Table 4
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (36 PATIENTS) - DOSE 1 DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	8 (22.2%)	2 (5.6%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		9 (25.0%)
SORENESS	8 (22.2%)	2 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		9 (25.0%)
STIFFNESS/TIGHTNESS	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
ECCHYMOSIS	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
SYSTEMIC	5 (13.9%)	5 (13.9%)	5 (13.9%)	4 (11.1%)	0 (0.0%)	0 (0.0%)		12 (33.3%)
WHOLE BODY/GENERAL	4 (11.1%)	3 (8.3%)	2 (5.6%)	2 (5.6%)	0 (0.0%)	0 (0.0%)		8 (22.2%)
FEVER (TEMP. NOT REPORTED)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
FATIGUE/WEAKNESS	2 (5.6%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (8.3%)
HEADACHE	1 (2.8%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)		3 (8.3%)
ACHINESS	0 (0.0%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
INTEGUMENTARY SYSTEM	1 (2.8%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)		2 (5.6%)
PRURITIS/ITCHING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)		1 (2.8%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (36 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
RASH, NOS	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	2 (5.6%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	2 (5.6%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
COUGH	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
BACK PAIN	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
DIGESTIVE SYSTEM	1 (2.8%)	2 (5.6%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	4 (11.1%)
DYSPEPSIA/HEARTBURN	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
DIARRHEA	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.6%)
NAUSEA	1 (2.8%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	2 (5.6%)
NERVOUS SYSTEM	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
VERTIGO/DIZZINESS	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)

Table 4 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (36 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	10 (27.8%)	7 (19.4%)	6 (16.7%)	4 (11.1%)	0 (0.0%)	0 (0.0%)	17 (47.2%)
PERSONS WITH NO COMPLAINTS	26 (72.2%)	29 (80.6%)	30 (83.3%)	32 (88.9%)	0 (0.0%)	0 (0.0%)	19 (52.8%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

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Table 4 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (35 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	8 (25.0%)	1 (3.1%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (28.1%)
PAIN	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
SORENESS	6 (18.8%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (18.8%)
TENDERNESS	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
SYSTEMIC	3 (9.4%)	2 (6.3%)	3 (9.4%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	9 (28.1%)
WHOLE BODY/GENERAL	3 (9.4%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
FATIGUE/WEAKNESS	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
HEADACHE	2 (6.3%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (9.4%)
INTEGUMENTARY SYSTEM	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
RASH, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
OTHER	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	2 (6.3%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (35 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
RHINITIS	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
MUSCULOSKELETAL	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
ARTHRALGIA, MONOARTICULAR	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
PERSONS WITH COMPLAINTS	9 (28.1%)	3 (9.4%)	5 (15.6%)	2 (6.3%)	0 (0.0%)	0 (0.0%)		15 (46.9%)
PERSONS WITH NO COMPLAINTS	23 (71.9%)	29 (90.6%)	27 (84.4%)	30 (93.8%)	0 (0.0%)	0 (0.0%)		17 (53.1%)
PERSONS WITH NO DATA	3 (8.6%)	3 (8.6%)	3 (8.6%)	3 (8.6%)	0 (0.0%)	0 (0.0%)		3 (8.6%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (35 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	5 (14.7%)	2 (5.9%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	7 (20.6%)
SORENESS	4 (11.8%)	2 (5.9%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	6 (17.6%)
NODULE FORMATION	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
SYSTEMIC	5 (14.7%)	4 (11.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (20.6%)
WHOLE BODY/GENERAL	3 (8.8%)	3 (8.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (17.6%)
SWEATING	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
FATIGUE/WEAKNESS	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
MALAISE	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
HEADACHE	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.9%)
ACHINESS	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
CHEST TIGHTNESS	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)
INTEGUMENTARY SYSTEM	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (35 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
URTICARIA/HIVES	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.9%)
MUSCULOSKELETAL	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.9%)
NECK STIFFNESS	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.9%)
DIGESTIVE SYSTEM	0 (0.0%)	2 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (5.9%)
DIARRHEA	0 (0.0%)	2 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (5.9%)
NAUSEA	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.9%)
VOMITING	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.9%)
PERSONS WITH COMPLAINTS	8 (23.5%)	6 (17.6%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)		10 (29.4%)
PERSONS WITH NO COMPLAINTS	26 (76.5%)	28 (82.4%)	33 (97.1%)	33 (97.1%)	0 (0.0%)	0 (0.0%)		24 (70.6%)
PERSONS WITH NO DATA	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)		1 (2.9%)

Table 5
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (36 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	30 (88.2%)	32 (91.4%)	34 (97.1%)	34 (97.1%)	0 (0.0%)	0 (0.0%)			28 (80.0%)
99 - 99.9	4 (11.8%)	3 (8.6%)	1 (2.9%)	1 (2.9%)	0 (0.0%)	0 (0.0%)			7 (20.0%)
TEMPERATURE TAKEN	34 (94.4%)	35 (97.2%)	35 (97.2%)	35 (97.2%)	0 (0.0%)	0 (0.0%)			35 (97.2%)
TEMPERATURE NOT TAKEN	2 (5.6%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	36 (100.0%)	36 (100.0%)			1 (2.8%)

Table 5 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (36 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (3.3%)	1 (3.2%)	1 (3.4%)	1 (3.1%)	0 (0.0%)	0 (0.0%)			1 (3.1%)
< 99	25 (83.3%)	28 (90.3%)	26 (89.7%)	27 (84.4%)	1 (100.0%)	0 (0.0%)			23 (71.9%)
99 - 99.9	2 (6.7%)	1 (3.2%)	2 (6.9%)	4 (12.5%)	0 (0.0%)	0 (0.0%)			6 (18.8%)
100 - 100.9	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (3.1%)
101 - 101.9	1 (3.3%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (3.1%)
TEMPERATURE TAKEN	30 (83.3%)	31 (86.1%)	29 (80.6%)	32 (88.9%)	1 (2.8%)	0 (0.0%)			32 (88.9%)
TEMPERATURE NOT TAKEN	6 (16.7%)	5 (13.9%)	7 (19.4%)	4 (11.1%)	35 (97.2%)	36 (100.0%)			4 (11.1%)

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Table 5 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (36 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	6 (18.8%)	6 (18.8%)	6 (18.2%)	6 (18.8%)	0 (0.0%)	0 (0.0%)		6 (18.2%)
< 99	23 (71.9%)	23 (71.9%)	25 (75.8%)	25 (78.1%)	0 (0.0%)	0 (0.0%)		21 (63.6%)
99 - 99.9	3 (9.4%)	2 (6.3%)	2 (6.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)		5 (15.2%)
100 - 100.9	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.0%)
TEMPERATURE TAKEN	32 (88.9%)	32 (88.9%)	33 (91.7%)	32 (88.9%)	0 (0.0%)	0 (0.0%)		33 (91.7%)
TEMPERATURE NOT TAKEN	4 (11.1%)	4 (11.1%)	3 (8.3%)	4 (11.1%)	36 (100.0%)	36 (100.0%)		3 (8.3%)

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Table 6

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (37 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	28 (77.8%)	33 (91.7%)	31 (86.1%)	32 (94.1%)	0 (0.0%)	0 (0.0%)			26 (72.2%)
99 - 99.9	8 (22.2%)	3 (8.3%)	5 (13.9%)	2 (5.9%)	0 (0.0%)	0 (0.0%)			10 (27.8%)
TEMPERATURE TAKEN	36 (97.3%)	36 (97.3%)	36 (97.3%)	34 (91.9%)	0 (0.0%)	0 (0.0%)			36 (97.3%)
TEMPERATURE NOT TAKEN	1 (2.7%)	1 (2.7%)	1 (2.7%)	3 (8.1%)	37 (100.0%)	37 (100.0%)			1 (2.7%)

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Table 6 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (37 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	21 (80.8%)	24 (96.0%)	21 (87.5%)	24 (88.9%)	0 (0.0%)	0 (0.0%)			22 (75.9%)
99 - 99.9	5 (19.2%)	1 (4.0%)	3 (12.5%)	3 (11.1%)	0 (0.0%)	0 (0.0%)			7 (24.1%)
TEMPERATURE TAKEN	26 (70.3%)	25 (67.6%)	24 (64.9%)	27 (73.0%)	0 (0.0%)	0 (0.0%)			29 (78.4%)
TEMPERATURE NOT TAKEN	11 (29.7%)	12 (32.4%)	13 (35.1%)	10 (27.0%)	37 (100.0%)	37 (100.0%)			8 (21.6%)

Table 6 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (37 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (2.9%)	1 (2.9%)	1 (3.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)			1 (2.9%)
< 99	27 (79.4%)	31 (91.2%)	30 (90.9%)	28 (84.8%)	0 (0.0%)	0 (0.0%)			23 (67.6%)
99 - 99.9	5 (14.7%)	2 (5.9%)	2 (6.1%)	4 (12.1%)	0 (0.0%)	0 (0.0%)			9 (26.5%)
100 - 100.9	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (2.9%)
TEMPERATURE TAKEN	34 (91.9%)	34 (91.9%)	33 (89.2%)	33 (89.2%)	0 (0.0%)	0 (0.0%)			34 (91.9%)
TEMPERATURE NOT TAKEN	3 (8.1%)	3 (8.1%)	4 (10.8%)	4 (10.8%)	37 (100.0%)	37 (100.0%)			3 (8.1%)

Table 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (36 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	29 (80.6%)	34 (94.4%)	33 (94.3%)	33 (94.3%)	0 (0.0%)	0 (0.0%)			28 (77.8%)
99 - 99.9	6 (16.7%)	2 (5.6%)	1 (2.9%)	2 (5.7%)	0 (0.0%)	0 (0.0%)			6 (16.7%)
100 - 100.9	1 (2.8%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			2 (5.6%)
TEMPERATURE TAKEN	36 (100.0%)	36 (100.0%)	35 (97.2%)	35 (97.2%)	0 (0.0%)	0 (0.0%)			36 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)	36 (100.0%)	36 (100.0%)			0 (0.0%)

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (35 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	27 (93.1%)	27 (96.4%)	28 (93.3%)	26 (89.7%)	0 (0.0%)	0 (0.0%)			26 (83.9%)
99 - 99.9	2 (6.9%)	1 (3.6%)	1 (3.3%)	2 (6.9%)	0 (0.0%)	0 (0.0%)			4 (12.9%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (3.3%)	1 (3.4%)	0 (0.0%)	0 (0.0%)			1 (3.2%)
TEMPERATURE TAKEN	29 (82.9%)	28 (80.0%)	30 (85.7%)	29 (82.9%)	0 (0.0%)	0 (0.0%)			31 (88.6%)
TEMPERATURE NOT TAKEN	6 (17.1%)	7 (20.0%)	5 (14.3%)	6 (17.1%)	35 (100.0%)	35 (100.0%)			4 (11.4%)

00283

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0798
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (35 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (3.4%)	1 (3.2%)	1 (3.2%)	1 (3.1%)	0 (0.0%)	0 (0.0%)			1 (3.1%)
< 99	24 (82.8%)	30 (96.8%)	29 (93.5%)	30 (93.8%)	0 (0.0%)	0 (0.0%)			26 (81.3%)
99 - 99.9	3 (10.3%)	0 (0.0%)	1 (3.2%)	1 (3.1%)	0 (0.0%)	0 (0.0%)			4 (12.5%)
100 - 100.9	1 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (3.1%)
TEMPERATURE TAKEN	29 (82.9%)	31 (88.6%)	31 (88.6%)	32 (91.4%)	0 (0.0%)	0 (0.0%)			32 (91.4%)
TEMPERATURE NOT TAKEN	6 (17.1%)	4 (11.4%)	4 (11.4%)	3 (8.6%)	35 (100.0%)	35 (100.0%)			3 (8.6%)

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Anti-HBs Responses to Vaccination with a Human Hepatitis B Vaccine Made by Recombinant DNA Technology in Yeast

In the United States, the currently licensed vaccine against hepatitis B virus (HEPTAVAX-B®; Merck Sharp & Dohme, West Point, Pa) consists of hepatitis B surface antigen (HBsAg) that is purified from the plasma of chronically infected humans. Antibodies to the group *a* determinant of this complex antigen effectively neutralize the various subtypes of hepatitis B virus (HBV), as shown in a number of controlled clinical trials [1–3]. Despite overwhelming evidence that documents the efficacy of this vaccine, widespread acceptance by those who are at greatest risk of contracting hepatitis B has been less than expected because of a number of unrelated factors. The plasma-derived vaccine is expensive to prepare. A number of physical and chemical inactivation steps are used in purification, and extensive safety testings are mandated by the Food and Drug Administration in laboratory animals, cell cultures, and chimpanzees before the product can be marketed. In addition, there are of necessity batch-to-batch variations in human source material. These problems would have been surmountable in the marketing of this vaccine were it not for two recent events that made potential vaccine candidates overly cautious about accepting this new product: the increased incidence of Guillain-Barré syndrome that followed administration of the swine influenza vaccine in 1976 and the emergence of AIDS in the homosexual population. The latter problem was particularly relevant because HEPTAVAX-B is a plasma-derived product obtained from HBsAg-positive individuals, some of whom are in high-risk groups for AIDS. This raised the question whether AIDS might be transmitted to recipients of this vaccine. Unfortunately, despite numerous studies [4, 5] that eventually have refuted this hypothesis (on the basis of the susceptibility of retroviruses to inactivation by the physical and chemical steps used in producing the vaccine and by the lack of cases of AIDs or antibody seroconversions to human T lymphotropic virus type III observed among vaccinees at low risk of exposure to this disease), many members of groups at risk of contracting hepatitis B have been reluctant to accept this vaccine.

Because of these problems, alternate sources of vaccine are being developed. Among the first to become available for human trials was a 25,000–30,000 molecular weight HBsAg polypeptide derived by disrupting the intact 22-nm HBsAg particle with a nonionic detergent [6]. Immunogenicity of this product was superior to that of the human HBsAg source from which it was prepared, especially during the initial stages of antibody development. More recently a number of other vaccines that do not depend on human plasma as their source of HBsAg have been produced [7]. These include chemically synthesized peptides from several antigenic domains of the HBV, products of recombinant DNA technology, and live vaccinia virus recombinants containing the HBsAg gene.

In this paper we report one-year follow-up data on the immunogenicity and reactogenicity of a nonglycosylated HBsAg hepatitis B vaccine, subtype adw, made by recombinant DNA technology (Merck). The vaccine, prepared in the yeast *Saccharomyces cerevisiae* (strain 2150-2-3) [8, 9] was administered in three different doses (5, 10, and 20 μg) to an adult at-risk population.

Subjects and Methods

After screening 359 Emergency Medical Service personnel in Houston, 105 adult men (median age, 29 years; range, 22–40), determined by RIA or enzyme immunoassay to be free of any seromarkers of hepatitis B infection (Abbott Laboratories, North Chicago, Ill), were admitted to the study. All had antibody to HBsAg (anti-HBs) sample-to-negative-mean (S/N) ratios ≤1.4, levels of antibody to hepatitis B core antigen (anti-HBc) ≤39% inhibition, and HBsAg S/N ratios ≤1.2. These values are substantially below the cutoff levels endorsed by the manufacturers. In addition, each participant was required to have serum levels of liver enzyme (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) ≤50 IU/liter, as determined by the Beckman System TR enzyme autoanalyzer (Beckman Instruments, Palo Alto, Calif). Participants were in good health at the time of enrollment, had not been previously vaccinated against hepatitis B, and had signed informed consent releases. The study was approved by the Baylor College of Medicine Human Investigations Committee.

