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HEMOCUE AB	WYETH

BUSINESS BRIEFS

- * **BAXTER INTERNATIONAL and the French biotechnology firm FLAMEL TECHNOLOGIES announced that they have entered into an agreement to formulate controlled release applications of blood clotting factor replacement therapies using Flamel's proprietary "Medusa" technology.** The partners will focus on developing longer-acting formulations with the objective of reducing the frequency of infusions required to treat blood clotting disorders in hemophilia. Pursuant to the agreement, Flamel will receive technology access fees totaling €2.5 million (\$3.6 million). Baxter will pay all development costs for the program and will control the exclusive right to negotiate a license to the "Medusa" platform.

"Medusa" uses biodegradable polymers to adsorb therapeutic large molecules through hydrophobic interaction to achieve a controlled release effect without loss of bioactivity. These polymers are robust over a wide pH range and can be stored as either stable liquid or stable dry forms that can be easily reconstituted in water.

- * In Japan, **the current prices of plasma** set by the Ministry of Health are ¥13,040 (\$135.66) per liter for plasma frozen within eight hour after collection, and ¥11,900 (\$123.80) for plasma frozen beyond that time frame.

- * Separately, **the Japanese Ministry of Health has projected that in 2009, albumin consumption will total 3,078,000 12.5 gram units (38.5 metric tons)**, about 5% lower than consumption in 2008. Recombinant albumin represents 1.4% of this volume. **IVIG consumption is expected to total 3.87 metric tons**, or 28.1 kilograms per million population. If these volume projections are realized, Japan's self-sufficiency level for albumin will be slightly over 60%, and over 90% for IVIG.

- * **BIOPURE has filed for Chapter 11 bankruptcy protection, and has entered into an agreement with OPK BIOTECH LLC to acquire most of its assets for \$2.6 million, pending approval of the U.S. bankruptcy court.** By last December the 25-year-old developer of bovine hemoglobin-based oxygen carrier products had terminated all but four of its full-time staff; a year earlier Biopure had 86 full-time employees. Its manufacturing facility in Cambridge was shut down last November, and its remaining inventory of a product for use in anemic dogs (*Oxyglobin*) was sold off in January.

Biopure lists assets of \$5.1 million and debts totaling \$2.7 million. The company has also received notice from the NASDAQ Stock Market that its common stock will be delisted. Biopure's fortunes have been battered by repeated refusals of the U.S. FDA to agree to allow the U.S. Naval Medical Research Center to evaluate the company's *Hemopure* "oxygen therapeutic" product in civilian trauma patients.

Announcement

The Marketing Research Bureau is pleased to announce the completion of a new report:

BLOOD COLLECTION & TRANSFUSION IN EUROPE & AFRICA - 2008

This study provides a quantitative and qualitative analysis of the blood collection, processing and transfusion markets in 35 countries in Western and Eastern Europe, and 21 African countries. It updates previously published studies on this subject. Topics of particular focus include:

- Organization of national blood transfusion services;
- Blood collections, component preparation and use;
- Automated collections of platelets and plasma;
- Leukocyte-reduction and other safety measures;
- Plasma for transfusion and fractionation. Volumes and virus inactivation;
- Blood bags market. Volumes, prices and major manufacturer's market shares;
- Apheresis machines. Market shares by major manufacturer;
- Price of blood products in the main countries;

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* **BAXTER INTERNATIONAL reports 13% growth in its BioScience unit revenues for the second quarter of 2009 (excluding the impact of foreign currency) with “strong double-digit gains” in revenues from its antibody therapies and other specialty plasma therapeutics.** Worldwide sales of non-immunoglobulin plasma protein therapies – including plasma-derived factor VIII, albumin, the alpha-1 proteinase inhibitor product *Aralast* and the anti-inhibitor coagulation complex *FEIBA* – gained 38%, excluding currency exchange effects. Recombinant factor VIII sales increased 11%, helped in part by differentiation with additional dosage forms and continuing conversion of U.S. customers in particular from *Recombinate* to the *ADVATE* product; conversion now stands at approximately 70%, versus 60% in the same quarter in 2008.

Antibody product sales, led by Baxter's *GAMMAGARD LIQUID* and *GAMMAGARD S/D* intravenous immunoglobulin products, grew 14% to \$344 million, again excluding foreign currency exchange. This strong performance is attributable to “strong global demand, favorable [product] mix and pricing,” according to a senior Baxter official.

