications. *Med*

- J Aust 1995; 163: 356–9.
- 34 *Hakala P, Hiippala S, Syrjala M, Randell T.* Massive blood transfusion exceeding 50 units of plasma poor red cells or whole blood: the survival rate and the occurrence of leukopenia and acidosis. *Injury* 1999; 30: 619–22.
- 35 *Reed RL, Ciavarella D, Heimbach DM, et al.* Prophylactic platelet administration during massive transfusion. *Ann Surg* 1986; 203: 40–8.
- 36 *Despotis GJ, Santoro SA, Spitznagel E, et al.* Prospective evaluation and clinical utility of on-site monitoring of coagulation in patients undergoing cardiac operation. *J Thorac Cardiovasc Surg* 1994; 107: 271–9.
- 37 *Michelson AD, MacGregor H, Barnard MR, Kestin AS, Rohrer MJ, Valeri CR.* Reversible inhibition of human platelet activation by hypothermia in vivo and in vitro. *Thromb Haemost* 1994; 71: 633–40.
- 38 *Rohrer MJ, Natale AM.* Effects of hypothermia on the coagulation cascade. *Crit Care Med* 1992; 20: 1402–5.
- 39 *Hewson JR, Neame PB, Kumar N, et al.* Coagulopathy related to dilution and hypotension during massive transfusion. *Crit Care Med* 1985; 13: 387–91.

APPENDIX 1*Working group*

Pr MICHALLET Mauricette, President, Lyon
 Dr NOUYRIGAT Emmanuel, Afssaps
 Dr DUMARCET Nathalie, Afssaps
 Dr BOURHIS Hean-Henri, Villejuif
 Pr CAZENAVE Jean-Pierre, Strasbourg
 Pr CLARIS Olivier, Lyon
 Dr DAVID Bernard, Afssaps
 Dr DECONINCK Eric, Besançon
 Dr DENIS Catherine, Afssaps
 Dr DJOUDI Rachid, Paris
 Pr DUFOUR Patrick, Strasbourg
 Dr FOLLEA Gilles, Nantes
 Dr KAPLAN-GOUET Cécile, Paris
 Pr LECOMPTE Thomas, Vandoeuvre les Nancy
 Dr LEFRERE François, Paris
 Pr MARIE Jean-Pierre, Paris
 Dr MERCADIER Anne, Paris
 Pr NATHAN-DENIZOT Nathalie, Limoges
 Dr OUNNOUGHENE Afssaps
 Pr SAMAMA Marc, Bobigny
 Dr SANDID Afssaps
 Pr SCHVED Jean-François, Montpellier
 Dr SUTTON Laurent, Paris
 Dr TRAINEAU Richard, Paris
 Dr VEY Norbert, Marseille

Review group

Dr CHABERNAUD Jean-Louis, Clamart
 Dr CLUET-DENNETIERE Sophie, Compiègne
 Dr DENNINGER Marie-Hélène, Clichy
 Dr FAVIER Rémi, Paris
 Dr FORESTIER François, Bordeaux
 Pr HARDY Jean-François, Montréal
 Dr HERNANDORENA José-Xavier, Bayonne
 Pr HERVE Patrick, Besançon
 Pr IFRAH Norbert, Angers
 Pr JANVIER Gérard, Pessac
 Pr JOUSSEMET Marcel, Clamart
 Dr LAPIERRE Valérie, Besançon
 Dr LASNE Dominique, Paris
 Dr LEPEU Gérard, Avignon
 Pr LONGROIS Dan, Nancy
 Pr MILPIED Noël, Nantes
 Pr MULLER Jean-Yves, Nantes
 Dr PIGNON Bernard, Reims
 Pr RIOU Bruno, Paris
 Dr SENSEBE Luc, Tours
 Pr SIE Pierre, Toulouse
 Pr SIMEONI Umberto, Marseille
 Pr STEIB Annick, Strasbourg
 Pr VAN DER LINDEN Philippe, Jumeat
 Pr TCHERNIA Gilbert, Le Kremlin Bicêtre

