TABLE 5. Comparison of confirmed-positive bacterial contamination rates of apheresis and WBP-derived samples utilizing the PLT-rich plasma (PRP) or buffy coat (BC) methods[7,16,23,24]

	WBPs				Apheresis PLTs		
Study	PLT pool size	PLT preparation	Products tested	Rate per million (95% CI)	Products tested	Rate per million (95% CI)	OR (95% CI)
This report	5	PRP	20,725	965 (542-1,388)	431,490	167 (128-205)	5.8 (3.5-9.5)
Kleinman et al.[7]	1	PRP	13,579	74 (0-218)	21,914	46 (0-135)	NS
Yomtovian et al.[17]	5	PRP	12,961	2,392 (1,550-3,234)	15,493	452 (117-787)	5.3 (2.3-12.0)
Schrezenmeier et al.[23]	5	BC	22,044	726 (370-1,081)	15,198	855 (390-1,320)	NS
Murphy et al.[24]	5	BC	30,407	329 (125-533)	12,823	312 (6-618)	NS
de Korte et al.[16]	5	BC	6,749	1,322 (397-2,519)	4,963	2,418 (1050-3,786)	NS

NS = not significant, $p \geq 0.05$.

plateletpheresis collections were assessed utilizing a standard protocol, the relative contamination rates are informative. Our finding that individual WBPs are likely contaminated at similar rates as plateletpheresis collections is substantiated by the report of Kleinman and colleagues,[7] who tested individual WBP and plateletpheresis products using the BacT/ALERT system and by Yomtovian and coworkers who tested pooled WBP and plateletpheresis products at issue using plate cultures[17] (Table 5). In all three cases, the WBPs were manufactured using the PLT-rich plasma method. These results are in contrast to those reported from Europe, where WBPs are produced using the buffy coat technique: In these reports, prestorage-pooled buffy coat PLTs have the same confirmed-positive contamination rate as similarly tested plateletpheresis (Table 5).[16,23,24] This difference has been ascribed to the overnight hold process in the manufacture of buffy coat PLTs, which may allow some bacteria to be inactivated by white cells before leukoreduction.[24]

We remain aware of the continued, residual risk of sepsis from bacterially contaminated WBP units. In 2007, the American Red Cross distributed 381,884, single WBP components and received one report of a severe septic reaction to a single WBP unit transfused to an infant, in which coagulase-negative *Staphylococcus* was implicated after pulsed-field gel electrophoresis demonstrated identical isolates from both the patient and residual product. We received no reports of septic reactions to PSPs in 2006 or 2007, although a false-negative QC culture result in 1 of 543 PSPs tested was detected by a transfusion service using a culture-based point-of-issue test. In this case, the PSP unit was transfused on Day 4 without reaction, but a 1- to 2-mL sample of the PSPs collected at the time of issue grew coagulase-negative *Staphylococcus* on plate culture at a titer of 2×10^4 colony-forming units per mL (M. Jacobs and R. Yomtovian, personal communication, 2008).[16]

In summary, the successful implementation of Acrodose PL PLTs by the American Red Cross now provides an alternative source of QC-cultured PLTs for transfusion. PSPs undoubtedly present lower bacterial risk to patients than WBPs that are pooled at the point of issue and tested with non–FDA-approved surrogate tests, such as pH or glucose content. Ongoing hemovigilance for septic transfusion reactions, however, will be required to document the relative safety of PSPs considering their approximately 5.8-fold higher rate in detectable contamination compared to that of plateletpheresis.