- * **In a joint venture with CADILA PHARMACEUTICALS, located in Ahmedabad, India, U.S.-based StemCyte announced that a first-of-its-kind public umbilical cord blood (UCB) bank will be operational on the hospital premises of an Apollo Hospitals facility in Ahmedabad by this November.** To be named **StemCyte Therapeutics India Pvt. Ltd.**, this new entity will process and store 25,000 UCB units to meet the cord blood transplant needs of patients throughout the world, including **India**. Additionally, Apollo Hospitals, in collaboration with StemCyte, has announced plans to establish a stem cell research institute in Gujarat, to be completed by year end 2009.

The partners' initial investment to establish the Ahmedabad UCB bank is about \$16 million. **The cost for processing one unit of stem cells is estimated at Rs. 25,000-30,000 (\$520-\$625).** While work is in progress on the facility, the companies are already contacting Indian gynecologists and transplant physicians to alert them about this new stem cell resource. Parent company StemCyte says its U.S. facility has already matched six to seven stem cell units, including four that belong to Ahmedabad, two to Chennai and one to Pune. "With this kind of a response, we are quite positive that the Ahmedabad facility will be a success," a StemCyte official said.

- * **The SOUTH AFRICAN NATIONAL BLOOD SERVICE (SANBS) has published its current 2009 prices for whole blood and blood components applicable to "state patients."** These prices are as follows:

	<u>Rands</u>	<u>US Dollars</u>
Red Cell Concentrate	990.15	128.59
Red Cell Concentrate, Leukocyte Depleted	1,617.85	210.11
Red Cell Conc., Pediatric, Leukocyte Depleted	915.08	118.84
Platelet Concentrate, Single Donor Apheresis	5,738.62	745.27
Platelet Concentrate, Leukocyte Depleted, Pooled	5,252.31	682.12
Platelet Concentrate, Pediatric	1,258.97	163.50
Platelet Concentrate Pooled	4,171.62	541.77
Whole Blood	1,096.54	142.41
Whole Blood, Leukocyte Depleted	1,724.25	223.93
Whole Blood, Pediatric	915.08	118.84
Cryoprecipitate (Fibrinogen-rich)	559.66	72.68
Frozen Plasma, Cryo Poor, Donor-retested	639.03	82.99
Quarantine FFP, Infant	663.35	86.15
Fresh Frozen Plasma, Donor-retested	792.11	102.87

SANBS' blood component prices for private-sector patients are generally set 20% to 24% higher than these rates.

BLOOD & BIOTECHNOLOGY

Below are selected highlights from the XXII Congress of the International Society on Thrombosis and Haemostasis held this month in Boston:

- * **CSL BEHRING reports that it has prepared recombinant factor IX fusion proteins (rFIX-FPs) with cleavable linker peptides, and has expressed them in mammalian cell culture.** These rFIX-FPs are the result of genetic fusion of albumin to the C-terminus of FIX via short linker peptides derived from the FIX activation sequence and purified by chromatographic methods.

In a clotting assay these rFIX-FPs with a cleavable linker showed a 10- to 30-fold increase in molar specific clotting activity when compared to fusion proteins with non-cleavable linkers prepared as controls. The terminal half-life of these rFIX-FPs was also significantly increased relative to rFIX. Together, these findings suggest a potential role for albumin fusion technology in development of improved factor IX products.

- * **BIOGEN IDEC subsidiary SYNTONICS PHARMACEUTICALS has initiated a 10-subject Phase I clinical trial to evaluate the safety and pharmacokinetics of its recombinant Fc and factor IX fusion protein as a potential treatment for hemophilia B.** Unlike other Fc fusion proteins already approved for human use, the company's long-acting factor IX agent uses a monomeric rather than dimeric Fc portion of the IgG molecule. In laboratory testing, functional properties of rFIX-Fc and a licensed recombinant factor IX (WYETH's *BeneFIX*) were very similar. Both were activated by factor IXa, and affinity of both clotting factors was comparable in the presence of phospholipids.

This Phase I/IIa non-randomized, open label, uncontrolled trial is enrolling 10 previously treated hemophilia B patients, who receive a single intravenous dose. A total of six dose levels – 1, 5, 12.5, 25, 50 and 100 IU/kg – will be evaluated. Syntonix expects to complete this study by October.