The 105 volunteers were weight matched within 4.5 kg [9a] into three groups of 35. Each member of each group received 5, 10, or 20 μg of an alum-adsorbed, DNA recombinant hepatitis B vaccine (lot no. 974/CK-446) containing 20 μg of HBsAg/ml. The vaccine was purified from

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We thank Dorothy Heiberg for her expert assistance in following the subjects and performing the analyses; the Emergency Medical Service division of the Houston Fire Department for their constructive suggestions and enthusiastic support of the project; and Esperanza Tafallo and Steven Rao for their excellent technical assistance.

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yeast extract by physical and chemical methods. Hydrophobic-interaction chromatography followed by gel-exclusion chromatography was the major procedure used to prepare the purified antigen. The removal of yeast components was demonstrated in vitro by immunologic methods and in vivo by anaphylactic testing in guinea pigs.

To deliver the inoculum, we used 0.5-ml syringes for the 5 or 10 μg doses and 1.0-ml syringes for the 20 μg dose. All doses were administered by the same person. The vaccine was thoroughly resuspended before use and inoculated im in the deltoid region with a one-inch, 23-gauge needle at months 0, 1, and 6. Blood samples were obtained at one, two, three, six, eight, and 12 months after the initial inoculation (100% participation). A prevaccination oral temperature was obtained, and participants were asked to take and record their temperature with the same calibrated thermometer 4 hr after inoculation and each morning for the next three days. They were also asked to record any local or systemic symptoms experienced during this time. Responses were received by mail from ~90% of the participants.

All blood samples were processed within 24 hr and assayed for liver enzymes. The unit of measurement for anti-HBs was mIU/ml and was determined by the method of Hollinger et al. [10]. On the basis of the statistical analysis of at least 1,000 normal human sera, a value ≥0.7 mIU/ml on replicate samples was considered evidence of the presence of anti-HBs for determination of seroconversion rates. This cutoff level was ≥5 SD above the mean value for the negative control samples. All samples taken at three and eight months were also tested for anti-HBc and HBsAg to rule out unsuspected infection with HBV that might have occurred during the course of the study.

Statistical calculations included Student's *t* test, McNemar's χ^2 test, analysis of variance, and Duncan's multiple range test [11].

Results

No local or systemic reactions of a serious nature were observed by the volunteers. After the first inoculation, 14% of the vaccinees experienced mild discomfort at the site of injection; this figure was 12% after the second and third inoculations. Temperature elevations ≥1.5 F above an individual's baseline level were recorded in 3.8%, 9.3%, and 3.4% of the participants after each of the three injections, respectively. Only four oral temperatures exceeded 100 F, the highest of which was 101.2 F. Among the systemic reactions recorded after the initial inoculation, headaches (10.5%), diarrhea or abdominal complaints (9.5%), and fatigue (7.6%) were noted most frequently. Rates declined substantially after the second and third injections. Such local and systemic reactions are similar to those observed among recipients of placebos in other studies [10].

None of the participants showed serological evidence of infection with HBV during the study. Ten (9.5%) volunteers had aminotransferase levels >50 IU/liter on one or more occasions over the one-year follow-up period. This rate is similar to that observed in a previous study [10]. Muscle trauma caused by excessive physical activity was felt to be the cause of the enzyme elevations in three of these ten participants; this hypothesis was based on an AST value that was higher than the ALT value and on creatine phosphokinase levels of 47,502, 844, and 533 IU/liter. A fourth volunteer sustained a lacerated liver following an auto accident that occurred two weeks before the blood specimen that showed elevated enzyme levels was taken, and three other men were taking medications that have been reported to cause liver damage. In the other three (2.9%) volunteers, the enzyme levels had returned to normal when their blood was retested one week later. There was nothing in their histories to explain these abnormalities.

Seroconversion rates and geometric mean antibody responses for all participants are shown by dose and time in tables 1 and 2. Seroconversion rates were significantly lower in the 5-μg dose group than in the 10- or 20-μg dose

Table 1. Seroconversion rates of anti-HBs by time and dose.

	Time (months)					
Dose	1°	2	3	6°	8	12
5 (n = 35)	8.6	34.3†	45.7†	62.9†	97.1	88.6‡
10 (n = 35)	28.6	80.0	94.3	94.3	97.1	97.1
20 (n = 35)	28.6	82.9	88.6	94.3	100.0	100.0

NOTE. Results are percentages of subjects who were positive at the noted time. Doses are in μg.

° Vaccine was administered at months 0, 1, and 6.

† $P < .002$, 5 μg compared with 10 or 20 μg.

‡ Four persons who were positive for anti-HBs at eight months became seronegative at 12 months, whereas the one person who had not responded by month 8 seroconverted.

Table 2. Geometric mean levels of anti-HBs (mIU/ml) by time and dose.

	Time (months)					
Dose	1°	2	3	6°	8	12
5 (n = 35)	0.1†	0.5‡	0.7‡	2.0‡	45.7‡	10.0‡
10 (n = 35)	0.3	5.1	6.9	14.0	388.6	76.0§
20 (n = 35)	0.4	7.3	9.4	26.4	519.5	184.6

NOTE. Doses are given in μg.

° Vaccine was administered at months 0, 1, and 6.

† $P < .02$, 5 μg compared with 10 or 20 μg.

‡ $P < .001$, 5 μg compared with 10 or 20 μg.

§ $P = .03$, 10 μg compared with 20 μg.

groups at two, three, and six months after the initial inoculation ($P < .002$). By eight months all but two of the participants had produced specific antibodies. One of these two volunteers, who received 5 μg of vaccine, did develop specific anti-HBs at a low level (1.3 mIU/ml) 12 months following his initial inoculation. Therefore, the total seroconversion rate for the 5-μg group through 12 months was 100%, even though four other vaccinees who were positive at eight months were negative at 12 months; this yielded a point prevalance rate of 88.6% (table 1).

Geometric mean concentrations of anti-HBs were considerably lower in the group receiving 5 μg of yeast-derived HBsAg than in the 10- or 20-μg dose groups after the first month ($P < .001$; table 2). Similar differences were observed when weight-matched group members were compared, most notably at six and eight months. No statistically significant differences were seen between the 10- and 20-μg groups during the first eight months in terms of seroconversion rates or geometric mean levels of antibody. At each bleeding interval, however, geometric mean levels of anti-HBs in the 10-μg group were lower than those seen in the 20-μg vaccinees, and a P value of .03 was obtained at 12 months (table 2).

Discussion

The reasons for the significantly larger differences in immune response seen between the 5-μg group and the other two groups in our study are not readily apparent. Lot-to-lot variation is not a factor since the same lot of vaccine was used to inoculate all three groups. The only known variable is the volume of inoculum administered. Thus, the lower doses of vaccine not only contained less HBsAg, but the total amount of alum administered was also reduced even though the protein-to-alum ratio remained constant among the three doses. Whether a finite amount of alum is essential for an optimal response cannot be ascertained in this study, but levels of alum should not vary significantly between batches of vaccine that use identical doses of vaccine. It is interesting that similar muted responses were not seen in another study that compared 5 μg and 10 μg of yeast-derived HBsAg, although a two-fold difference in the geometric mean levels of antibody was reported [12]. Since the RIA activity of equimolar preparations of purified yeast HBsAg has been reported to vary by as much as 2.5 times [8], this might account for the interstudy differences observed at critical threshold levels.

As expected, a decline in anti-HBs concentration was observed in 96% of the subjects between the eighth and 12th months. To examine the slope of this response more completely, we determined the natural logarithms of the differences in the anti-HBs levels after dividing by the number of months between observations for each subject in the three dose groups. Similar data were obtained for adults participating in previous vaccine studies that used 40 μg of an HBsAg plasma-derived vaccine [10] and 20 or 40 μg of HEPTAVAX-B [9a], and the results were compared by analysis of variance. No significant differences in the rate of decline were found between these four groups when equivalent levels of peak anti-HBs responses were evaluated.

When geometric mean levels of anti-HBs at eight months were compared for two different plasma-derived vaccines, values ranged from 2,980 to 3,322 mIU/ml for 40 μg of vaccine to 1,975 mIU/ml for 20 μg of HBsAg [9a, 10] vs. 46 (5 μg), 389 (10 μg), and 520 (20 μg) mIU/ml for the yeast-derived product. These findings lead us to conclude that the lower antibody levels detected in adults receiving the yeast-derived vaccine may be related to the immunogenicity of the product. It is noteworthy that Dandolos et al. [13] reported similar discrepancies in anti-HBs levels between yeast- and plasma-derived vaccines, in which equivalent doses of antigen could be compared, although immune responses were significantly lower with our lot of recombinant vaccine. Since a butyl agarose method was used to remove contaminating yeast antigens from the final product in both of these studies, it is unlikely that this could account for the reduced immunogenicity found in our study. Two other studies [12, 14] did not permit equivalent time and dose comparisons between the two types of vaccines. Variations between lots, dissimilarities in the lipid content of the antigen produced in the yeast as compared with plasma-derived antigen, reduced antigenicity when compared with human HBsAg, and the fact that the yeast-derived HBsAg is not glycosylated [7, 8] may be factors responsible for the relatively lower anti-HBs response seen with the yeast-derived product. Further field trials in different at-risk groups seem appropriate before a specific adult dose of this vaccine is recommended. Nevertheless, several small trials in humans have shown that the vaccine is safe, and we anticipate that durable levels of protection should be achieved if sufficient immunogen is incorporated in the vaccine.

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The Epidemiology of *Clostridium difficile* with Use of a Typing Scheme: Nosocomial Acquisition and Cross-Infection Among Immunocompromised Patients

Gastrointestinal disturbance, particularly diarrhea, is one of the commonest side effects of the use of antibiotics. Up to 20%–25% of antibiotic-associated diarrhea occurs in conjunction with a fecal isolate of *Clostridium difficile* [1]. This organism is the major cause of pseudomembranous colitis and antibiotic-associated colitis but is also carried in the gastrointestinal tract of 2%–4% of the normal adult population and can be isolated from the feces of 30%–75% of asymptomatic neonates [2].

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Clusters of antibiotic-associated colitis have been noted [3], and early animal studies suggested that environmental contamination and cross-infection might be important in the etiology of outbreaks of antibiotic-associated diarrhea [4]. However, convincing evidence for the cross-infective potential of *C. difficile*, as well as its demonstration as a predominantly nosocomial infection, has been prevented due to lack of a reliable typing scheme for this organism [5].

Various typing schemes have been suggested [6–10]. Among these, Tabaqchali et al. [8] reported a well-defined scheme for typing this organism on the basis of the incorporation of [^{35}S]methionine into bacterial proteins and have described to date nine distinct groups within the *C. difficile* species (A-E, W-Z), as demonstrated by the radiolabeled protein profile obtained by using SDS-PAGE followed by autoradiography. We have applied this technique to isolates obtained from a prospective six-month study of immunocompromised and general medical patients in an attempt to assess the carriage and acquisition of *C. difficile* among hospital patients. The effect of isolation and containment procedures on the spread of *C. difficile* was also studied.

IMMUNOGENICITY AND REACTOGENICITY OF NEW HEPATITIS B VACCINES. FB Hollinger, Y Sanchez, C Troisi, GR Dreesman, and JL Melnick, Baylor College of Medicine, Houston, TX.

An HBsAg/gdx polypeptide (PP) vaccine and a recombinant DNA vaccine produced in yeast (*SD) are being evaluated. The PP vaccine was prepared from 22-nm HBsAg particles, packaged in a micellar form and alum-adsorbed. The starting material (NIH/40) contained 300 HBsAg RIA equivalent units (RSU) based on a HEPTAVAX-B standard of 100 HBsAg RSU. 3 lots containing 5, 1, and 0.2 HBsAg RSU were compared to 2 intact particle vaccines. Vaccine was administered at 0, 1, and 6 months to 52 weight-matched adults. RESULTS: Local and systemic reactions were insignificant. The anti-HBs seroconversion rate at 4 weeks for the 5 RSU PP vaccine group (90%) was considerably better than that seen with HEPTAVAX-B. By 12 weeks, all vaccine recipients in the 1 and 5 RSU PP vaccine groups had seroconverted versus 50% of the 0.2 RSU group ($p<0.02$) which reached 100% seroconversion by month 7. Throughout follow-up, geometric mean (GM) anti-HBs levels (mIU/ml) in the 5 RSU PP group were significantly higher than in the other PP vaccine groups. At 1 month the GM anti-HBs level for the 5 RSU PP group was 8.9, whereas the 300 RSU NIH/40 vaccine group had a GM antibody level of 5.2. By 3 months, the respective anti-HBs levels were 202 vs 90, rising to 8910 and 3450 by 7 months. The 1 RSU PP vaccine produced antiHBs responses comparable to the 100 RSU HEPTAVAX-B vaccine. Thus, the polypeptide vaccines, with substantially lower RIA HBsAg reactivity, produced superior anti-HBs responses when compared with 22-nm HBsAg vaccines. These studies confirm our previous findings in chimpanzees that critical antigenic determinants are associated with these polypetides, and they provide a link to future vaccine studies using synthetic HBsAg macromolecules. The rapid anti-HBs response that follows the initial inoculation suggests that such an immunogen may be beneficial in postexposure prophylaxis where the early development of immunity is advantageous. Preliminary data through 6 months also will be presented on the immunogenicity of 3 doses (5, 10, and 20 mcg) of an HBSAg vaccine made by recombinant DNA technology in yeast (*SD).

Hollinger FB, Sanchez Y, Troisi C, Dreesman GR, Melnick JL. Immunologenicity and reactogenicity of new hepatitis B vaccines. Hepatology 1984; 4:1027 (Abstract).

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 801
PURPOSE:	To evaluate antibody and clinical responses to the vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #972/C-K444 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Edward J. Septimus, M.D. Suite 740 7777 Southwest Freeway Houston, TX 77074
STUDY LOCATION:	Suite 740 7777 Southwest Freeway Houston, TX 77074
DATE INITIATED:	February 16, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 22 health care personnel of either sex (excluding pregnant woman), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and had not previously received any hepatitis B vaccine.
PROCEDURE:	Eligible participants receive a 1.0 ml (10 mg HBsAg) intramuscular injection of vaccine at 0, 1 and 6 months. Vaccine recipients are asked to record their temperature daily for five days after each injection of vaccine and also to record any local or systemic complaints that they may have during this period.

Study 801

PROCEDURE: (Cont.) A blood specimen (10-15 ml) is obtained from each participant approximately two weeks before the first vaccination. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12 and 24 months. The samples are assayed for HBsAg, anti-HBc, anti-HBs, yeast antibody and ALT. Samples with anti-HBs titers ≥ 25 mIU/ml are tested for the proportions of anti-a and anti-d activity.