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医薬部外品　研究報告　調査報告書
化粧品

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一般的名称	①乾燥抗HBs人免疫グロブリン ②ポリエチレングリコール処理抗HBs人免疫グロブリン		研究報告の公表状況	CDC/MMWR 2009; 58(5): 105-109	公表国 アメリカ	
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研究報告の概要

カリフォルニア州において Confidential Morbidity Reports (CMR) のデータの入手が常に可能になった 1995 年以降に収集された、2000-2007 年の間のコクシジオイデス症の報告症例数および入院数の増加、ならびに最も高い罹患率について報告する。
コクシジオイデス症は、土壌中の真菌である Coccidioides immitis または Coccidioides posadasii の浮遊胞子を吸い込むことによって感染する。1995-2000 年の間、カリフォルニア州でのコクシジオイデス症の報告症例数は、人口 100,000 人当たりで毎年平均 2.5 であった。しかし、2000-2006 年の報告数は 3 倍を超え、人口 100,000 人当たり 2.4 から 8.0 に増加した。この増加を特徴付けるため、カリフォルニア州公衆衛生局は 2000-2007 年の症例および入院データ、ならびに 2008 年の予備的症例報告データを分析した。その結果の示すところによれば、2000-2006 年の間、カリフォルニア州におけるコクシジオイデス症の報告症例数および入院数は毎年増加しており、2007 年に減少した。2000-2007 年の間の年間症例数は Kern 郡が最も高く（人口 100,000 人当たり 150.0）、入院率は非ヒスパニックの黒人が最も高く、人口 100,000 人当たりで 3.0 から 7.5 に増加した。
カリフォルニア州のコクシジオイデス症の増加は隣のアリゾナ州および米国全体に観察された増加と類似している。アリゾナ州は毎年米国のコクシジオイデス症例全体の約 60%を報告しており、1999 年の 1,812 症例（人口 100,000 人当たり 37）から 2006 年の 5,535 症例（人口 100,000 人当たり 91）と実質的な増加を報告した。米国全体では、コクシジオイデス症報告症例数は 1996 年の 1,697 症例（人口 100,000 人当たり 0.64）から 2006 年の 8,917 症例（人口 100,000 人当たり 6.79）に増加した。コクシジオイデス症報告数が最近増加している理由については、十分に解明されていない。

報告企業の意見	今後の対応
コクシジオイデス症はカルフォルニア州で最近３倍以上に大幅増加し、米国全体においても同じ傾向にあることについての報告である。 コクシジオイデス・イミチスは、コクシジオイデス症の原因となる真菌であり、宿主の体内で観察される最も小さな単位は2～5μmの内生胞子である。万一、原料血漿にコクシジオイデス・イミチスが混入したとしても、除菌ろ過等の製造工程にて十分に除去されると考えている。	本報告は本剤の安全性に影響を与えないと考えるので、特段の措置はとらない。

使用上の注意記載状況・その他参考事項等

代表として静注用ヘブスブリンーIH の記載を示す。
2. 重要な基本的注意
(1) 本剤の原材料となる血液については、HBs抗原、抗HCV抗体、抗HIV-1抗体、抗HIV-2抗体陰性で、かつALT（GPT）値でスクリーニングを実施している。更に、プールした試験血漿については、HIV-1、HBV及びHCVについて核酸増幅検査(NAT)を実施し、適合した血漿を本剤の製造に使用しているが、当該NATの検出限界以下のウイルスが混入している可能性が常に存在する。本剤は、以上の検査に適合した高力価の抗HBs抗体を含有する血漿を原料として、Cohnの低温エタノール分画で得た画分からポリエチレングリコール4000処理、DEAEセファデックス処理等により抗HBs人免疫グロブリンを濃縮・精製した製剤であり、ウイルス不活化・除去を目的として、製造工程において60℃、10時間の液状加熱処理及びウイルス除去膜によるろ過処理を施しているが、投与に際しては、次の点に十分注意すること。

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Increase in Coccidioidomycosis --- California, 2000--2007