- * Separately, **SYNTONICS PHARMACEUTICALS reportedly hopes to file an U.S. Investigational New Drug (IND) application by year-end 2009, asking the U.S. FDA for permission to evaluate the safety and pharmacokinetics of a new recombinant factor VIII:Fc monomer fusion protein.**

- * **An investigational long-acting recombinant factor IX (rFIX) variant developed by NOVO NORDISK achieved a nearly five-fold longer functional half-life than WY-ETH'S *BeneFIX* product in a pharmacokinetics study in minipigs.** In groups of six animals infused with 0.2 mg/kg (which corresponds to a prophylactic dose of 50 IU/kg), the average estimated clearance for the company's 40 kilodalton polyethylene glycol-conjugated rFIX (40K PEG-rFIX) was 1.7 ± 0.2 mL/h/kg versus 12 ± 1 mL/h/kg for *BeneFIX*. Estimated half-lives of the two products were 76 ± 3 hours and 16 ± 5 hours, respectively. In a separate study utilizing hemophilia B mice, the terminal half-life was estimated to be 41 hours and 17 hours for 40K PEG-rFIX and *BeneFIX*, respectively.

Using a two-compartment model to simulate repeated dosing of 0.2 mg/kg, Novo Nordisk scientists determined that once-weekly dosing of their 40K PEG-rFIX resulted in small fluctuations in peak and trough levels of rFIX than dosing every second day with *BeneFIX*. They concluded that once-weekly dosing with 40K PEG-rFIX is a feasible regimen for prophylaxis, with the goal of maintaining the factor IX level between 1% and 5% of normal.

- * Pursuing the principle that a human pattern of post-translational modifications, such as glycosylation, could result in improved function and a reduced risk of immunogenicity, **OCTAPHARMA has developed and described the first human cell line to express recombinant factor VIII.** This B domain-deleted factor VIII protein, produced in "HEK293F" cells, was found to be optimally sulphated and demonstrated a 60% higher affinity in binding to vWF in relation to other recombinant factor VIII products expressed in CHO or BHK cell lines.

Interactions with thrombin, Factor Xa, factor IXa, activated protein C and phospholipid were shown to be similar to those of plasma-derived factor VIII. Preclinical safety and efficacy, as well as *in vivo* survival results, were all "very satisfying," according to Octapharma collaborators based in Stockholm and Berlin. The company received U.S. FDA approval of an Investigational New Drug (IND) application for its human cell line-derived recombinant factor VIII in March 2009. Plans for an on-demand treatment study involving U.S. patients with severe hemophilia are underway, while a second trial evaluating prophylactic treatment with the product was initiated in **Russia** this March. Marketing authorizations for the product will be first submitted to the Russian health authorities in 2010, then to the **EMEA** in 2011, and finally to the **U.S. FDA** in 2013.

- * **At least three unique new factor IX variants with factor VIII bypassing activity may offer a new factor VIII inhibitor bypassing strategy,** according to **GERMAN RED CROSS** researchers who have developed these products and evaluated them in a hemophilic mouse model. Created using certain combined mutations, these factor IX variants were shown to provide 17% of normal clotting activity in the absence of factor VIII. This bypassing activity was also confirmed in plasma obtained from patients with high titers of inhibitor antibodies.

- * **In hemophilic mouse studies, Bayer HealthCare reported that its novel factor VIIa analogue “BAY86-6150” (Bay7) effectively reduced blood loss to levels comparable to that seen in normal mice at five to 10-fold lower doses than *NovoSeven*.** This finding coincides with *in vitro* data documenting superior clotting activity, for Bay7, also presented at this meeting. The half-life of Bay7, as measured by a soluble tissue factor-based prothrombin time, was shown to be approximately five-fold longer than that of *NovoSeven*.

Using a prophylactic treatment model, a dose of 1 mg/kg of *NovoSeven* protected about 50% of treated mice from a lateral vein injury inflicted at one hour post-dosing, while 1 mg/kg of Bay7 achieved comparable or better protection following tail vein transection inflicted at six hours post-dosing. “To our knowledge, this is the first demonstration of prolonged prophylactic efficacy of a novel rFVIIa in animal models,” Bayer collaborators asserted.