Validation Committee

Pr BOUVENOT Gilles, President, Marseille
 Pr BERGMANN Jean-François, Vice-President, Paris
 Dr CARON Jacques, Lille
 Pr CAULIN Charles, Paris
 Pr CHOUTET Patrick, Tours
 Pr DUPUIS Bernard, Lille
 Pr JOLLIET Pascale, Nantes
 Dr AMBROSI Pierre, Marseille
 Dr ATLAN Pierre, Paris
 Pr BANNWARTH Bernard, Bordeaux
 Dr CAMELLI Bruno, Paris
 Dr CUCHERAT Michel, Lyon
 Dr DEMOLIS Pierre, le Kremlin Bicêtre
 Dr DENIS Catherine, Afssaps
 Pr DIQUET Bertrand, Angers
 Dr DUMARCET Nathalie, Afssaps
 Dr GUEYFFIER François, Lyon
 Dr HANSLIK Thomas, Boulogne Billancourt
 Dr LE ROUX Gérard, Epinay sous Sénart
 Dr LIEVRE Michel, , Lyon
 Dr MEYER François, Afssaps
 Pr PETIT Michel, Sotteville-lès-Rouen
 Dr REVEILLAUD Olivier, Bièvres
 Pr RICHIÉ Christian, Brest
 Dr ROSTOKER Guy, Afssaps
 Dr TREMOLIERES François, Mantes-la-Jolie
 Pr TROUVIN Jean-Hugues, Afssaps
 Dr WONG Olivier, Paris

APPENDIX 2

Drugs most often involved in abnormal platelet function in surgical patients

<i>Type of surgery</i>	<i>Drug therapy</i>	<i>Situation</i>	<i>Hemorrhagic risk</i>	<i>Level of evidence</i>
Hip surgery	Aspirin 100 mg with prophylactic heparin	Preoperative	Increased risk and exposure to transfusion	1
	Aspirin and other NSAIDs (without heparin)	Preoperative	Possible increase in risk and exposure to transfusion	3
	Aspirin (alone)	Postoperative	No increased risk or exposure to transfusion	1
	NSAIDs with prophylactic heparin	Postoperative	No increased risk or exposure to transfusion	1
	NSAIDs	Postoperative	No increased risk or exposure to transfusion	2
Knee surgery	Aspirin (alone)	Postoperative	No increased risk or exposure to transfusion	1
	NSAIDs	Postoperative	No increased risk or exposure to transfusion	2
Cardiac surgery	Aspirin and other NSAIDs	Preoperative	Modest increase in risk with few changes in transfusion requirements	2–4
	Abciximab (plus aspirin)	Preoperative	Possible increase in risk and exposure to transfusion	3
	Eptifibatide, tirofiban (plus aspirin)	Preoperative	Possible increase in risk and exposure to transfusion, but less than with abciximab	3
	Thienopyridine	Preoperative	Possible increase in risk or exposure to transfusion	4
Carotid artery surgery	Aspirin	Preoperative	No increased risk of cervical hematoma or intracranial bleeding*	3
Tonsillectomy	NSAIDs including aspirin	Pre- or postoperative	Possible increased risk and revision procedures for hemostasis	1–3
Ophthalmology Anterior chamber, avascular structures (lens, cornea) Strabismus surgery	Aspirin	Preoperative	Small increase in risk	2
Intracranial surgery Prostate via abdominal approach	NSAIDs	Postoperative	No increased risk	2
	All platelet function inhibitors	Preoperative	Increased risk	3–4
	NSAIDs	Postoperative	Low increase in risk with no increase in transfusion requirements	2
Transurethral prostatic resection	Aspirin	Preoperative	Possible increase in risk and transfusion requirements	3
	Ticlopidine	Pre- or postoperative	Increased risk and transfusion requirements	2
	Aspirin and other NSAIDs	Preoperative	Contradictory findings	2–3
	NSAIDs if patient is less than 75 yr old	Postoperative by less than 5 days	No increased risk or revision procedures for hemostasis	3
Gastrointestinal and general surgery	Thienopyridines	Preoperative	High increase in risk	3–4
General	Aspirin	Before	No increase in the incidence or severity of hemorrhage during delivery	2
Vaginal delivery Cesarean	NSAIDs	?	No increased risk	2

* For carotid surgery, the only randomized placebo-controlled trial studied the pre- and postoperative administration (one single dose) of low-dose aspirin (75 mg), and pre-operative anticoagulation with heparin was neutralized by postoperative administration of protamine.