RESULTS:

HEALTH CARE PERSONNEL:

10 mcg Lot #972/C-K444 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
22	21	21

2. Serologic Results:

Serologic data are available for 21 participants at 7/8 months. 100% (21/21) of the vaccinees seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10) at that time. The GMT at 7/8 months was 280.8 mIU/ml (all vaccinees and responders by either cutoff).

Among participants with serology data at 12 months, 86% (18/21) were positive for anti-HBs (mIU/ml ≥10). The GMT for all vaccinees at that time was 139.7 mIU/ml, while it was 256.0 mIU/ml for those with a titer of mIU/ml ≥10.

See Table 1 for anti-HBs responses for other time intervals.

3. Clinical Complaints:

Clinical follow-up data are available for 21 participants after each injection. The overall frequencies of complaints follow.

Study 801

RESULTS (CONT.):

Type	Frequency in % by Injection No. 1	2	3
Injection Site	14(3/22)	10(2/21)	29(6/21)
Systemic	32(7/22)	29(6/21)	43(9/21)

Refer to Table 2 for listings of specific clinical complaints by injection number. Maximum temperature data are provided in Table 3.

There were no serious or alarming adverse reactions attributable to vaccination.

ALT Elevations

ALT levels 2-7 times the upper level of normal were observed in post-vaccination blood samples taken from three subjects. All elevations were transient and returned to normal. None of those participants were seropositive for HBsAg or anti-HBC. The ALT elevations in two of the subjects were attributed to infectious mononucleosis and cholecystitis. The third case was asymptomatic.

Reactions reported to the DoBRR

A 26-year old female became aware that she was pregnant after receiving one injection of vaccine. She experienced a spontaneous abortion at 18 weeks after fetal death in utero. No microscopic examination was completed on the fetus. The investigator stated the fetal death and abortion were probably not/possibly related to vaccination.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK444
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	25%	(5/20)	10%	(2/20)	0.8	10.1	47.3
2 MONTHS	81%	(17/21)	52%	(11/21)	10.5	24.4	53.9
3 MONTHS	84%	(16/19)	63%	(12/19)	18.8	37.1	74.1
6 MONTHS	89%	(17/19)	79%	(15/19)	37.1	60.3	82.1
7/8 MONTHS	100%	(21/21)	100%	(21/21)	280.8	280.8	280.8
12 MONTHS	100%	(21/21)	86%	(18/21)	139.7	139.7	256.0

00293

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	2 (9.1%)	2 (9.1%)	1 (4.5%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	3 (13.6%)
SORENESS	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.1%)
TENDERNESS	0 (0.0%)	2 (9.1%)	1 (4.5%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	2 (9.1%)
WARMTH	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)
SYSTEMIC	4 (18.2%)	2 (9.1%)	5 (22.7%)	2 (9.1%)	2 (9.1%)	2 (9.1%)	7 (31.8%)
WHOLE BODY/GENERAL	4 (18.2%)	1 (4.5%)	4 (18.2%)	2 (9.1%)	1 (4.5%)	1 (4.5%)	6 (27.3%)
FATIGUE/WEAKNESS	1 (4.5%)	0 (0.0%)	2 (9.1%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	4 (18.2%)
MALAISE	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)
EDEMA, FACE	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)
HEADACHE	3 (13.6%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	4 (18.2%)
ACHINESS	1 (4.5%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.1%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (4.5%)

00294

able 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
MONONUCLEOSIS, INFECTIOUS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)		1 (4.5%)
RESPIRATORY	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		2 (9.1%)
RHINITIS	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.1%)
DYSPNEA (SHORT OF BREATH)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		1 (4.5%)
MUSCULOSKELETAL	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
ARTHRALGIA (OTHER)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	2 (9.1%)	2 (9.1%)		4 (18.2%)
DYSPEPSIA/HEARTBURN	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
DIARRHEA	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
NAUSEA	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	1 (4.5%)		2 (9.1%)
ABDOMEN DISTENDED	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	1 (4.5%)	1 (4.5%)		1 (4.5%)
OTHER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)		1 (4.5%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
EARACHE	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
HEARING IMPAIRMENT	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
PERSONS WITH COMPLAINTS	5 (22.7%)	4 (18.2%)	6 (27.3%)	3 (13.6%)	2 (9.1%)	2 (9.1%)		8 (36.4%)
PERSONS WITH NO COMPLAINTS	17 (77.3%)	18 (81.8%)	16 (72.7%)	19 (86.4%)	20 (90.9%)	20 (90.9%)		14 (63.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 2 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	2 (9.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.5%)
SORENESS	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
PRURITIS (ITCHING)	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
SYSTEMIC	3 (14.3%)	4 (19.0%)	3 (14.3%)	1 (4.8%)	2 (9.5%)	1 (4.8%)		6 (28.6%)
WHOLE BODY/GENERAL	2 (9.5%)	4 (19.0%)	3 (14.3%)	1 (4.8%)	1 (4.8%)	1 (4.8%)		5 (23.8%)
FATIGUE/WEAKNESS	1 (4.8%)	4 (19.0%)	3 (14.3%)	1 (4.8%)	1 (4.8%)	1 (4.8%)		5 (23.8%)
HEADACHE	2 (9.5%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		3 (14.3%)
RESPIRATORY	1 (4.8%)	0 (0.0%)	1 (4.8%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		2 (9.5%)
RHINITIS	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (4.8%)
SINUSITIS	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
MUSCULOSKELETAL	0 (0.0%)	2 (9.5%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.5%)
ARTHRALGIA (OTHER)	0 (0.0%)	2 (9.5%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.5%)

00297

Table 2 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
MYALGIA	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (4.8%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (4.8%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (4.8%)
PERSONS WITH COMPLAINTS	3 (14.3%)	5 (23.8%)	3 (14.3%)	1 (4.8%)	2 (9.5%)	1 (4.8%)		7 (33.3%)
PERSONS WITH NO COMPLAINTS	18 (85.7%)	16 (76.2%)	18 (85.7%)	20 (95.2%)	19 (90.5%)	20 (95.2%)		14 (66.7%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	3 (14.3%)	2 (9.5%)	2 (9.5%)	1 (4.8%)	1 (4.8%)	2 (9.5%)		6 (28.6%)
PAIN	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
SORENESS	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)		2 (9.5%)
TENDERNESS	1 (4.8%)	1 (4.8%)	2 (9.5%)	1 (4.8%)	1 (4.8%)	1 (4.8%)		2 (9.5%)
NODULE FORMATION	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
PRURITIS (ITCHING)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
ECCHYMOSIS	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)		1 (4.8%)
OTHER	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
SYSTEMIC	3 (14.3%)	4 (19.0%)	3 (14.3%)	1 (4.8%)	2 (9.5%)	3 (14.3%)		9 (42.9%)
WHOLE BODY/GENERAL	2 (9.5%)	4 (19.0%)	3 (14.3%)	1 (4.8%)	2 (9.5%)	2 (9.5%)		8 (38.1%)
FLUSH	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
FATIGUE/WEAKNESS	0 (0.0%)	2 (9.5%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.5%)

00299

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
HEADACHE	0 (0.0%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	2 (9.5%)	2 (9.5%)	4 (19.0%)
ACHINESS	2 (9.5%)	2 (9.5%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (14.3%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)	1 (4.8%)	2 (9.5%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	1 (4.8%)
SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)	1 (4.8%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)	1 (4.8%)	2 (9.5%)
MUSCULOSKELETAL	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)
ARTHRALGIA (OTHER)	0 (0.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
MYALGIA	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
DIGESTIVE SYSTEM	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)
ABDOMINAL PAINS/CRAMPS	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
NAUSEA	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)
UROGENITAL SYSTEM	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
OTHER	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.8%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)		2 (9.5%)
EARACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	0 (0.0%)		1 (4.8%)
EYE PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)		1 (4.8%)
PERSONS WITH COMPLAINTS	6 (28.6%)	6 (28.6%)	5 (23.8%)	2 (9.5%)	3 (14.3%)	5 (23.8%)		12 (57.1%)
PERSONS WITH NO COMPLAINTS	15 (71.4%)	15 (71.4%)	16 (76.2%)	19 (90.5%)	18 (85.7%)	16 (76.2%)		9 (42.9%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (22 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	21 (95.5%)	20 (90.9%)	19 (90.5%)	20 (90.9%)	19 (90.5%)	21 (95.5%)			18 (81.8%)
99 - 99.9	1 (4.5%)	2 (9.1%)	2 (9.5%)	2 (9.1%)	2 (9.5%)	0 (0.0%)			3 (13.6%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)			1 (4.5%)
TEMPERATURE TAKEN	22 (100.0%)	22 (100.0%)	21 (95.5%)	22 (100.0%)	21 (95.5%)	22 (100.0%)			22 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (4.5%)	0 (0.0%)			0 (0.0%)

Table 3 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (21 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	20 (95.2%)	20 (95.2%)	19 (90.5%)	21 (100.0%)	21 (100.0%)	20 (95.2%)		17 (81.0%)
99 - 99.9	1 (4.8%)	1 (4.8%)	2 (9.5%)	0 (0.0%)	0 (0.0%)	1 (4.8%)		4 (19.0%)
TEMPERATURE TAKEN	21 (100.0%)	21 (100.0%)	21 (100.0%)	21 (100.0%)	21 (100.0%)	21 (100.0%)		21 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0801
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (21 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	16 (76.2%)	17 (85.0%)	17 (81.0%)	16 (88.9%)	19 (95.0%)	19 (95.0%)			13 (61.9%)
99 - 99.9	4 (19.0%)	1 (5.0%)	3 (14.3%)	2 (11.1%)	1 (5.0%)	0 (0.0%)			5 (23.8%)
100 - 100.9	1 (4.8%)	1 (5.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (4.8%)
101 - 101.9	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)			2 (9.5%)
TEMPERATURE TAKEN	21 (100.0%)	20 (95.2%)	21 (100.0%)	18 (85.7%)	20 (95.2%)	20 (95.2%)			21 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	1 (4.8%)	0 (0.0%)	3 (14.3%)	1 (4.8%)	1 (4.8%)			0 (0.0%)

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 803
PURPOSE:	To evaluate antibody and clinical responses to the vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #972/C-K444 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Franklyn N. Judson, M.D. Denver Department of Health and Hospitals Disease Control Service 605 Bannock Street Denver, CO 80204-4507
SECONDARY INVESTIGATORS:	David Cohn, M.D. Denver Department of Health and Hospitals Disease Control Service 605 Bannock Street Denver, CO 80204-4507 Morton Davidson, M.D. New York University Medical Center University Hospital 560 First Avenue New York, NY 10016
STUDY LOCATION:	Denver Department of Health and Hospitals Disease Control Service 605 Bannock Street Denver, CO 80204-4507
DATE INITIATED:	January 16, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 31 health care personnel of either sex (excluding pregnant woman), who were negative for HBsAg, anti-HBc and anti-HBs, had normal ALT level and had not previously received any hepatitis B vaccine.

Study 803

PROCEDURE:

Eligible participants receive a 1.0 ml (10 mg HBsAg) intramuscular injection of vaccine at 0, 1 and 6 months. Vaccine recipients are asked to record their temperature daily for five days after each injection of vaccine and also to record any local or systemic complaints that they may have during this period.

A blood specimen (10-15 ml) was obtained from each participant approximately two weeks before the first vaccination. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12 and 24 months. The samples are assayed for HBsAg, anti-HBc, anti-HBs, yeast antibody and ALT. Samples with anti-HBs titers $\geq$ 25 mIU/ml are tested for the proportions of anti-a and anti-d activity.

STUDY RESULTS:

HEALTH CARE PERSONNEL:

10 mcg Lot #972/C-K444 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
31	30	30

One person had a low titer of anti-HBs when the first dose of vaccine was given.

2. Serologic Results:

Serologic data are available for 26 study participants at 7/8 months. Eighty-five percent (22/26) of the subjects seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10) at that time. The GMT for all vaccinees at 7/8 months was 584.6 mIU/ml, while it was 2136.0 mIU/ml for responders with titers of mIU/ml $\geq$10.

Study 803

STUDY RESULTS: (Cont.)

Among participants with serology data at 12 months, 81% (22/27) were positive for anti-HBs (mIU/ml ≥10). At that time the GMT was 147.1 mIU/ml for all vaccinees and 513.5 mIU/ml for those with a titer of mIU/ml ≥10.

See Table 1 for anti-HBs responses for other time intervals.

3. Clinical Complaints:

Clinical follow-up data are available for 30 participants following each injection. The overall frequencies of complaints are presented below.

Type of Complaint	Frequency in % by Injection No. 1	2	3
Injection Site	29(9/31)	33(10/30)	30(8/27)
Systemic	36(11/31)	20(6/30)	4(1/27)

Refer to Table 2 for listings of specific complaints after each injection. Maximum temperature data are provided in Table 3.

There were no serious or alarming adverse reactions attributable to vaccine.

ALT Elevations

Four participants had transient elevations in ALT levels (1.5 times the upper limit of normal). In two individuals transient elevation occurred at one month after vaccination, in the other two individuals elevation occurred at 2 and 8 months respectively. ALT levels returned to normal in all cases. An additional individual had an elevated ALT (1.5-2.0 times the upper limit of normal) at 12 months after vaccination. A repeat serology drawn two weeks later was returning

Study 803

STUDY RESULTS (CONT.):

toward normal. In all cases the reasons for the elevations are unknown. The subjects were not ill and were negative for HBsAg and anti-HBc.