Coccidioidomycosis is an infection resulting from inhalation of airborne spores of Coccidioides immitis or Coccidioides posadasii, soil-dwelling fungi endemic to California's San Joaquin Valley, southern regions of Arizona, Utah, Nevada, and New Mexico; western Texas; and regions of Mexico and Central and South America (1). Of an estimated 150,000 new infections annually in the United States (2), approximately 60% are asymptomatic (1). Patients with symptoms usually experience a self-limited influenza-like illness (ILI), although some develop severe pneumonia. Fewer than 1% of patients develop disseminated disease. Infection usually produces immunity to reinfection. During 1995--2000, the number of reported coccidioidomycosis cases in California averaged 2.5 per 100,000 population annually. However, from 2000 to 2006, the incidence rate more than tripled, increasing from 2.4 to 8.0 per 100,000 population. To characterize this increase, the California Department of Public Health (CDPH) analyzed case and hospitalization data for the period 2000--2007 and preliminary case report data for 2008. The results indicated that, during 2000--2006, the number of reported cases and hospitalizations for coccidioidomycosis in California increased each year, before decreasing in 2007. Annual incidence during 2000--2007 was highest in Kern County (150.0 cases per 100,000 population), and the hospitalization rate was highest among non-Hispanic blacks, increasing from 3.0 to 7.5 per 100,000 population. Health-care providers should maintain heightened suspicion for coccidioidomycosis in patients who live or have traveled in areas where the disease is endemic and who have signs of ILI, pneumonia, or disseminated infection.

Coccidioidomycosis is a reportable disease in California, although laboratories are not required to report. During 1991--1995, California experienced a large epidemic of coccidioidomycosis in the San Joaquin Valley; since 1995, cases of coccidioidomycosis have been reported consistently to local health departments in California using Confidential Morbidity Reports (CMRs). For the analysis summarized in this report, CDPH reviewed case and hospitalization data for the period 2000--2007 using CMRs and California Patient Discharge Data Set (CPDDS) data. Preliminary CMR case data for 2008 also were analyzed. CMRs include data on the patient's county of residence, sex, and dates of birth, illness onset, diagnosis, and case report. CPDDS data include inpatient discharge diagnoses from all California nonfederal hospitals. Cases with codes for coccidioidomycosis (114--114.5 and 114.9) from the *International Classification of Diseases, Ninth Edition* were selected. Duplicate records were removed so that the CMR data set retained only the first report of a case and the CPDDS retained only the first report of a patient's hospitalization. For the 3% of reported CMR cases with no date of illness onset or diagnosis, year of illness onset was presumed to be year of case report. CMR data were used to calculate incidence rates of reported cases overall and by age, sex, region, and county. Because 34% of reported CMR cases had missing data on race, incidence rates by race were not calculated. CPDDS data were used to calculate rates of first hospitalization overall and by age, sex, race/ethnicity, region, and county. California Department of Finance population projections were used for denominators (*3*). Negative binomial regression was used to test for statistical significance of change in rates of reported cases and hospitalizations during 2000--2006, the period of annual increase in reported cases and hospitalizations. Fatality rates among hospitalized patients were calculated by using CPDDS data for 2000--2007.

After remaining stable since 1995, reported coccidioidomycosis cases in California increased from 816 in 2000 (incidence rate: 2.4 per 100,000 population) to 2,981 in 2006 (8.0 per 100,000 population) ($p<0.001$) (Figure 1), before decreasing in 2007 to 2,791 cases (7.4 per 100,000 population). Preliminary 2008 CMR data indicated that 1,718 cases were reported in California during January 1--December 6, 2008, compared with 2,210 and 2,426 cases reported during the same period in 2006 and 2007, respectively.

During 2000--2007, estimated average annual incidence was highest among adults aged 40--49 years (3,518 cases [8.0 per 100,000 population]) versus other age groups (Table). A total of 10,909 (65%) cases were reported in male patients, for an average annual rate of 7.6 per 100,000 population, compared with 5,848 cases in females (4.0 per 100,000 population) (Table). The greatest incidence occurred in the San Joaquin Valley region, where coccidioidomycosis is endemic. A total of 12,855 (76%) of California's 16,970 cases were reported from the San Joaquin Valley during 2000--2007. Reported cases from this region increased from 490 (14.7 per 100,000 population) in 2000 to 2,135 (53.9 per 100,000 population) in 2007. Within the region, Kern County reported the highest incidence every year. Rates of reported cases in Kern County averaged 150.0 per 100,000 population during 2000--2007 (Figure 2), peaking in 2004 at 195.3 per 100,000 population.