- * Using enzymatic “GlycoPEGylation” technology licensed from **NEOSE TECHNOLOGIES**, **NOVO NORDISK has developed and characterized the PEGylation profile of its novel long-acting recombinant factor VIIa (LA-rFVIIa).** An analysis of three pilot clinical batches of LA-rFVIIa yielded the following results:

<i>Batch</i>	<i>Non-PEG LA-rFVIIa (%)</i>	<i>Mono-PEG LA-rFVIIa (%)</i>	<i>Di-PEG LA-rFVIIa (%)</i>	<i>Product-related impurities</i>
#1	0.7	95.5	1.3	2.4
#2	0.4	92.3	4.2	3.1
#3	0.8	94.9	2.1	2.2

LA-rFVIIa is mainly mono-PEGylated, with minor amounts of non- and di-pegylated product. Peptide mapping confirmed that the primary structure of LA-rFVIIa is identical to rFVIIa, except for the generated PEGylated peptides. The investigators have concluded that the PEGylation process of rFVIIa generates a well-characterized and consistent product.

- * **NOVO NORDISK has also reported the results of a randomized, placebo-controlled dose-escalation trial to evaluate the safety and pharmacokinetics of its long-acting recombinant factor VIIa product (LA-rFVIIa).** Five cohorts of eight subjects were randomized to receive a dose of 12.5 to 100 µg/kg (n = 6) or placebo (n = 2). This first human trial of the company’s 40K-glycopegylated product follows studies in hemophilic mice that documented similar maximal efficacy of LA-rFVIIa and conventional recombinant factor VIIa (*NovoSeven*), and a significantly prolonged duration of action as measured by thromboelastography (TEG) and tail bleeding time. (*continued*)

In these human subjects, LA-rFVIIa has an overall mean plasma half-life of 15 hours, with a frequency of adverse events that was similar to placebo in all dosage groups. A pharmacological effect was apparent by a dose-dependent statistically significant decrease in the mean prothrombin time in all LA-rFVIIa groups compared to placebo. The investigators have concluded that this agent is a candidate for bleeding prophylaxis of patients with hemophilia and inhibitors.

- * **INSPIRATION BIOPHARMACEUTICALS has initiated multinational clinical studies to evaluate its investigational recombinant factor IX product for use in on-demand and prophylaxis use in patients with hemophilia B.** Subjects have been enrolled at participating centers in the U.S. and Israel, with other sites in the UK, France and Italy expected to initiate enrollment this month. Initially, 34 patients will be crossed over between the company's "IB1001" and WYETH'S *BeneFIX* recombinant factor IX product to evaluate pharmacokinetics, safety and thrombogenicity.

Fifty-five patients will then enroll in a prophylaxis protocol, while 20 others will receive on-demand therapy. Efficacy and safety in major surgical procedures will also be evaluated. "IB1001" has been extensively tested in rats, rabbits and normal and hemophilic dogs with "excellent" safety results. There was no evidence of hemostatic activation nor any differences between "IB1001" and *BeneFIX* or CSL BEHRING'S *Mononine* product at any dose. Inspiration reports that the circulating half-life and recovery profile for "IB1001" was similar to *BeneFIX* in preclinical evaluations. The Laguna Niguel, California-based biotechnology firm expects to complete enrollment in late 2009.

RESEARCH AND DEVELOPMENT

- * **A combination of rituximab and intravenous immunoglobulin (IVIG) improved kidney allograft function in all four patients suffering from chronic antibody-mediated rejection of their kidney allografts,** according to Swiss investigators reporting in the June 27 issue of *Transplantation*. Donor-specific antibodies were significantly reduced in two of the four subjects.

However, one patient experienced an acute rejection episode that occurred twelve months after this treatment, and another had severe lung toxicity possibly associated with rituximab administration. The authors concluded that combination rituximab-IVIG therapy may be a useful strategy for treatment of chronic antibody-mediated kidney allograft rejection, but further randomized multicenter studies are necessary to establish its efficacy and safety profile.

- * **Immunotherapy with intravenous immunoglobulin (IVIG) in conjunction with exchange transfusion importantly improved clinical outcome and reduced the need for liver transplantation in newborns with neonatal hemochromatosis (NH)**, according to investigators at Children's Memorial Hospital in Chicago. Sixteen infants with liver failure due to NH received high-dose IVIG; 13 also received exchange transfusion (ET) therapy. Their outcomes were compared with 131 historical control patients treated conventionally. Liver disease severity, estimated by prothrombin time, was similar in subjects receiving ET/IVIG and the historical controls, and medical therapy was equivalent with the exception of the ET/IVIG therapy.