Reactions Reported to the OoBRR

One subject had onset of biparietal headache, upset stomach, confusion, and expressive aphasia two days after receiving the first injection of vaccine. Neurologic and vital signs were within normal limits. A CAT scan of the head was also normal. His WBC was slightly elevated (13,000) with a shift to the left. All symptoms resolved within 2 days. The event was not considered to be vaccine related.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK444
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	43%	(12/28)	21%	(6/28)	1.8	11.8	26.5
2 MONTHS	76%	(22/29)	62%	(18/29)	17.4	58.0	107.4
3 MONTHS	78%	(21/27)	63%	(17/27)	23.8	74.1	131.7
6 MONTHS	86%	(24/28)	79%	(22/28)	53.3	121.2	163.9
7/8 MONTHS	85%	(22/26)	85%	(22/26)	584.6	2136.0	2136.0
12 MONTHS	85%	(23/27)	81%	(22/27)	147.1	431.9	513.5

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	8 (25.8%)	3 (9.7%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		9 (29.0%)
PAIN ON INJECTION	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
PAIN	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
SORENESS	7 (22.6%)	3 (9.7%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		8 (25.8%)
SYSTEMIC	6 (19.4%)	4 (12.9%)	4 (12.9%)	4 (12.9%)	2 (6.5%)	3 (9.7%)		11 (35.5%)
WHOLE BODY/GENERAL	4 (12.9%)	1 (3.2%)	2 (6.5%)	2 (6.5%)	1 (3.2%)	1 (3.2%)		6 (19.4%)
CHILLS	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
FATIGUE/WEAKNESS	2 (6.5%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)		2 (6.5%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)		2 (6.5%)
LIGHTHEADED	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
INTEGUMENTARY SYSTEM	2 (6.5%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)		2 (6.5%)
PAPULAR RASH	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PRURITIS/ITCHING	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)
RESPIRATORY	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	2 (6.5%)	2 (6.5%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)
UPPER RESPIRATORY INFECT., NOS	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)
MUSCULOSKELETAL	1 (3.2%)	2 (6.5%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	2 (6.5%)
ARTHRALGIA (OTHER)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)
MYALGIA	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)
OTHER	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
DYSPEPSIA/HEARTBURN	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
NERVOUS SYSTEM	0 (0.0%)	1 (3.2%)	2 (6.5%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
PARESTHESIAS	0 (0.0%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
THOUGHT IMPAIRMENT	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
OTHER	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
PERSONS WITH COMPLAINTS	13 (41.9%)	7 (22.6%)	4 (12.9%)	4 (12.9%)	2 (6.5%)	3 (9.7%)		18 (58.1%)
PERSONS WITH NO COMPLAINTS	18 (58.1%)	24 (77.4%)	27 (87.1%)	27 (87.1%)	29 (93.5%)	28 (90.3%)		13 (41.9%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00312

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (30 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	7 (23.3%)	8 (26.7%)	5 (16.7%)	3 (10.0%)	2 (6.7%)	1 (3.3%)	10 (33.3%)
PAIN ON INJECTION	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
PAIN	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
SORENESS	4 (13.3%)	5 (16.7%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (16.7%)
TENDERNESS	1 (3.3%)	2 (6.7%)	2 (6.7%)	2 (6.7%)	1 (3.3%)	1 (3.3%)	2 (6.7%)
NODULE FORMATION	0 (0.0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
LYMPHADENOPATHY, REGIONAL	0 (0.0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	1 (3.3%)
SYSTEMIC	4 (13.3%)	3 (10.0%)	5 (16.7%)	4 (13.3%)	1 (3.3%)	1 (3.3%)	6 (20.0%)
WHOLE BODY/GENERAL	2 (6.7%)	2 (6.7%)	2 (6.7%)	2 (6.7%)	1 (3.3%)	1 (3.3%)	3 (10.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)
LIGHTHEADED	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
ACHINESS	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	1 (3.3%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (30 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
INTEGUMENTARY SYSTEM	1 (3.3%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
PRURITIS/ITCHING	0 (0.0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
RASH, NOS	0 (0.0%)	1 (3.3%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
OTHER	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
RESPIRATORY	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
UPPER RESPIRATORY INFECT., NOS	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	2 (6.7%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
DIARRHEA	0 (0.0%)	0 (0.0%)	2 (6.7%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
PERSONS WITH COMPLAINTS	9 (30.0%)	10 (33.3%)	8 (26.7%)	6 (20.0%)	3 (10.0%)	2 (6.7%)		12 (40.0%)
PERSONS WITH NO COMPLAINTS	21 (70.0%)	20 (66.7%)	22 (73.3%)	24 (80.0%)	27 (90.0%)	28 (93.3%)		18 (60.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 2 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (30 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	7 (25.9%)	4 (14.8%)	2 (7.4%)	1 (3.7%)	0 (0.0%)	0 (0.0%)		8 (29.6%)
PAIN ON INJECTION	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
PAIN	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
SORENESS	5 (18.5%)	2 (7.4%)	1 (3.7%)	1 (3.7%)	0 (0.0%)	0 (0.0%)		5 (18.5%)
TENDERNESS	0 (0.0%)	2 (7.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (7.4%)
WARMTH	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
PRURITIS (ITCHING)	0 (0.0%)	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
SYSTEMIC	0 (0.0%)	1 (3.7%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (3.7%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
ILLNESS, NOS	0 (0.0%)	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
PERSONS WITH COMPLAINTS	7 (25.9%)	4 (14.8%)	3 (11.1%)	1 (3.7%)	0 (0.0%)	0 (0.0%)		8 (29.6%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (30 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO COMPLAINTS	20 (74.1%)	23 (85.2%)	24 (88.9%)	26 (96.3%)	27 (100.0%)	27 (100.0%)	19 (70.4%)
PERSONS WITH NO DATA	2 (6.9%)	2 (6.9%)	2 (6.9%)	2 (6.9%)	2 (6.9%)	2 (6.9%)	2 (6.9%)

Table 3
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (31 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	28 (90.3%)	27 (90.0%)	27 (90.0%)	27 (87.1%)	29 (96.7%)	26 (92.9%)			24 (77.4%)
99 - 99.9	3 (9.7%)	3 (10.0%)	3 (10.0%)	4 (12.9%)	1 (3.3%)	2 (7.1%)			7 (22.6%)
TEMPERATURE TAKEN	31 (100.0%)	30 (96.8%)	30 (96.8%)	31 (100.0%)	30 (96.8%)	28 (90.3%)			31 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	3 (9.7%)			0 (0.0%)

00317

Table 3 (cont)
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (30 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (3.3%)	0 (0.0%)	1 (3.4%)	1 (3.6%)	1 (3.6%)	1 (3.8%)			0 (0.0%)
< 99	26 (86.7%)	26 (92.9%)	25 (86.2%)	26 (92.9%)	25 (89.3%)	23 (88.5%)			24 (80.0%)
99 - 99.9	3 (10.0%)	1 (3.6%)	3 (10.3%)	1 (3.6%)	2 (7.1%)	2 (7.7%)			5 (16.7%)
101 - 101.9	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (3.3%)
TEMPERATURE TAKEN	30 (100.0%)	28 (93.3%)	29 (96.7%)	28 (93.3%)	28 (93.3%)	26 (86.7%)			30 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	2 (6.7%)	1 (3.3%)	2 (6.7%)	2 (6.7%)	4 (13.3%)			0 (0.0%)

Table 3 (cont)
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0803
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (30 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	22 (91.7%)	19 (79.2%)	21 (87.5%)	24 (96.0%)	21 (91.3%)	22 (95.7%)			19 (76.0%)
99 - 99.9	2 (8.3%)	5 (20.8%)	2 (8.3%)	1 (4.0%)	1 (4.3%)	1 (4.3%)			5 (20.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (4.3%)	0 (0.0%)			1 (4.0%)
TEMPERATURE TAKEN	24 (80.0%)	24 (80.0%)	24 (80.0%)	25 (83.3%)	23 (76.7%)	23 (76.7%)			25 (83.3%)
TEMPERATURE NOT TAKEN	6 (20.0%)	6 (20.0%)	6 (20.0%)	5 (16.7%)	7 (23.3%)	7 (23.3%)			5 (16.7%)

00319

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 807
PURPOSE:	To compare antibody and clinical responses to yeast recombinant and plasma-derived hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINES:	1. Yeast Recombinant Hepatitis B Vaccine Lot 972/C-K444 (10 mcg HBsAg/ml) 2. Plasma-Derived Hepatitis B Vaccine Lot 1510J (20 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Solko W. Schalm, M.D. Department of Internal Medicine and Gastroenterology University Hospital Dijkzigt Rotterdam, The Netherlands
SECONDARY INVESTIGATOR:	Dr. Rudolf A. Heytink Department of Virology Erasmas University Rotterdam, The Netherlands
STUDY LOCATION:	University Hospital Dijkzigt Rotterdam, The Netherlands
DATE STUDY INITIATED:	April 4, 1984
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 50-60 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.
STUDY PROCEDURE:	Eligible study participants receive a 1.0 ml intramuscular injection of yeast recombinant (10 mcg HBsAg) or plasma-derived (20 mcg HBsAg) vaccine at 0, 1, and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

Study 807

STUDY PROCEDURE (CONT.):

A blood sample is obtained from each study participant approximately two to three weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 7, 9 and 12 months. Blood samples are obtained at 24 months from those participants who have seroconverted.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer ≥25 mIU/ml may be tested to determine anti-a and anti-d subtype specificity.

RESULTS:

HEALTH CARE PERSONNEL

Yeast Recombinant Hepatitis B Vaccine:

10 mcg Lot 972/C-K444 at 0, 1, and 6 months

Plasma-Derived Hepatitis B Vaccine:

20 mcg Lot 1510J at 0, 1, and 6 months

1. Number Vaccinated:

	Injection No.		
Vaccine	1	2	3
Yeast Recombinant	31	31	31
Plasma-Derived	25	25	25

2. Serologic Results:

Serologic data at 7-8 months are available for 31 recipients of the yeast recombinant vaccine and 22 recipients of the plasma-derived vaccine.

At 7-8 months, 100% of recipients of both the yeast recombinant (31/31) and plasma-derived (22/22) vaccines seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees and responders

Study 807

RESULTS (CONT.):

(S/N ≥2.1 and ≥10 mIU/ml) was 885.1 mIU/ml for those persons who received the yeast recombinant vaccine, and 6164.4 mIU/ml for those who received the plasma-derived vaccine.

By 12 months 94% (29/31) of recipients of the yeast recombinant and 100% (24/24) of recipients of the plasma-derived vaccines retained on anti-HBs titer of mIU/ml ≥10. The GMTs for all vaccinees at that time was 112.4 mIU/ml (yeast recombinant vaccine) and 1029.2 mIU/ml (plasma-derived vaccine).

Anti-HBs responses at 1 through 12 months are included in Table 1.

3. Clinical Results:

Clinical follow-up data are available for 36 recipients of the yeast recombinant vaccine and 25 recipients of the plasma-derived vaccine following each injection. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 2-5. In summary:

Vaccine	Clinical Complaint	% Frequency by Injection No. 1	2	3
Yeast - Recombinant	Injection Site	10(3/31)	3(1/31)	7(2/31)
	Systemic	16(5/31)	7(2/31)	10(3/31)
Plasma	Injection Site	12(3/25)	4(1/25)	8(2/25)
	Systemic	20(5/25)	12(3/25)	0(0/25)

No serious or alarming adverse reactions attributable to vaccination have been reported.

PUBLICATIONS:

Heijtink RA, Kruining J, Baker M, Schalm SW. Immune response after vaccination with recombinant hepatitis B vaccine as compared to that after plasma-derived vaccine. Antiviral Res 1985; Supplement 1:273-9.

Heijtink RA, Schalm SW. Anti-HBs/a determination after hepatitis B vaccination. Submitted for publication to Lancet.

Study 807

Table 1

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Recombinant Hepatitis B Vaccine Lot 972/C-K444 or 20 mcg Doses of Plasma-Derived Hepatitis B Vaccine Lot 1510J at 0, 1, and 6 Months in Study 807

Time (Months)	Yeast Recombinant Vaccine					Plasma-Derived Vaccine				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders				All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1	19 (6/31)	13 (4/31)	0.7	16.7	36.4	56 (14/25)	44 (11/25)	3.3	21.4	36.6
2	77 (24/31)	39 (12/31)	5.3	12.4	44.6	100 (22/22)	77 (17/22)	59.1	59.1	148.0
3	89 (25/28)	71 (20/28)	21.5	35.9	60.7	100 (21/21)	95 (20/21)	135.0	135.0	161.9
6	94 (29/31)	84 (26/31)	48.4	68.8	94.8	100 (25/25)	100 (25/25)	271.9	271.9	271.9
7/8	100 (31/31)	100 (31/31)	885.1	885.1	885.1	100 (22/22)	100 (22/22)	6164.4	6164.4	6164.4
9	100 (31/31)	100 (31/31)	363.1	363.1	363.1	100 (24/24)	100 (24/24)	2899.4	2899.4	2899.4
12	100 (31/31)	94 (29/31)	112.4	112.4	140.5	100 (24/24)	100 (24/24)	1029.2	1029.2	1029.2

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (3.2%)	2 (6.5%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	3 (9.7%)
PAIN	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
STIFFNESS/TIGHTNESS	1 (3.2%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
SYSTEMIC	1 (3.2%)	1 (3.2%)	1 (3.2%)	1 (3.2%)	2 (6.5%)	1 (3.2%)	5 (16.1%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	3 (9.7%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	2 (6.5%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	1 (3.2%)
INFLUENZA, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	1 (3.2%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	2 (6.5%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (3.2%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
MUSCULOSKELETAL	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
BACK PAIN	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
PERSONS WITH COMPLAINTS	1 (3.2%)	3 (9.7%)	1 (3.2%)	2 (6.5%)	2 (6.5%)	1 (3.2%)	7 (22.6%)
PERSONS WITH NO COMPLAINTS	30 (96.8%)	28 (90.3%)	30 (96.8%)	29 (93.5%)	29 (93.5%)	30 (96.8%)	24 (77.4%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
PAIN	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
SYSTEMIC	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
WHOLE BODY/GENERAL	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
FATIGUE/WEAKNESS	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
PERSONS WITH COMPLAINTS	2 (6.5%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
PERSONS WITH NO COMPLAINTS	29 (93.5%)	30 (96.8%)	31 (100.0%)	31 (100.0%)	31 (100.0%)	31 (100.0%)	29 (93.5%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

00326

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (3.2%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
PAIN	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
STIFFNESS/TIGHTNESS	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
SYSTEMIC	1 (3.2%)	1 (3.2%)	2 (6.5%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	3 (9.7%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
HEADACHE	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.5%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
DIARRHEA	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
NERVOUS SYSTEM	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
VERTIGO/DIZZINESS	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)
PERSONS WITH COMPLAINTS	2 (6.5%)	2 (6.5%)	3 (9.7%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	5 (16.1%)
PERSONS WITH NO COMPLAINTS	29 (93.5%)	29 (93.5%)	28 (90.3%)	30 (96.8%)	31 (100.0%)	31 (100.0%)	26 (83.9%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (31 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (31 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	1 (3.6%)	1 (3.7%)	1 (3.7%)	1 (3.7%)	1 (3.7%)	1 (3.8%)		1 (3.2%)
< 99	23 (82.1%)	22 (81.5%)	23 (85.2%)	25 (92.6%)	24 (88.9%)	24 (92.3%)		21 (67.7%)
99 - 99.9	4 (14.3%)	3 (11.1%)	3 (11.1%)	0 (0.0%)	0 (0.0%)	1 (3.8%)		6 (19.4%)
100 - 100.9	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	0 (0.0%)		2 (6.5%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (3.7%)	0 (0.0%)		1 (3.2%)
TEMPERATURE TAKEN	28 (90.3%)	27 (87.1%)	27 (87.1%)	27 (87.1%)	27 (87.1%)	26 (83.9%)		31 (100.0%)
TEMPERATURE NOT TAKEN	3 (9.7%)	4 (12.9%)	4 (12.9%)	4 (12.9%)	4 (12.9%)	5 (16.1%)		0 (0.0%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (31 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	22 (78.6%)	24 (85.7%)	25 (96.2%)	21 (95.8%)	23 (95.8%)	23 (100.0%)		20 (71.4%)
99 - 99.9	5 (17.9%)	4 (14.3%)	0 (0.0%)	1 (4.2%)	1 (4.2%)	0 (0.0%)		7 (25.0%)
100 - 100.9	1 (3.6%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
TEMPERATURE TAKEN	28 (90.3%)	28 (90.3%)	26 (83.9%)	24 (77.4%)	24 (77.4%)	23 (74.2%)		28 (90.3%)
TEMPERATURE NOT TAKEN	3 (9.7%)	3 (9.7%)	5 (16.1%)	7 (22.6%)	7 (22.6%)	8 (25.8%)		3 (9.7%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (31 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	5 (19.2%)	5 (19.2%)	5 (19.2%)	5 (19.2%)	5 (20.0%)	5 (19.2%)		5 (18.5%)
< 99	17 (65.4%)	20 (76.9%)	17 (65.4%)	19 (73.1%)	19 (76.0%)	19 (73.1%)		18 (66.7%)
99 - 99.9	4 (15.4%)	1 (3.8%)	4 (15.4%)	1 (3.8%)	1 (4.0%)	2 (7.7%)		3 (11.1%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)		1 (3.7%)
TEMPERATURE TAKEN	26 (83.9%)	26 (83.9%)	26 (83.9%)	26 (83.9%)	25 (80.6%)	26 (83.9%)		27 (87.1%)
TEMPERATURE NOT TAKEN	5 (16.1%)	5 (16.1%)	5 (16.1%)	5 (16.1%)	6 (19.4%)	5 (16.1%)		4 (12.9%)