In California, coccidioidomycosis cases requiring hospitalization increased from 611 in 2000 (1.8 per 100,000 population) to 1,587 in 2006 (4.3 per 100,000 population) ($p<0.001$), before decreasing to 1,368 (3.6 per 100,000 population) in 2007 (Figure 1). Hospitalizations for coccidioidomycosis were highest among persons aged 60--79 years, averaging 5.8 per 100,000 population during 2000--2007 (Table). By race/ethnicity, hospitalizations were highest among non-Hispanic blacks, compared with non-Hispanic whites, Hispanics, and Asians/Pacific Islanders. From 2000 to 2007, hospitalizations among non-Hispanic blacks increased from 66 (3.0 per 100,000 population) to 169 (7.5 per 100,000 population). Hospitalizations among non-Hispanic whites increased from 297 (1.9 per 100,000 population) in 2000 to 570 (3.5 per 100,000 population) in 2007; hospitalizations among Hispanics increased from 182 (1.6 per 100,000 population) to 485 (3.6 per 100,000 population), and hospitalizations among Asians/Pacific Islanders increased from 36 (0.9 per 100,000 population) to 86 (1.9 per 100,000 population).

By geographic region, hospitalizations for coccidioidomycosis in the San Joaquin Valley increased from 230 (6.9 per 100,000 population) in 2000 to 701 (17.7 per 100,000 population) in 2007. Within the region, Kern County reported the highest hospitalization rates, increasing from 121 (18.2 per 100,000 population) in 2000 to 285 (34.9 per 100,000 population) in 2007, and peaking in 2005 at 353 hospitalizations (45.8 per 100,000 population). Overall in California, during 2000--2007, a total of 752 (8.7%) of the 8,657 persons hospitalized for coccidioidomycosis died.

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Editorial Note:

This report describes increases in reported coccidioidomycosis cases and hospitalizations during 2000--2007 and the highest incidence rate in California since 1995, the first year that CMR data were available consistently. The number of reported cases and hospitalizations decreased in 2007, and preliminary data indicate those decreases might have continued in 2008. However, rates of coccidioidomycosis in California remain substantially higher than during 1995--2000. These increased rates likely are real, rather than surveillance artifact, because no major changes in diagnosis or reporting of coccidioidomycosis in California occurred before or during the period studied.

Increases in coccidioidomycosis in California are similar to those observed in neighboring Arizona and in the United States overall. Arizona, which annually reports approximately 60% of all coccidioidomycosis cases in the United States, reported a substantial increase in coccidioidomycosis from 1,812 cases (37 per 100,000 population) in 1999 to 5,535 cases (91 per 100,000 population) in 2006 (*4*). In the United States overall, the number of reported coccidioidomycosis cases increased from 1,697 (0.64 per 100,000 population) in 1996 to 8,917 (6.79 per 100,000 population in 2006) (*5*). Reasons for these recent increases in reported coccidioidomycosis are not fully understood. Some previous increases have been associated with local environmental and climatic variations (*6*). Other hypothesized causes include aerosolization of spores caused by soil disturbance during periods of increased construction activity (*4*), growing numbers of persons who are immunocompromised or have other risk factors for severe disease (*7*), and immigration of previously unexposed persons from areas where coccidioidomycosis is not endemic (*2*). Recent increases in coccidioidomycosis in California are partially attributable to several hundred cases reported from two San Joaquin Valley prisons (*8*) with inmates from areas where the disease is not endemic. Multiple clusters also have been reported at California military bases, where personnel often have intensive dust exposure (*9*). Such exposure is hypothesized to increase the risk for infection; local outbreaks of coccidioidomycosis have been noted after dust storms (*1*).

Coccidioidomycosis hospitalization rates in California were highest among persons aged 60--79 years, which is consistent with previous reports that older age might be a risk factor for severe coccidioidomycosis (*7*).