Seventy-five percent (12 of 16) ET/IVIG subjects experienced a good outcome – defined as survival without liver transplantation – in contrast with a good outcome in just 17% (23 of 171) historical control patients. Four subjects died, including two following liver transplant and two without liver transplant. Survivors followed for more than one year are within normal limits for measures of growth, development and liver function, the authors report. Their findings appear in the June 26 online issue of the *Journal of Pediatrics*.

- * **In the context of Canada's publicly funded health care system, intravenous immunoglobulin (IVIG) may not be a cost-effective option for treatment of adults with persistent chronic immune thrombocytopenic purpura (ITP) in lieu of oral prednisone**, collaborators from McMaster University and St. Joseph's Healthcare concluded. Using a Markov model developed based on a systematic clinical and economic review and recommendations of **Canadian** clinical experts, the incremental costs of IVIG versus prednisone were estimated to be Can\$8,080 (\$7,300), while the estimated benefit in quality-adjusted life-years (QALYs) was 0.0071.

This yielded an incremental cost-effectiveness ratio of Can\$1.13 million (\$1.02 million) per QALY. The probability of IVIG being cost-effective was zero if the maximum willingness-to-pay (WTP) value for an additional QALY was below Can\$40,000, and was only 20% if the WTP was increased to Can\$100,000. Their analysis was published in *Clinical Therapeutics*.

- * **ProFibrix has initiated a Phase II clinical trial of its novel dry powder-form topical fibrinogen/thrombin tissue sealant, and reports the "successful treatment" of initial patients experiencing mild to moderate bleeding during liver surgery.** *FibroCaps* offers several major advantages over existing liquid tissue sealants, including readiness for immediate use and room temperature stability, according to the Leiden, **Netherlands**-based company.

ProFibrix expects to file an Investigation New Drug (IND) application for its *FibroCaps* product in the first half of 2010 and conduct a combined Phase II/III pivotal study in various surgical indications.

- * **In 26 patients with von Willebrand disease managed with long-term prophylaxis with LFB's *Wilfactin* plasma-derived von Willebrand factor concentrate, a significant reduction in bleeds was observed for every patient when compared with the prior period without long-term prophylaxis.** This prospective observational postmarketing study was implemented in **France** following marketing authorization for *Wilfactin* in 2004.

Indications for long-term prophylaxis were arthropathy prophylaxis, gastrointestinal bleeding, epistaxis, menorrhagia or psoas hematoma relapses. The average number of infusions was two per week, ranging from one to three weekly. For joint bleeds and gastrointestinal bleeds – the two main indications for prophylaxis – the median dose was (continued) 46-48 IU RCo/kg per infusion. In addition to the reduction in bleeds, overall tolerability was very good; none of the patients on long-term prophylaxis experienced drug-related adverse events. No vWF inhibitor development or thrombosis events were reported for any patient. “These findings confirm that [*Wilfactin*] may be efficient and safe for management of [a] long-term prophylaxis regimen, with an important impact on quality of life,” participating investigators concluded.

- * **Administration of human fibrinogen reduced postoperative blood loss by 32% and resulted in a significantly higher hemoglobin concentration 24 hours after coronary artery bypass graft (CABG) surgery,** according to researchers at Sahlgrenska University Hospital in Gothenburg, **Sweden**. Twenty CABG patients with low preoperative plasma fibrinogen levels (<3.8 g/L) were randomized to receive an infusion of 2 grams of **CSL BEHRING'S *Haemocomplettan P*** fibrinogen concentrate or no infusion before surgery. Patients who received fibrinogen supplementation experienced a mean of 565 ± 150 ml of postoperative blood loss versus 830 ± 268 ml in the control group (p = 0.01). Mean hemoglobin levels were 110 versus 98 grams per liter, respectively.

There was no evidence of postoperative hypercoagulability, but the investigators acknowledge that larger trials will be needed to ensure safety of the product in this setting. Interestingly, prophylactic fibrinogen concentrate infusion did not influence global postoperative hemostasis as assessed by thromboelastometry.

- * **The acute hemolysis rarely associated with administration of Rho(D) immune globulin products for treatment of immune thrombocytopenic purpura (ITP) cannot be experimentally reproduced using hemolysin assays to evaluate seven anti-D lots,** including four lots that had been implicated in acute hemolytic episodes. Despite testing of each lot against 73 different red blood cell specimens, no hemolysis endpoint was observed in any of the hemolysin assays.