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	3 (12.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	3 (12.0%)
PAIN	2 (8.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	2 (8.0%)
STIFFNESS/TIGHTNESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SYSTEMIC	1 (4.0%)	3 (12.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	5 (20.0%)
WHOLE BODY/GENERAL	1 (4.0%)	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
ILLNESS, NOS	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
MUSCULOSKELETAL	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
BACK PAIN	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
DIARRHEA	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	4 (16.0%)	4 (16.0%)	2 (8.0%)	2 (8.0%)	1 (4.0%)	1 (4.0%)	7 (28.0%)
PERSONS WITH NO COMPLAINTS	21 (84.0%)	21 (84.0%)	23 (92.0%)	23 (92.0%)	24 (96.0%)	24 (96.0%)	18 (72.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PAIN	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SYSTEMIC	3 (12.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	3 (12.0%)
WHOLE BODY/GENERAL	3 (12.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)
FATIGUE/WEAKNESS	3 (12.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)
ILLNESS, NOS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
MUSCULOSKELETAL	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
BACK PAIN	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)
STOMATITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)
NERVOUS SYSTEM	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
VERTIGO/DIZZINESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	4 (16.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	4 (16.0%)
PERSONS WITH NO COMPLAINTS	21 (84.0%)	23 (92.0%)	24 (96.0%)	25 (100.0%)	24 (96.0%)	25 (100.0%)	21 (84.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
PAIN	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
PERSONS WITH COMPLAINTS	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
PERSONS WITH NO COMPLAINTS	23 (92.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	23 (92.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 5

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH MAX TEMP
< 99	19 (82.6%)	18 (78.3%)	20 (87.0%)	16 (80.0%)	18 (81.8%)	20 (95.2%)		14 (58.3%)
99 - 99.9	3 (13.0%)	5 (21.7%)	3 (13.0%)	4 (20.0%)	3 (13.6%)	0 (0.0%)		7 (29.2%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)		1 (4.2%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)		1 (4.2%)
102 - 102.9	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
TEMPERATURE TAKEN	23 (92.0%)	23 (92.0%)	23 (92.0%)	20 (80.0%)	22 (88.0%)	21 (84.0%)		24 (96.0%)
TEMPERATURE NOT TAKEN	2 (8.0%)	2 (8.0%)	2 (8.0%)	5 (20.0%)	3 (12.0%)	4 (16.0%)		1 (4.0%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 2								DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5											
NORMAL	5 (21.7%)	5 (20.8%)	5 (20.8%)	5 (23.8%)	5 (21.7%)	5 (22.7%)											5 (20.8%)
< 99	16 (69.6%)	17 (70.8%)	17 (70.8%)	15 (71.4%)	17 (73.9%)	16 (72.7%)											16 (66.7%)
99 - 99.9	2 (8.7%)	2 (8.3%)	1 (4.2%)	1 (4.8%)	1 (4.3%)	1 (4.5%)											2 (8.3%)
101 - 101.9	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)											1 (4.2%)
TEMPERATURE TAKEN	23 (92.0%)	24 (96.0%)	24 (96.0%)	21 (84.0%)	23 (92.0%)	22 (88.0%)											24 (96.0%)
TEMPERATURE NOT TAKEN	2 (8.0%)	1 (4.0%)	1 (4.0%)	4 (16.0%)	2 (8.0%)	3 (12.0%)											1 (4.0%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE

STUDY : 0807
TREATMENT :
LOT NUMBER : 1510J
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	10 (47.6%)	10 (45.5%)	10 (45.5%)	10 (45.5%)	10 (45.5%)	10 (47.6%)		10 (45.5%)
< 99	9 (42.9%)	11 (50.0%)	10 (45.5%)	12 (54.5%)	10 (45.5%)	11 (52.4%)		10 (45.5%)
99 - 99.9	2 (9.5%)	1 (4.5%)	2 (9.1%)	0 (0.0%)	2 (9.1%)	0 (0.0%)		2 (9.1%)
TEMPERATURE TAKEN	21 (84.0%)	22 (88.0%)	22 (88.0%)	22 (88.0%)	22 (88.0%)	21 (84.0%)		22 (88.0%)
TEMPERATURE NOT TAKEN	4 (16.0%)	3 (12.0%)	3 (12.0%)	3 (12.0%)	3 (12.0%)	4 (16.0%)		3 (12.0%)

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A. Billiau, E. De Clercq and H. Schellekens (eds.)

IMMUNE RESPONSE AFTER VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE AS COMPARED TO THAT AFTER PLASMA-DERIVED VACCINE

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SUMMARY

Thirty-one individuals (health care workers) were vaccinated with recombinant hepatitis B vaccine (10 µg dose) and their immune response (anti-HBs) was compared to that of twenty-five health care workers after vaccination with plasma-derived vaccine (20 µg dose). Although the seroconversion rate and the percentage of anti-HBs/a antibodies at month 7 were comparable, the geometric mean titre of anti-HBs at month 7 was considerably lower for the recombinant vaccine group (857.4 vs. 6736.5 IU/l). However, vaccinees from the two groups showing seroconversion at month 1 had comparable titres at month 7. Raising the dose of HBsAg in the recombinant vaccine may favourably influence the seroconversion rate at month 1 and thereby the immune response after three injections.

INTRODUCTION

Only six years ago, a plasma-derived vaccine was introduced to overcome the worldwide problem of hepatitis B infections.[1] General acceptance of the vaccine, however, has been hampered by the high costs and in particular by doubts about the suitability of infectious plasma as its source. Public concern has waned considerably since the discovery of human T-cell leukaemia virus as a possible cause of the acquired immune deficiency syndrome and the possibility of investigating the efficacy of inactivation of this virus in vaccine preparation procedures.[2] Meanwhile, an alternative for the latter objective has been found in the preparation of hepatitis B surface antigen by recombinant DNA technology in the yeast *Saccharomyces cerevisiae*.[3] Although the yeast recombinant DNA produced HBsAg polypeptides, unlike the native HBsAg, are not glycosylated, the vaccine thus prepared has proven to induce protective antibodies during chimpanzee challenge studies.[4] Its safety and immunicity in man has been demonstrated by several groups of investigators.[5 6 7 8] One of these studies is presented here.

Soon after the introduction of the plasma-derived vaccine it was uncertain whether an HBsAg/adw vaccine would protect against HBsAg/ayw virus infections. Nowadays it is generally known from chimpanzee studies as well as experiments in man[3 9 10] that the antibodies directed against the main determinant a provide cross protection for infections with strains not incorporated in the vaccine.

However, in the plasma-derived vaccine studies[11 12] it was found that the relative proportion of anti-HBs antibodies is variable, which may partially account for hepatitis B infections in the first few months after vaccination. Therefore, the need to monitor the development of anti-HBs/a antibodies after vaccination is stressed.

MATERIAL AND METHODS

Population

The study population consisted of 56 health care workers. Recombinant vaccine was given to 31 individuals (17 female, 14 male; mean age 32 ± 2 yr, range 20-59); plasma-derived vaccine was given to 25 individuals (13 female, 12 male; mean age 30 ± 2 yr, range 22-53). Participants to this study were negative for HBsAg, anti-HBc, and anti-HBs and had a normal alanine transferase level at the entrance to the study.

Vaccine

Participants were vaccinated at 0, 1, and 6 months with either a 10 µg HBsAg/adw dose of the recombinant hepatitis B vaccine (Merck, Sharp and Dohme, lot 972/C-K444) or a 20 µg HBsAg/adw dose of the plasma-derived vaccine (Merck, Sharp and Dohme, lot 1510 J). Recombinant HBsAg used here was purified by hydrophobic interaction chromatography.[8 7]

Assays

HBsAg, anti-HBc, anti-HBs were measured in commercially available kits (Ausria II, Corab, and Ausab; Abbott Laboratories, North Chicago, USA). The concentration of anti-HBs was calculated by the method of Hollinger et al.[13] and expressed in IU/l after comparison with the WHO standard preparation (125 IU/l), obtained from the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands. Calculations were made for positive results in Ausab only (sample/negative control ratio ≥ 2.1). Samples containing more than 200 IU/l were diluted and retested. Dilutions were made in the negative control serum from Ausab. Estimation of the proportion of anti-HBs/a antibodies was performed according to the method of Hoofnagle et al.[14] In short, undiluted or diluted sera containing 1000-2000 cpm in Ausab were incubated for 2 h at room temperature with pooled HBsAg/ad, HBsAg/ay, and normal human serum, respectively. Pooled sera

included reference sera from Dr.A.M.Courouce-Pauty as mentioned in an earlier study.[15] Reduction of cpm after incubation with HBsAg/ay strains measured the anti-HBs/a proportion of the total amount of anti-HBs, since the vaccine consisted of HBsAg/adw only. The proportion of anti-HBs/d(w) antibodies was obtained by subtracting the reduction percentage after incubation with HBsAg/ay pooled serum from the reduction percentage after incubation with HBsAg/ad pooled serum.

RESULTS

Table I shows a delayed seroconversion rate for the recombinant vaccine group as compared to the plasma-derived vaccine group in the course of the vaccine study. Similar results were obtained for titres $\geq$ 10 IU/l, the supposed protective level of antibodies.

TABLE I

SEROCONVERSION RATE AFTER VACCINATION WITH RECOMBINANT (10 µg) AND PLASMA-DERIVED (20 µg) VACCINE IN HEALTH CARE WORKERS

Month	Recombinant vaccine	Plasma-derived vaccine	Recombinant vaccine	Plasma-derived vaccine
	Percentage seroconversion		Percentage anti-HBs $\geq$ 10 IU/l	
1	19(6/31)	56(14/25)	13(4/31)	40(10/25)
2	77(24/31)	96(22/23)	39(12/31)	74(17/23)
3	90(28/31)	100(25/25)	74(23/31)	96(24/25)
6	94(29/31)	100(25/25)	87(27/31)	100(25/25)
7	100(31/31)	100(22/22)	100(31/31)	100(22/22)

Geometric mean titres of anti-HBs were significantly lower in the recombinant vaccine group as compared to the plasma-derived vaccine group at month 2, 3, 6, and 7 (Table II).

After three injections females had significantly ($p < 0.05$) higher anti-HBs titres than males in the recombinant vaccine group (1412 vs. 468 IU/l) but not in the plasma-derived vaccine group (6036 vs. 7519 IU/l).

All vaccinees were negative for HBsAg and anti-HBc at 7 months and had normal alanine transferase levels in all sera obtained. Table III illustrates the increase of the relative proportion of anti-HBs/a antibodies from about 60% at month 1 to about 100% at month 7 following the first injection for both vaccine groups as measured by specific absorption. In any sample at

TABLE II

GEOMETRIC MEAN TITRES OF ANTI-HBs AFTER VACCINATION WITH RECOMBINANT VACCINE (10 µg) AND PLASMA-DERIVED VACCINE (20 µg)

Month	Recombinant vaccine GMT in IU/l	Plasma-derived vaccine GMT in IU/l
1	16.8(n= 6)[*]	19.7(n=14)
2	13.7(n=24)	61.8(n=22)[°]
3	34.8(n=28)	177.7(n=25)[°]
6	69.0(n=29)	291.1(n=25)[°]
7	857.4(n=31)	6736.5(n=22)[°]

[*] Responders only [°] $p < 0.05$ Wilcoxon's rank sum test

TABLE III

DETERMINATION OF SUBDETERMINANT SPECIFIC ANTIBODIES AFTER VACCINATION WITH RECOMBINANT VACCINE (10 µg) AND PLASMA-DERIVED VACCINE (20 µg) AS DETERMINED BY SPECIFIC ABSORPTION

Month	Recombinant vaccine			Plasma-derived vaccine		
	No. samples	% anti-HBs/a (range)	% anti-HBs/d	No. samples	% anti-HBs/a (range)	% anti-HBs/d
1	4	60(19- 92)[*]	39	6	57(22- 99)	42
2	9	81(40- 98)	17	15	83(25- 99)	17
3	18	95(74-100)	5	23	88(26-100)	11
6	26	99(89-100)	1	24	94(43-100)	6
7	31	99(90-100)	1	22	97(91-100)	3

[*] Determination of anti-HBs/a and anti-HBs/d was limited by the minimum amount of 25 IU/l anti-HBs.

month 7 the proportion of anti-HBs/a antibodies was at least 90%. In sera with anti-HBs $\geq$ 10 IU/l at month 1, two out of four in the recombinant vaccine group and three out of six in the plasma-derived vaccine group had less than 50% anti-HBs/a. In only two cases, one in each group, the anti-HBs/a percentage at month 1 was above 90, suggesting an anamnestic response. Geometric mean titres for those vaccinees with a positive anti-HBs response

at month 1 increased to 11158 IU/l (n=6) in sera from the recombinant vaccine group and to 13748 IU/l (n=13) in sera from the plasma-derived vaccine group, both at month 7.

DISCUSSION

Table IV compares the results of the immunicity of recombinant hepatitis B vaccine of Merck, Sharp and Dohme in our study with results of others as recently published. [5 6 7 8] Several lots of vaccine with minor differences in the purification procedure were used. Comparison is made in some studies with earlier results using plasma-derived vaccine from the same manufacturer. In our study vaccination with recombinant vaccine and plasma-derived vaccine took place simultaneously. Serum samples could therefore be handled similarly and investigated with the same batch of reagents.

We found anti-HBs development during the first six months following the first injection very similar to Scolnick et al.[5] and Jilg et al.[6]. After the booster injection at month 6 we found a lower geometric mean titre than observed by others. The proportion of anti-HBs/a antibodies, however, was very similar for the two vaccine groups and increased from 60% at month 1 to about 100% at month 7.

Interestingly, we noted high titres of anti-HBs at month 7 for those vaccinees who had already shown seroconversion at month 1. Titres in this subgroup were comparable to those in early responders in the plasma-derived vaccine group. Since we had the lowest seroconversion rate at month 1 observed so far for recombinant vaccine (19%), this may explain the low geometric mean titre at month 7. The reason for the initial low conversion rate in our study is unknown. Sex and age differences with other study groups may have contributed. Sex and age effects may have their most pronounced influence on vaccination of weak responders.[16 17] The highest seroconversion rate (67%) and the highest geometric mean titre (2749 IU/l) at month 7 were observed by Papaevangelou et al.[9] in male recruits aged 17-19 years.

If our observations can be confirmed in more extended studies, equalizing the dose of HBsAg in the recombinant vaccine preparation to that of the plasma-derived vaccine may favourably influence the seroconversion rate at month 1 and the amount of anti-HBs produced after three injections.

ACKNOWLEDGEMENT

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TABLE IV

IMMUNE RESPONSE AFTER VACCINATION WITH RECOMBINANT AND PLASMA-DERIVED HEPATITIS B VACCINE AS COMPARED FROM LITERATURE

Authors	Dose	Geometric mean titres in IU/l Month 1	3	6	7	No.	Mean age	No. of men	No. of women	Lot no.
Recombinant vaccine										
Scolnick et al.[5]	10 µg	8	56	68	1905	15	33,23-53	10	5	934
Jilg et al.[6]	10 µg	9	29	68	2135	30	25,21-34	13	17	934
Papaevangelou et al.[8]	10 µg	11	198	189	2749	55	17-19	55		979
Davidson and Krugman[7]	10 µg	42	145	321	1911	51	21-30			972
Present study	10 µg	17	35	69	857	31	32,20-59	14	17	972
Plasma-derived vaccine										
Jilg et al.[6]	20 µg	15	164	263	4299	41	25,21-32	18	23	
Present study	20 µg	20	177	291	6737	25	30,22-53	12	13	
Papaevangelou et al.[8]	10 µg	4	278	492	9227	50				

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PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 808
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 972/C-K444 (10 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Richard E. Sampliner, M.D. Chief, Gastroenterology 111 G, Veterans Administration Medical Center Tucson, Arizona 85723
SECONDARY INVESTIGATOR:	Timothy R. Morgan, M.D. Chief, Gastroenterology Veterans Administration Medical Center Tucson, Arizona 85723
STUDY LOCATION:	Veterans Administration Medical Center Tucson, Arizona 85723 Arizona Health Sciences Center Tucson, Arizona 85723
DATE STUDY INITIATED:	April 3, 1984
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 25 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc, anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.
STUDY PROCEDURE:	Eligible study participants receive a 1.0 ml (10 mcg HBsAg) intramuscular injection of vaccine at 0, 1 and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

Study 808

STUDY PROCEDURE: (Contd)

A blood sample is obtained from each study participant approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12, and 24 months.

All samples are assayed for HBsAg, anti-HBc, anti-HBs and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer ≥25 mIU/ml may be tested for anti-a and anti-d subtype specificity.

RESULTS:

HEALTH CARE PERSONNEL

10 mcg Lot 972/C-K444 at 0, 1 and 6 months.

1. Number Vaccinated:

Injection No.		
1	2	3
25	25	25

One person who was initially anti-HBs positive received vaccine. The subject did not display a boost in titer after one injection of vaccine. A >50 fold rise in titer was seen after two injections.

One person who was anti-HBc positive prior to vaccination and 1 month post vaccination received vaccine. In all subsequent serum samples the person was anti-HBc negative. The subject remained HBsAg negative with normal ALT levels through 9 months of follow-up and became anti-HBs positive at 2 months. There has been no report of clinical illness in this individual.

2. Serologic Results:

Serologic data at 7-8 months are available for 23 study participants.

Study 808

RESULTS: (Contd)

At 7-8 months, 96% (22/23) vaccine recipients seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 1711.5 mIU/ml at that time. Among responders with a titer of S/N ≥2.1 and mIU/ml ≥10 the GMT was 2535.7 mIU/ml at 7-8 months.

By 12 months 95% (19/20) of the vaccinees retained an anti-HBs titer of S/N ≥2.1 and mIU/ml ≥10. The GMT for all vaccinees was 631.7 mIU/ml at that time.

Anti-HBs responses at 1 through 12 months are included in Table 1.

3. Clinical Results:

Clinical follow-up data are available for 25 study participants following the first two injections and for 24 participants following the third injection of vaccine. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 2 and 3. In summary:

	% Frequency by Injection No.		
Clinical Complaint	1	2	3
Injection Site	20 (5/25)	12 (3/25)	21 (5/24)
Systemic	36 (9/25)	8 (2/25)	0 (0/24)

No serious or alarming adverse reactions attributable to vaccination have been reported.

ALT Elevations

Alanine aminotranferase levels were normal in all vaccine recipients except for elevations approximately 1.5 - 2 times normal, in three participants. Case no. (b)(6) had an ALT level of 62

Study 808

RESULTS: (Contd)

at 8 months. To date subsequent ALT levels for this individual have not been reported. Case nos. (b)(6) had transient ALT levels of 64 and 90, respectively, at 1 month. All subsequent samples through 8 months of follow-up were normal. A reason for the ALT elevations was not ascertained. None of the subjects has showed any clinical or serologic signs (HBsAg or anti-HBc)of hepatitis B.

HBV Markers (Anti-HBc)

One vaccine recipient had a 2 month post-vaccination serum sample positive for anti-HBc. The same serum sample was reported negative on retest. All subsequent samples through 12 months were negative. The subject remained HBsAg negative with normal ALT levels. There has been no report of clinical illness in this individual.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK444
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	46%	(11/24)	33%	(8/24)	2.6	27.9	61.6
2 MONTHS	87%	(20/23)	70%	(16/23)	57.6	126.8	270.8
3 MONTHS	90%	(19/21)	81%	(17/21)	65.0	114.4	186.9
6 MONTHS	91%	(21/23)	83%	(19/23)	83.3	136.8	195.0
7/8 MONTHS	96%	(22/23)	96%	(22/23)	1711.5	2535.7	2535.7
12 MONTHS	95%	(19/20)	95%	(19/20)	631.7	945.1	945.1

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	5 (20.0%)	3 (12.0%)	2 (8.0%)	2 (8.0%)	2 (8.0%)	1 (4.0%)	5 (20.0%)
PAIN	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
SORENESS	3 (12.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	4 (16.0%)
TENDERNESS	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	2 (8.0%)
NODULE FORMATION	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
ECCHYMOSIS	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SYSTEMIC	4 (16.0%)	4 (16.0%)	2 (8.0%)	3 (12.0%)	2 (8.0%)	2 (8.0%)	9 (36.0%)
WHOLE BODY/GENERAL	3 (12.0%)	1 (4.0%)	2 (8.0%)	3 (12.0%)	1 (4.0%)	0 (0.0%)	4 (16.0%)
FEVER (TEMP. NOT REPORTED)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
FATIGUE/WEAKNESS	2 (8.0%)	1 (4.0%)	2 (8.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	2 (8.0%)
HEADACHE	2 (8.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
RESPIRATORY	0 (0.0%)	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	3 (12.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SINUSITIS	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)
MUSCULOSKELETAL	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	4 (16.0%)
MYALGIA	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
NECK PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)
SHOULDER PAIN	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
NECK STIFFNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)
MYASTHENIA	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PERSONS WITH COMPLAINTS	8 (32.0%)	5 (20.0%)	4 (16.0%)	5 (20.0%)	4 (16.0%)	3 (12.0%)	10 (40.0%)
PERSONS WITH NO COMPLAINTS	17 (68.0%)	20 (80.0%)	21 (84.0%)	20 (80.0%)	21 (84.0%)	22 (88.0%)	15 (60.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	2 (8.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)
SORENESS	2 (8.0%)	2 (8.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)
SYSTEMIC	2 (8.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
WHOLE BODY/GENERAL	1 (4.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
FEVER (TEMP. NOT REPORTED)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
FATIGUE/WEAKNESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
HEADACHE	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
DIGESTIVE SYSTEM	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
ABDOMINAL PAINS/CRAMPS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
NERVOUS SYSTEM	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
VERTIGO/DIZZINESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PERSONS WITH COMPLAINTS	3 (12.0%)	3 (12.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	4 (16.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO COMPLAINTS	22 (88.0%)	22 (88.0%)	24 (96.0%)	24 (96.0%)	25 (100.0%)	25 (100.0%)	21 (84.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

00355

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	5 (20.8%)	1 (4.2%)	2 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (20.8%)
SORENESS	4 (16.7%)	1 (4.2%)	2 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (16.7%)
TENDERNESS	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
PERSONS WITH COMPLAINTS	5 (20.8%)	1 (4.2%)	2 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (20.8%)
PERSONS WITH NO COMPLAINTS	19 (79.2%)	23 (95.8%)	22 (91.7%)	24 (100.0%)	23 (100.0%)	24 (100.0%)		19 (79.2%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
< 99	20 (83.3%)	21 (84.0%)	23 (92.0%)	22 (88.0%)	20 (90.9%)	18 (85.7%)			18 (72.0%)
99 - 99.9	4 (16.7%)	4 (16.0%)	2 (8.0%)	3 (12.0%)	2 (9.1%)	2 (9.5%)			6 (24.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)			1 (4.0%)
TEMPERATURE TAKEN	24 (96.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	22 (88.0%)	21 (84.0%)			25 (100.0%)
TEMPERATURE NOT TAKEN	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (12.0%)	4 (16.0%)			0 (0.0%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (5.3%)		1 (4.8%)
< 99	19 (90.5%)	19 (90.5%)	19 (90.5%)	18 (85.7%)	19 (90.5%)	17 (89.5%)		15 (71.4%)
99 - 99.9	1 (4.8%)	1 (4.8%)	1 (4.8%)	2 (9.5%)	1 (4.8%)	1 (5.3%)		5 (23.8%)
TEMPERATURE TAKEN	21 (84.0%)	21 (84.0%)	21 (84.0%)	21 (84.0%)	21 (84.0%)	19 (76.0%)		21 (84.0%)
TEMPERATURE NOT TAKEN	4 (16.0%)	4 (16.0%)	4 (16.0%)	4 (16.0%)	4 (16.0%)	6 (24.0%)		4 (16.0%)

00358

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0808
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH MAX TEMP
< 99	14 (100.0%)	13 (92.9%)	13 (100.0%)	12 (100.0%)	10 (90.9%)	13 (100.0%)		12 (85.7%)
99 - 99.9	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)		2 (14.3%)
TEMPERATURE TAKEN	14 (56.0%)	14 (56.0%)	13 (52.0%)	12 (48.0%)	11 (44.0%)	13 (52.0%)		14 (56.0%)
TEMPERATURE NOT TAKEN	11 (44.0%)	11 (44.0%)	12 (48.0%)	13 (52.0%)	14 (56.0%)	12 (48.0%)		11 (44.0%)

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 809
PURPOSE:	To evaluate antibody and clinical responses to various doses of vaccine in the following initially seronegative populations: 1. Healthy Children (1-11 years of age) 2. Healthy Adults
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot # 972/C-K444 (10 mcg HBsAg/ml) 985/C-K732 (5 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Drs. Stanley Plotkin and Stuart Starr Division of Preventive Medicine Joseph Stokes, Jr. Research Institute Children's Hospital of Philadelphia 34th Street and Civic Center Blvd. Philadelphia, PA 19104
STUDY LOCATIONS:	The Pediatric Medical Associates 420 Township Line Road Havertown, PA 19083 George A. Starkweather, M.D. 1001 Pennsylvania Avenue Havertown, PA 19083
DATE INITIATED:	February 2, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population consists of healthy children (ages 1-11 years) and healthy adults who are negative for HBsAg, anti-HBc, and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.
PROCEDURE:	Children in the study receive a 0.5 ml (5 mcg HBsAg) or a 0.25 ml (2.5 mcg HBsAg) intramuscular injection of lot # 972/C-K444 vaccine at 0, 1 and 6 months or a 0.5 ml (2.5 mcg HBsAg) or 0.25 ml (1.25 mcg HBsAg) injection of lot # 985/C-K732 vaccine according to the

Study 809

PROCEDURE (Contd): the same time schedule. Adults receive a 1.0 ml (10 mcg HBsAg) intramuscular injection of lot # 972/C-K444 vaccine at 0, 1 and 6 months. Vaccine recipients (or the parent or guardian in the case of a minor) are asked to record their temperature daily for five days after each injection of vaccine and to record any local or systemic complaints that they may have during this period.

A blood specimen (10-15 ml) is obtained from each prospective vaccine recipient one to two weeks before the first vaccination. Post-vaccination bleedings are obtained at 1, 3, 7 and 12 months from some of the children and at 2, 6, 8 and 12 months from others. Post-vaccination bleedings are obtained from adult vaccine recipients at 1, 2, 3, 6, 8, 12 and 24 months. The samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may also be tested for yeast antibody and those with an anti-HBs titer $\geq$ 25 mIU/ml may be tested for the proportions of anti-a and anti-d activity.

RESULTS:

HEALTHY ADULTS:

10 mcg Lot # 972/C-K444 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
18	17	17

2. Serologic Results:

Serologic data are available for 11 participants at 7/8 months. One hundred percent (11/11) of the subjects seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10) at that time. The GMT at 7/8 months for all vaccinees was 955.7 mIU/ml.

Among the participants with serology data available at 12 months, 100% (12/12) were positive for anti-HBs (mIU/ml $\geq$10). The GMT for all vaccinees was 448.7 mIU/ml.

Study 809

RESULTS (Contd): Refer to Table 1 for anti-HBs responses and GMTs for other time intervals.

3. Clinical Complaints:

Clinical follow-up data are available for at least 17 participants after each injection. The overall frequencies of complaints are presented below.

Type of Complaint	Frequency in % by Injection No. 1	2	3
Injection Site	17(3/18)	24(4/17)	6(1/17)
Systemic	6(1/18)	6(1/17)	12(2/17)

Refer to Table 2 for listings of specific clinical complaints by injection number. Maximum temperature data are provided in Tables 3.