U.S. FDA investigators, reporting in the June issue of *Transfusion*, concluded that these results did not support the acute hemolytic transfusion reaction (AHTR) model to explain rare hemolysis episodes in patients who receive anti-D products.

- * **The rate of inhibitor antibody development is significantly lower in previously untreated patients with hemophilia A who receive plasma-derived factor VIII products and those treated with recombinant factor VIII products**, according to a systematic review of 20 trials in the clinical literature. This gap persisted when isolating only patients with severe hemophilia A, as is shown in their findings:

	<i>Inhibitor rates with plasma-derived FVIII (95% CI)</i>	<i>Inhibitor rates with recombinant FVIII (95% CI)</i>
All trials	14.0 (9.7 to 20.0)	25.0 (20.4 to 30.8)
Prospective trials	9.3 (5.3 to 15.8)	22.8 (16.5 to 30.6)
Severe hemophilia A	17.0 (10.9 to 25.5)	32.1 (23.5 to 42.0)
High titer inhibitors	8.8 (4.7 to 15.9)	12.3 (9.9 to 16.7)

The Milan-based investigators proposed that prospective confirmation of these findings is warranted.

PLASMA FRACTIONATION NOTES

- * **India's Union Cabinet has approved a proposal to build a plasma fractionation facility capable of processing more than 150,000 liters of plasma annually, in the city of Chennai.** Located on the Bay of Bengal, this new Chennai plant is part of an ongoing national AIDS control program designed to ensure access of needy patients to plasma derivatives. Expected to open by or before 2012, the plant's output is intended to reduce **India's** dependence on imports of factors VIII and IX and generate savings on expenditure in foreign currencies.

PRODUCT SAFETY UPDATE

- * While mediating a 10% reduction in endogenous thrombin potential, a 30% decrease in peak thrombin and 20% to 35% loss of factor VIII, fibrinogen and factor XI activity, **methylene blue (MB) treatment of plasma was not associated with an altered rate of clot formation or an important change in clot firmness in relation to untreated plasma**, according to UK researchers at the National Blood Service. Surprisingly, clot firmness in MB-treated plasma exceeded conventional plasma by 20%, as assessed by rotational thromboelastography.

These findings were presented in a recent issue of *Transfusion*.

- * **Methylene blue (MB) treatment of plasma and cryoprecipitate does not appear to be associated with an altered rate of clot formation or an important change in clot firmness, despite known reductions in clotting factors, according to UK researchers at the National Blood Service in Cambridge.** MB treatment resulted in a 10% reduction in endogenous thrombin potential and 30% decrease in peak thrombin as well as a 20% to 35% loss of factor VIII, fibrinogen and factor XI activity.

Despite these effects, there was no impact on clot formation rate in relation to untreated plasma, and a 20% *increase* in clot firmness as assessed by rotational thromboelastography. The factor VIII and fibrinogen content of MB-treated cryo was reduced by 30% and 40% respectively, but this was not associated with altered clot time or rate of clot formation; there was an 8% decrease in clot firmness. This report appeared in a recent issue of *Transfusion*.

NEW PRODUCTS

- * **GE HEALTHCARE has introduced two new albumin and IgG depletion columns.** The “HiTrap Albumin & IgG Depletion” and “Albumin and IgG Depletion SpinTrap” pre-packed columns efficiently remove these two classes of proteins from human serum and plasma. Both columns deplete >95% of albumin and >90% of IgG by means of a mixture of anti-HSA Sepharose High Performance and Protein G Sepharose High Performance, in a medium consisting of highly cross-linked agarose beads with covalently immobilized affinity ligands. For more information, visit www.gehealthcare.com.
- * **r² Diagnostics (South Bend, IN) has launched its new “Thrombotek PSe Kit,” a clotting assay for quantification of Protein S activity in human plasma.** This test can be performed as a simple factor assay, and is suitable for manual and fully automated methods. With a lower limit of detection of 1% Protein S activity,

“Thrombotek PSe” offers excellent precision and linearity between 10% Protein S to 156% Protein S levels. For more information, call 1-574-288-4377 or visit www.r2diagnostics.com.