There were no serious or alarming reactions attributable to vaccine.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0989
POPULATION : HEALTHY ADULTS
DOSE : 10 MCG
LOT : CR443
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL STATUS : NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	7.1%	(1/14)	0%	(0/14)	0.4	1.9	
2 MONTHS	67%	(4/6)	33%	(2/6)	7.7	32.7	184.9
3 MONTHS	71%	(5/7)	71%	(5/7)	7.2	25.9	25.9
6 MONTHS	93%	(14/15)	80%	(12/15)	33.7	44.9	66.0
7/8 MONTHS	100%	(11/11)	100%	(11/11)	955.7	955.7	955.7
12 MONTHS	100%	(12/12)	92%	(11/12)	448.7	448.7	697.5

00363

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (18 PATIENTS) - DOSE 1							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	3 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (16.7%)
SORENESS	2 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (11.1%)
STIFFNESS/TIGHTNESS	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.6%)
SYSTEMIC	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.6%)
WHOLE BODY/GENERAL	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.6%)
FEVER (TEMP. NOT REPORTED)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.6%)
HEADACHE	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.6%)
PERSONS WITH COMPLAINTS	3 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (16.7%)
PERSONS WITH NO COMPLAINTS	15 (83.3%)	18 (100.0%)	18 (100.0%)	18 (100.0%)	18 (100.0%)	18 (100.0%)		15 (83.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (17 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	4 (23.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (23.5%)
SORENESS	4 (23.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (23.5%)
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)	0 (0.0%)		1 (5.9%)
PERSONS WITH COMPLAINTS	4 (23.5%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		4 (23.5%)
PERSONS WITH NO COMPLAINTS	13 (76.5%)	17 (100.0%)	17 (100.0%)	16 (94.1%)	16 (94.1%)	16 (94.1%)		13 (76.5%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00365

Table 2 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (17 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
SORENESS	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
SYSTEMIC	1 (5.9%)	1 (5.9%)	2 (11.8%)	2 (11.8%)	1 (5.9%)	0 (0.0%)		2 (11.8%)
RESPIRATORY	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	0 (0.0%)		1 (5.9%)
UPPER RESPIRATORY INFECT., NOS	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	0 (0.0%)		1 (5.9%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (5.9%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
NECK PAIN	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
SHOULDER PAIN	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
ARM PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
OTHER	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)		1 (5.9%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (17 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
PERSONS WITH COMPLAINTS	1 (5.9%)	1 (5.9%)	3 (17.6%)	2 (11.8%)	1 (5.9%)	0 (0.0%)		3 (17.6%)
PERSONS WITH NO COMPLAINTS	16 (94.1%)	16 (94.1%)	14 (82.4%)	15 (88.2%)	16 (94.1%)	17 (100.0%)		14 (82.4%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (18 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	2 (18.2%)	3 (21.4%)	3 (23.1%)	3 (23.1%)	3 (21.4%)	3 (21.4%)			3 (21.4%)
< 99	7 (63.6%)	10 (71.4%)	10 (76.9%)	8 (61.5%)	11 (78.6%)	9 (64.3%)			6 (42.9%)
99 - 99.9	1 (9.1%)	1 (7.1%)	0 (0.0%)	2 (15.4%)	0 (0.0%)	2 (14.3%)			4 (28.6%)
101 - 101.9	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (7.1%)
TEMPERATURE TAKEN	11 (61.1%)	14 (77.8%)	13 (72.2%)	13 (72.2%)	14 (77.8%)	14 (77.8%)			14 (77.8%)
TEMPERATURE NOT TAKEN	7 (38.9%)	4 (22.2%)	5 (27.8%)	5 (27.8%)	4 (22.2%)	4 (22.2%)			4 (22.2%)

Table 3 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (17 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	0 (0.0%)	1 (10.0%)	1 (10.0%)	1 (10.0%)	1 (11.1%)	2 (22.2%)			0 (0.0%)
< 99	10 (100.0%)	8 (80.0%)	7 (70.0%)	8 (80.0%)	8 (88.9%)	6 (66.7%)			6 (60.0%)
99 - 99.9	0 (0.0%)	1 (10.0%)	2 (20.0%)	1 (10.0%)	0 (0.0%)	1 (11.1%)			4 (40.0%)
TEMPERATURE TAKEN	10 (58.8%)	10 (58.8%)	10 (58.8%)	10 (58.8%)	9 (52.9%)	9 (52.9%)			10 (58.8%)
TEMPERATURE NOT TAKEN	7 (41.2%)	7 (41.2%)	7 (41.2%)	7 (41.2%)	8 (47.1%)	8 (47.1%)			7 (41.2%)

Table 3 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 10 MCG
PATIENT CLASS: HEALTHY ADULTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (17 PATIENTS) - DOSE 3 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	1 (12.5%)	1 (12.5%)	2 (28.6%)	1 (12.5%)	2 (25.0%)	1 (12.5%)			1 (12.5%)
< 99	6 (75.0%)	6 (75.0%)	4 (57.1%)	7 (87.5%)	5 (62.5%)	7 (87.5%)			6 (75.0%)
99 - 99.9	1 (12.5%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)			0 (0.0%)
101 - 101.9	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (12.5%)
TEMPERATURE TAKEN	8 (47.1%)	8 (47.1%)	7 (41.2%)	8 (47.1%)	8 (47.1%)	8 (47.1%)			8 (47.1%)
TEMPERATURE NOT TAKEN	9 (52.9%)	9 (52.9%)	10 (58.8%)	9 (52.9%)	9 (52.9%)	9 (52.9%)			9 (52.9%)

PROGRAM: Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 811.

PURPOSE: To evaluate antibody and clinical responses to several dose levels of commercial hepatitis B plasma derived vaccine (H-B-VAX) and yeast recombinant hepatitis B vaccine in the following populations who are initially seronegative for hepatitis B virus markers:

1. Predialysis Patients
2. Health Care Personnel

VACCINE: Yeast Recombinant Hepatitis B Vaccine
Lot # 974/C-K446 (20 mcg HBsAg/ml)

Hepatitis B Plasma Vaccine
Lot # 1510J (20 mcg HBsAg/ml)

PRINCIPAL INVESTIGATOR:
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Study 811

SECONDARY INVESTIGATORS: (Cont.)	K. Zaruba, M.D., P.D. Hemodialysis Station City Hospital Waid Zurich W. Herwig, M.D. Hemodialysis Station Kantonsspital Chur H.-J. Gloor, M.D. Hemodialysis Station Kantonsspital Schaffhausen J. Nadig, M.D. Hemodialysis Unit Kantonsspital Winterthur H. I. Joller-Jemelka, M.D. Section of Clinical Immunology Department of Medicine University Hospital Zurich
STUDY LOCATION:	University Hospital Haldeliweg 4 CH - 8044 Zurich Switzerland
DATE INITIATED:	April 10, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	One study population consists of 59 predialysis patients who have renal disease with functional impairment or end-stage renal disease that will shortly require dialysis treatment. The other population is comprised of 11 health care personnel. Subjects in both populations must be adults of either sex (pregnant women excluded). They must be initially negative for all hepatitis B serologic markers, have a normal ALT level, and must not previously have received any hepatitis B vaccine.

Study 811

PROCEDURE:

Patients are randomly assigned to one of 5 groups. Health care personnel constitute a sixth group.

Group	Vaccine/Dose/Regimen
1	Recombinant vaccine; 0.5 ml (10 mcg) at 0, 1 and 6 months
2	Recombinant vaccine; 1.0 ml (20 mcg) at 0, 1 and 6 months
3	Recombinant vaccine; 2x1.0 ml (40 mcg) at 0, 1 and 6 months
4	H-B-VAX; 1.0 ml (20 mcg) at 0, 1 and 6 months
5	H-B-VAX; 2x1.0 ml (40 mcg) at 0, 1 and 6 months
6	Recombinant vaccine; 0.5 ml (10 mcg) at 0, 1 and 6 months

All injections will be intramuscular. Patients in Groups 3 and 5 will have the vaccine administered in divided dose (i.e., 2 injections - one injection in each of two contralateral limbs).

Vaccine recipients will be asked to record their temperature for 5 days after each injection and to note any local or systemic complaints. Study participants will be bled 1 to 10 days prior to vaccination to verify eligibility for the study.

Follow-up samples will be obtained at 1, 3, 6 and 8 months following the initial vaccine injection. Blood samples will also be obtained at 12 and 24 months from subjects who are positive for anti-HBs at 8 months. All serum samples will be assayed for anti-HBc, anti-HBs, HBsAg and ALT by the investigator, and may be assayed for yeast antibody at MSDRL. In addition, participants who show an anti-HBs titer $\geq$ 25 mIU/ml will have their serum tested to determine the proportions of anti-a and anti-d activity.

Study 811

RESULTS:

HEALTH CARE PERSONNEL

10 mcg Lot #974/C-K446 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
11	8	8

2. Serologic Results:

Serology data are available for seven participants at 7/8 months. Eighty-six percent (6/7) of the subjects seroconverted for anti-HBs (S/N ≥2.1) at that time. Eighty-three percent (5/6) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT at 7/8 months for all vaccinees was 275.1 mIU/ml and 1076.6 mIU/ml for responders with a titer of mIU/ml ≥10.

Among subjects with serology data available at 12 months, 83% (5/6) were positive for anti-HBs (mIU/ml ≥10). The GMT at that time was 44.1 mIU/ml for all vaccinees and 324.9 mIU/ml for responders with a titer of mIU/ml ≥10.

Refer to Table 1 for anti-HBs responses and GMTs through 12 months of follow-up.

3. Clinical Complaints:

Clinical follow-up data are available for at least six participants after each injection. The overall frequencies of complaints are presented below.

Type of Complaint	Frequency in % by Injection No.		
	1	2	3
Injection Site	0(0/7)	0(0/7)	0(0/6)
Systemic	28(2/7)	0(0/7)	17(1/6)

Study 811

RESULTS (CONT.): Listings of specific clinical complaints are not presently available. There have been no reports of serious or alarming reactions attributable to vaccine.

Table 1.

Antibody Responses Among Health Care Personnel
Following Vaccination with 10 mcg Injections of Yeast Recombinant
Hepatitis B Vaccine Lot # 974/C-K446 at 0, 1, and 6 Months
in Study B11

Time (Months)	% (Proportion) with Anti-HBs		GMT (mIU/ml)		
	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	Responders S/N ≥ 2.1	Responders mIU/ml ≥ 10
1	0 (0/9)	0 (0/9)	0.3	---	---
3	38 (3/8)	38 (3/8)	2.4	77.5	77.5
6	38 (3/8)	25 (2/8)	2.2	63.1	225.0
7/8	86 (6/7)	83 (5/6)*	275.1*	1076.6*	1076.6*
12	83 (5/6)	83 (5/16)	44.1	324.9	324.9

* Based on 6 subjects (5 responders) for whom numeric titers are available.

STUDY 813

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 813
PURPOSE:	To evaluate antibody and clinical responses to several dose levels of yeast recombinant hepatitis B vaccine among the following populations: 1. Health Care Personnel (Seronegative) 2. Preimmune Adults
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 972/C-K444 (10 mcg HBsAg/ml) Lot 81954I/18071/C-L220 (10 mcg HBsAg/0.5 ml) Lot 85860/22123/C-M125 (20 mcg HBsAg/ml) Lot 85861/22124/C-M126 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Morton Davidson, M.D. New York University Medical Center University Hospital 560 First Avenue New York, NY 10016
SECONDARY INVESTIGATOR:	Saul Krugman, M.D. Professor Department of Pediatrics New York University Medical Center 550 First Avenue New York, NY 10016
STUDY LOCATION:	New York University Medical Center University Hospital 560 First Avenue New York, NY 10016
DATE INITIATED:	February 1, 1984
DATE COMPLETED:	In progress.

Study 813

STUDY POPULATIONS: Under the original protocol and subsequent addenda, the following groups of health care personnel are included in the study. Participants may be of either sex, but pregnant women are excluded. Initially seronegative subjects have not previously received any hepatitis B vaccine.

Addendum No.	Characteristics	Number	Vaccine Lot No.#	Regimen
Initial protocol	Initially seronegative	50	972/C-K444	10 mcg (1.0 ml) at 0, 1, and 6 months
Add. #1	Initially seronegative	50	972/C-K444	5 mcg (0.5 ml) at 0, 1, and 6 months
Add. #2	Initially seronegative	50	972/C-K444	2.5 mcg (0.25 ml) at 0, 1, and 6 months
Add. #3	Initially seronegative	50	81954I/18071/ C-L220	10 mcg (0.5 ml) at 0, 1, and 6 months
Add. #4	Initially seronegative	50	81954I/18071/ C-L220	5 mcg (0.25 ml) at 0, 1, and 6 months
Add. #5	Initially seronegative; ≥40 years of age	50	85860/22123/ C-M125	20 mcg (1.0 ml) at 0, 1, and 6 months
Add. #5	Initially seronegative; ≥40 years of age	50	85861/22124/ C-M126	10 mcg (1.0 ml) at 0, 1, and 6 months
Add. #6	Vaccinated 3-5 yrs previously with plasma derived hepatitis B vaccine (HEPTAVAX-B)	100	85861/22124/ C-M126	10 mcg (1.0 ml) at time 0
Add. #7	Vaccinated previously with three 2.5 mcg doses of recombinant vaccine under Add. #2.	50	85861/22124/ C-M126	5 mcg (0.5 ml) or 10 mcg (1.0 ml) at time 0

Study 813

PROCEDURE:

Participants receive intramuscular injections of vaccine according to the regimens outlined above under STUDY POPULATIONS. Those enrolled under addendum #5 who fail to develop antibody following 3 injections of vaccine or have only a transient response that becomes negative by 12 months after the first dose may receive a fourth injection of vaccine.

Participants will be asked to record their temperature for 5 days after each injection of vaccine and to note any local or systemic complaints. Unexpected or serious reactions are to be reported immediately to the study physician.

Blood samples will be obtained from the initially seronegative groups prior to and on the day of the first vaccination. Follow-up samples will be obtained 1, 2, 3, 6, 8, 12 and 24 months after the initial injection of vaccine (initial protocol and addenda #1-5). Follow-up samples from persons vaccinated under addendum #6 are only taken 1 month after vaccination while persons enrolled under addendum #7 have blood samples taken 2 weeks, 4 weeks, and 6 months after vaccination.

Blood samples will be assayed for HBsAg, anti-HBc, anti-HBs and ALT by Dr. Krugman's laboratory and may be assayed for yeast antibody by the Merck Sharp and Dohme Research Laboratories. Samples with an anti-HBs titer $\geq$25 mIU/ml may be tested to determine the relative proportions of anti-a and anti-d activity.

RESULTS:

HEALTH CARE PERSONNEL:

2.5 mcg lot 972/C-K444 at 0, 1, and 6 months
5.0 mcg lot 972/C-K444 at 0, 1, and 6 months
5.0 mcg lot 1807I/C-L220 at 0, 1, and 6 months
10.0 mcg lot 972/C-K444 at 0, 1, and 6 months
10.0 mcg lot 1807I/C-L220 at 0, 1, and 6 months
10.0 mcg lot 22124/C-M126 at 0, 1, and 6 months
20.0 mcg lot 22123/C-M125 at 0, 1, and 6 monts

Study B13

RESULTS:

1. Number Vaccinated:

Dose Level	Lot	Injection No. 1	2	3	
2.5 mcg	C-K444	61	61	60	(Addendum #2)
5.0 mcg	C-K444	60	59	58	(Addendum #1)
5.0 mcg	C-L220	61	61	57	(Addendum #4)
10.0 mcg	C-K444	62	59	53	(Initial Protocol)
10.0 mcg	C-L220	62	62	56	(Addendum #3)
10.0 mcg	C-M126	7	3	--	(Addendum #5)
20.0 mcg	C-M125	7	4	--	(Addendum #5)

2. Serologic Results:

Seven/eight month serologic data are available for 40, 43, and 36 participants in the 2.5 mcg, 5 mcg, and 10 mcg dose regimens, respectively. Anti-HBs responses at that time are summarized below:

Dose Level	% with Anti-HBs S/N ≥2.1	% with Anti-HBs mIU/ml ≥10	GMT (mIU/ml) All Vaccinees	GMT (mIU/ml) Responders S/N ≥2.1	GMT (mIU/ml) Responders mIU/ml ≥10
2.5 mcg	100 (40/40)	97 (39/40)	291.5	291.5	321.5
5 mcg	98 (42/43)	95 (41/43)	523.8	625.7	693.9
10 mcg	100 (36/36)	100 (36/36)	1509.3	1509.3	1509.3

Serologic results are not presently available for the 7 participants who have received 20 mcg injections of vaccine.

Refer to Table 1 for anti-HBs responses and GMTs, by dose regimen, through 12 months of follow-up.