RECENT U. S. PATENTS

- * **Methods for Diagnosing and Evaluating Treatment of Blood Disorders. #7,514,229.** Assigned to The Board of Trustees of the Leland Stanford Junior University (Palo Alto, CA). A method of staging a blood disorder combining a hematologic sample from a patient suspected of having a blood disorder (from a group of seven disorders specified in the patent) with specific binding members that are sufficient to distinguish the distribution of hematopoietic stem and progenitor cell subsets between hematopoietic stem cells (HSC); common myeloid progenitors (CMP); megakaryocyte erythroid progenitors (MEP); granulocyte macrophage progenitors (GMP); and determining the distribution of hematopoietic stem and progenitor cells between said subsets; wherein the distribution of hematopoietic stem and progenitor cells is indicative of the phenotype of said blood disorder.

- * **Platelet-Derived Growth Factor Protection of Cardiac Myocardium. #7,514,261.** Assigned to Cornell Research Foundation, Inc. (Ithaca, NY). A culture comprising isolated bone marrow cells, PDGF AB, VEGF, heparin and cardiac myocytes derived therefrom, wherein the concentrations of PDGF, VEGF and FGF in the culture are sufficient to generate myocytes from the bone marrow cells.

- * **Chimeric Immunogens. #7,514,535.** Assigned to **Sanofi Pasteur Limited** (Toronto, Canada). A chimeric protein including a protein from parainfluenza virus (PIV) and a protein from respiratory syncytial virus (RSV), which comprises a PIV-3F protein or a fragment thereof having fusion activity linked to a RSV G protein or a fragment thereof having attachment activity.

- * **Methods of Inhibiting Amyloid Toxicity. #7,517,525.** Assigned to **Elan Pharmaceuticals, Inc.** (San Francisco, CA). A method of inhibiting amyloid toxicity in a human patient, comprising administering an effective dosage of one or more agents under conditions such that the one or more agents inhibits amyloid toxicity; wherein they are selected from an antibody and a molecule that comprises an antibody fragment; wherein the antibody or fragment binds to an α V β 1 integrin; and wherein the patient is suffering from an amyloidogenic disease.

- * **Glycosylation Engineering of Antibodies for Improving Antibody-Dependent Cellular Cytotoxicity. #7,517,670.** Assigned to **GlycArt Biotechnology AG** (Schlieren-Zürich, Switzerland). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, through a glycoengineering process described in the patent.

- * **Methods and Compositions for Concentrating Secreted Recombinant Protein. #7,517,671.** Assigned to **New England Biolabs, Inc.** (Ipswich, MA). A method of obtaining a concentrated preparation of a secreted recombinant protein, involving transforming host expression cells with a shuttle vector containing a DNA encoding a fusion protein comprising a chitin-binding domain and a target protein; expressing the fusion protein in the host expression cells and secreting the fusion protein therefrom; and binding the secreted fusion protein to a preparation of chitin by means of the chitin binding domain, so as to obtain a concentrated preparation of the secreted recombinant protein.

- * **Non-Neutralizing Anti-APC Antibodies. #7,517,965.** Assigned to **Chugai Seiyaku Kabushiki Kaisha** (Tokyo, Japan). An antibody against protein C or activated protein C (aPC), comprising the heavy chain complementarity determining regions (CDRs) 1, 2 and 3 having the sequences of SEQ ID NOs: 9, 10 and 11, respectively; and light chain CDRs specified in the patent.

- * **Factor VII or VIIa-Like Molecules. #7,517,974.** Assigned to **Bayer Healthcare LLC** (Tarrytown, NY). A nucleic acid comprising a nucleotide sequence which encodes a polypeptide comprising an amino acid sequence which (a) differs from the hFVII or hFVIIa sequence SEQ ID NO:1 in 1-15 amino acid residues and (b) comprises an introduced *in vivo* N-glycosylation site relative to SEQ ID NO:1, wherein the introduced *in vivo* N-glycosylation site comprises the substitution T106N.

- * **Antibody Immunization Therapy for Treatment of Atherosclerosis. #7,521,046.** Assigned to **BIOINVENT International AB** (Lund, Sweden). A purified or recombinant antibody or antigen binding fragment capable of binding oxidized fragments of apolipoprotein B100, wherein the antibody or antigen body fragment comprises a variable heavy region encoded by a nucleic acid sequence specified in the patent.

- * **Universal Red Blood Cells, Methods of Preparing Same, and Uses Thereof. #7,521,174.** Assigned to Albert Einstein College of Medicine of Yeshiva University (Bronx, NY). A method of preparing red blood cells involving a polyethylene glycol (PEG) attachment of a molecular weight of 5 K daltons, followed by chemical attachment of a PEG having a molecular weight of 20 K daltons.

- * **Enumeration of White Blood Cells. #7,521,143.** Assigned to **Hemocue AB** (Ängelholm, Sweden). A method for volumetric enumeration of white blood cells in a blood sample, involving use of a hemolysing agent and a staining agent to react with the sample, followed by irradiation, digital imaging and digital analysis.

- * **Method and Apparatus for Preparing an Acellular Red Blood Cell Substitute. #7,521,417.** Assigned to **Northfield Laboratories, Inc.** (Evanston, IL). A packaged pharmaceutical composition comprising a presterilized bag containing an aqueous solution of pyridoxylated and polymerized mammalian hemoglobin, with molecular weight distribution specified in the patent.

- * **Albumin Fusion Proteins. #7,521,424.** Assigned to **Human Genome Sciences, Inc.** (Rockville, MD). A method of treating memory loss in a patient, comprising administering an albumin fusion protein comprising two or tandemly oriented glucagon-like peptide-1 (GLP-1) polypeptides fused to albumin, said albumin fusion protein having an increased serum plasma half-life compared with GLP-1 that is not fused to said albumin or a fragment or variant thereof, and said albumin fusion protein has GLP-1 activity.

- * **Method of Generating and/or Increasing an Immune Response Against RSV. #7,524,627.** Assigned to **Pierre Fabre Medicament** (Boulogne-Billancourt, France). A method of generating and/or increasing an immunogenic response directed against respiratory syncytial virus (RSV) comprising administering an immunogenic peptide derived from the G protein of RSV subgroup A, wherein the immunogenic peptide comprises a sequence selected from a group of sequences specified in the patent.

- * **Multivalent Immunoglobulin-Based Bioactive Assemblies. #7,527,787.** Assigned to **IBC Pharmaceuticals, Inc.** (Morris Plains, NJ). A hexameric stably tethered structure comprising an IgG antibody attached to two AD2 moieties of SEQ ID NO:4 and four antigen-binding antibody fragments of the same or different IgG with each fragment attached to a DDD2 moiety of SEQ ID NO:2; the AD2 moieties bound to the DDD2 moieties.

- * **Preparation of Platelet Analogs. #7,531,357.** Assigned to **Bio-Rad Laboratories, Inc.** (Hercules, CA). A process for the manufacture of human platelet analogs for use as reference controls in automated blood cell analyzers, involving treating a single lot of red blood cells of a non-human vertebrate that have been reduced in size by extraction of cellular fluid and fixed with a fixing agent, to cause said single lot of cells to display by optical measurement a log normal size distribution simulating that of human platelets.

- * **Therapeutic Preparation of Very High Purity FVIIa and Method for Obtaining Same. #7,531,513.** Assigned to **Grifols, S.A.** (Barcelona, Spain). A therapeutic preparation of factor VIIa (FVIIa) having a purity of at least 6000 IU/mg of protein, wherein the FVIIa is purified from human plasma and wherein said preparation is free of proteins of non-human origin.

MEETINGS

September 11-13, 2009
22nd Annual European Haemophilia Consortium Conference 2009
 Reval Hotel Lietuva
 Vilnius, Lithuania
 Tel: +370 5 2101 436
 Website: www.ehc2009.eu

September 24-25, 2009
WFH Global Forum 2009
 Delta Montreal
 Montreal, Canada
 Tel: 514-875-7944
 Email: mbrookker@wfh.org
 Website: www.wfh.org

October 1-2, 2009
Advisory Committee on Blood, Safety and Availability
 Hilton Rockville Hotel
 1750 Rockville Pike
 Rockville, MD
 Tel: 301-468-1100
 Website: www.hhs.gov/ophs/bloodsafety/

October 24-27, 2009
AABB Annual Meeting
 The Convention and Visitors Bureau
 New Orleans, LA
 Tel: 301-907-6977
 Email: aabb@aabb.org
 Website: www.aabb.org

October 25, 2009
PPTA Business Forum
 Marriott New Orleans
 555 Canal Street
 New Orleans, LA
 Tel: 202-789-3100
 Email: ppta@pptaglobal.org
 Website: www.plasmaproteinforum.com

October 29-30, 2009
NHF 2009 Meeting
 San Francisco Convention Center
 San Francisco, CA
 Tel: 212-328-3700
 Email: handi@hemophilia.org
 Website: www.hemophilia.org

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