Study 813

RESULTS: (Contd)

3. Clinical Complaints

Clinical follow-up data are available for at least 60, 78, 77, and 2 participants after each injection in the 2.5 mcg, 5 mcg, 10 mcg, and 20 mcg dose regimens, respectively. The overall frequencies of complaints are presented below

Type of Complaint	Dose Level	Frequency in % by Injection 1	2	3
Injection site	2.5 mcg	21 (13/61)	12 (7/61)	5 (3/60)
	5 mcg	22 (27/121)	11 (13/119)	12 (9/78)
	10 mcg	30 (38/129)	15 (18/119)	17 (13/77)
	20 mcg	0 (0/6)	0 (0/2)	
Systemic	2.5 mcg	13 (8/61)	3 (2/61)	2 (1/60)
	5 mcg	17 (20/121)	13 (15/119)	6 (5/78)
	10 mcg	16 (20/129)	11 (13/119)	5 (4/77)
	20 mcg	17 (1/6)	50 (1/2)	

Refer to Tables 2 through 5 for listings of specific clinical complaints by injection and dose regimen. Maximum temperature data are presented in Tables 6 through 9.

Reaction Possibly Related to Vaccine

A 23 year-old female developed pruritic hives on her back and legs within 24 hours of receiving the first 10 mcg injection of vaccine lot C-L220. All symptoms resolved by day 4 post vaccination. The subject received the second injection of vaccine and within 24 hours again developed hives on her back, arms and left hand. All symptoms resolved by day 4 post vaccination. She received the third injection of vaccine with no evidence of hives. The subject's medical history is significant for an allergy to contrast dye (developed hives during administration of dye for CAT scan). The development of hives post injections one and two is considered probably vaccine related.

Study 813

PUBLICATIONS:

Davidson M, Krugman S. Immunogenicity of recombinant yeast hepatitis B vaccine. Lancet 1985; 1:108-9.

Davidson M, Krugman S. Recombinant yeast hepatitis B vaccine: Side effects and immunogenicity compared with plasma-derived hepatitis B vaccine. Submitted for publication to Hepatitis Scientific Memoranda.

Table 1

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10, 5, and 2.5 mcg Injections of Yeast Recombinant Hepatitis B Vaccine at 0, 1, and 6 Months in Study 813

	10 mcg					5 mcg					2.5 mcg				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
Time Months	S/N≥2.1	mIU/ml≥10	All Vaccinees	----Responders -- S/N≥2.1	mIU/ml≥10	S/N≥2.1	mIU/ml≥10	All Vaccinees	----Responders---- S/N≥2.1	mIU/ml≥10	S/N≥2.1	mIU/ml≥10	All Vaccinees	--- Responders - S/N≥2.1	mIU/ml≥10
1	46(48/104)	24(25/104)	2.0	18.4	63.9	35(37/105)	20(21/105)	1.3	18.3	59.8	27(16/60)	15(9/60)	1.0	23.6	65.9
2	89(86/97)	72(70/97)	24.9	43.7	70.9	85(84/99)	55(54/99)	14.4	28.7	79.8	71(37/52)	44(23/52)	7.0	25.2	65.0
3	92(87/95)	86(82/95)	56.5	89.1	108.1	92(93/101)	80(81/101)	30.9	46.0	63.7	86(48/56)	63(35/56)	17.0	33.3	63.2
6	97(89/92)	93(86/92)	95.7	116.2	129.2	93(94/101)	84(85/101)	45.8	66.6	85.0	86(49/57)	70(40/57)	17.2	32.1	46.9
7/8	100(36/36)	100(36/36)	1509.3	1509.3	1509.3	98(42/43)	95(41/43)	523.8	625.7	693.9	100(40/40)	97(39/40)	291.5	291.5	321.5
12	96(43/45)	96(43/45)	313.5	433.1	433.1	98(56/57)	91(52/57)	212.5	239.0	326.7	96(45/47)	87(41/47)	98.1	127.0	172.3

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (61 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	11 (18.0%)	8 (13.1%)	5 (8.2%)	2 (3.3%)	2 (3.3%)	2 (3.3%)		13 (21.3%)
SORENESS	2 (3.3%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (4.9%)
TENDERNESS	9 (14.8%)	7 (11.5%)	4 (6.6%)	2 (3.3%)	2 (3.3%)	2 (3.3%)		9 (14.8%)
ERYTHEMA (REDNESS)	2 (3.3%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)		2 (3.3%)
WARMTH	2 (3.3%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)		2 (3.3%)
PRURITIS (ITCHING)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
SYSTEMIC	0 (0.0%)	3 (4.9%)	2 (3.3%)	3 (4.9%)	3 (4.9%)	4 (6.6%)		8 (13.1%)
WHOLE BODY/GENERAL	0 (0.0%)	2 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)		3 (4.9%)
SWEATING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)		1 (1.6%)
FATIGUE/WEAKNESS	0 (0.0%)	2 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)		3 (4.9%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	2 (3.3%)	1 (1.6%)	1 (1.6%)	2 (3.3%)		2 (3.3%)
RHINITIS	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.6%)		1 (1.6%)

00384

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (61 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)		1 (1.6%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	1 (1.6%)		1 (1.6%)
MUSCLE STIFFNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	1 (1.6%)		1 (1.6%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (1.6%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	1 (1.6%)		3 (4.9%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)		1 (1.6%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	1 (1.6%)		2 (3.3%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
DIMINISHED APPETITE	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
PERSONS WITH COMPLAINTS	11 (18.0%)	10 (16.4%)	7 (11.5%)	5 (8.2%)	5 (8.2%)	6 (9.8%)		20 (32.8%)
PERSONS WITH NO COMPLAINTS	50 (82.0%)	51 (83.6%)	54 (88.5%)	56 (91.8%)	56 (91.8%)	55 (90.2%)		41 (67.2%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00385

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (61 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	5 (8.2%)	3 (4.9%)	3 (4.9%)	1 (1.6%)	1 (1.6%)	0 (0.0%)		7 (11.5%)
SORENESS	2 (3.3%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.3%)
TENDERNESS	3 (4.9%)	2 (3.3%)	2 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (6.6%)
ERYTHEMA (REDNESS)	1 (1.6%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
PRURITIS (ITCHING)	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	0 (0.0%)		1 (1.6%)
SYSTEMIC	1 (1.6%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	0 (0.0%)	0 (0.0%)		2 (3.3%)
WHOLE BODY/GENERAL	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
HEADACHE	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (1.6%)	1 (1.6%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
WHEEZES	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
PERSONS WITH COMPLAINTS	6 (9.8%)	3 (4.9%)	4 (6.6%)	2 (3.3%)	1 (1.6%)	0 (0.0%)		9 (14.8%)

Table 2 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (61 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO COMPLAINTS	55 (90.2%)	58 (95.1%)	57 (93.4%)	59 (96.7%)	60 (98.4%)	61 (100.0%)	52 (85.2%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (60 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	3 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.0%)
TENDERNESS	3 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.0%)
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		1 (1.7%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		1 (1.7%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)		1 (1.7%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)		1 (1.7%)
PERSONS WITH COMPLAINTS	3 (5.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		4 (6.7%)
PERSONS WITH NO COMPLAINTS	57 (95.0%)	60 (100.0%)	60 (100.0%)	59 (98.3%)	59 (98.3%)	59 (98.3%)		56 (93.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (121 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	22 (18.2%)	12 (9.9%)	4 (3.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)		27 (22.3%)
INFLAMMATION	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
PAIN	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (1.7%)
SORENESS	14 (11.6%)	8 (6.6%)	3 (2.5%)	1 (0.8%)	0 (0.0%)	0 (0.0%)		17 (14.0%)
TENDERNESS	6 (5.0%)	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		7 (5.8%)
STIFFNESS/TIGHTNESS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
PRURITIS (ITCHING)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (1.7%)
ECCHYMOSIS	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
SYSTEMIC	14 (11.6%)	9 (7.4%)	6 (5.0%)	4 (3.3%)	4 (3.3%)	3 (2.5%)		20 (16.5%)
WHOLE BODY/GENERAL	9 (7.4%)	4 (3.3%)	4 (3.3%)	3 (2.5%)	3 (2.5%)	3 (2.5%)		13 (10.7%)
FEVER (TEMP. NOT REPORTED)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
SWEATING	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (121 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
FLUSH	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
FATIGUE/WEAKNESS	6 (5.0%)	2 (1.7%)	3 (2.5%)	2 (1.7%)	2 (1.7%)	2 (1.7%)		9 (7.4%)
MALAISE	3 (2.5%)	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (3.3%)
HEADACHE	2 (1.7%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		4 (3.3%)
LIGHTHEADED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
RESPIRATORY	3 (2.5%)	3 (2.5%)	1 (0.8%)	2 (1.7%)	2 (1.7%)	1 (0.8%)		5 (4.1%)
PHARYNGITIS (SORE THROAT)	1 (0.8%)	2 (1.7%)	1 (0.8%)	2 (1.7%)	1 (0.8%)	1 (0.8%)		3 (2.5%)
UPPER RESPIRATORY INFECT., NOS	2 (1.7%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)		2 (1.7%)
WHEEZES	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
MUSCULOSKELETAL	2 (1.7%)	3 (2.5%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (2.5%)
ARTHRITIS, MONOARTICULAR	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
ARTHRALGIA, MONOARTICULAR	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
ARTHRALGIA (OTHER)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (121 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
BACK PAIN	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
OTHER	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DIGESTIVE SYSTEM	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
NAUSEA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
ABDOMEN DISTENDED	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
NERVOUS SYSTEM	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
VERTIGO/DIZZINESS	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
IRRITABILITY	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
PERSONS WITH COMPLAINTS	34 (28.1%)	20 (16.5%)	9 (7.4%)	5 (4.1%)	4 (3.3%)	3 (2.5%)	41 (33.9%)
PERSONS WITH NO COMPLAINTS	87 (71.9%)	101 (83.5%)	112 (92.6%)	116 (95.9%)	117 (96.7%)	118 (97.5%)	80 (66.1%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (120 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	11 (9.2%)	5 (4.2%)	3 (2.5%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		13 (10.9%)
PAIN	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
SORENESS	8 (6.7%)	4 (3.4%)	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		8 (6.7%)
TENDERNESS	2 (1.7%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		3 (2.5%)
WHEAL/WHEAL AND FLARE	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
SYSTEMIC	3 (2.5%)	8 (6.7%)	7 (5.9%)	4 (3.4%)	3 (2.5%)	3 (2.5%)		15 (12.6%)
WHOLE BODY/GENERAL	2 (1.7%)	3 (2.5%)	1 (0.8%)	1 (0.8%)	2 (1.7%)	2 (1.7%)		9 (7.6%)
FEVER (TEMP. NOT REPORTED)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
FLUSH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)		1 (0.8%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)		2 (1.7%)
FATIGUE/WEAKNESS	1 (0.8%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (1.7%)		4 (3.4%)
MALAISE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.8%)

Table 3 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (120 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
HEADACHE	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.5%)
RESPIRATORY	0 (0.0%)	3 (2.5%)	4 (3.4%)	1 (0.8%)	0 (0.0%)	1 (0.8%)	5 (4.2%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	2 (1.7%)	3 (2.5%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	4 (3.4%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	2 (1.7%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
HEMIC AND LYMPHATIC	1 (0.8%)	1 (0.8%)	2 (1.7%)	2 (1.7%)	2 (1.7%)	1 (0.8%)	3 (2.5%)
LYMPHADENOPATHY, GENERAL	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	2 (1.7%)	1 (0.8%)	2 (1.7%)
LYMPHADENOPATHY, CERVICAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DIGESTIVE SYSTEM	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
DIARRHEA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
NAUSEA	0 (0.0%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
PERSONS WITH COMPLAINTS	13 (10.9%)	12 (10.1%)	9 (7.6%)	4 (3.4%)	3 (2.5%)	3 (2.5%)	24 (20.2%)
PERSONS WITH NO COMPLAINTS	106 (89.1%)	107 (89.9%)	110 (92.4%)	115 (96.6%)	116 (97.5%)	116 (97.5%)	95 (79.8%)

Table 3 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

	TOTAL VACCINEES (120 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						
CLINICAL COMPLAINTS	0	1	2	3	4	5	NUMBER WITH COMPLAINTS
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (115 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	8 (10.3%)	3 (3.8%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)		9 (11.5%)
SORENESS	2 (2.6%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.6%)
TENDERNESS	5 (6.4%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)		6 (7.7%)
PRURITIS (ITCHING)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
SYSTEMIC	2 (2.6%)	3 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (6.4%)
WHOLE BODY/GENERAL	1 (1.3%)	3 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (5.1%)
FATIGUE/WEAKNESS	0 (0.0%)	2 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.6%)
MALAISE	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
HEADACHE	1 (1.3%)	2 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (3.8%)
ACHINESS	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
HEMIC AND LYMPHATIC	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.3%)
LYMPHADENOPATHY, GENERAL	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.3%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (115 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH COMPLAINTS	9 (11.5%)	6 (7.7%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)		13 (16.7%)
PERSONS WITH NO COMPLAINTS	69 (88.5%)	72 (92.3%)	77 (98.7%)	77 (98.7%)	78 (100.0%)	78 (100.0%)		65 (83.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (132 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	27 (20.9%)	17 (13.2%)	10 (7.8%)	3 (2.3%)	2 (1.6%)	2 (1.6%)		38 (29.5%)
PAIN	2 (1.6%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (2.3%)
SORENESS	13 (10.1%)	7 (5.4%)	4 (3.1%)	2 (1.6%)	1 (0.8%)	1 (0.8%)		18 (14.0%)
TENDERNESS	11 (8.5%)	7 (5.4%)	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		15 (11.6%)
ERYTHEMA (REDNESS)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
ECCHYMOSIS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
RASH, NOS	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
SYSTEMIC	10 (7.8%)	11 (8.5%)	8 (6.2%)	6 (4.7%)	3 (2.3%)	3 (2.3%)		20 (15.5%)
WHOLE BODY/GENERAL	5 (3.9%)	3 (2.3%)	2 (1.6%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		8 (6.2%)
FEVER (TEMP. NOT REPORTED)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (1.6%)
FATIGUE/WEAKNESS	3 (2.3%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)		4 (3.1%)
MALAISE	1 (0.8%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (1.6%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (132 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
HEADACHE	1 (0.8%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (1.6%)
INFECTIOUS SYNDROMES	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
INFLUENZA, NOS	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
INTEGUMENTARY SYSTEM	1 (0.8%)	2 (1.6%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.3%)
URTICARIA/HIVES	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
PRURITIS/ITCHING	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
RASH, NOS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
RESPIRATORY	1 (0.8%)	2 (1.6%)	2 (1.6%)	2 (1.6%)	2 (1.6%)	2 (1.6%)	5 (3.9%)
RHINITIS	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.6%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	1 (0.8%)	2 (1.6%)	1 (0.8%)	2 (1.6%)	1 (0.8%)	3 (2.3%)
UPPER RESPIRATORY INFECT., NOS	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	3 (2.3%)
HEMIC AND LYMPHATIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
LYMPHADENOPATHY, CERVICAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

Table 4 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (132 PATIENTS) - DOSE 1						NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION						
	0	1	2	3	4	5	
MUSCULOSKELETAL	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
NECK STIFFNESS	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DIGESTIVE SYSTEM	3 (2.3%)	2 (1.6%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.9%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DIARRHEA	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)
NAUSEA	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)
VOMITING	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
OTHER	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
UROGENITAL SYSTEM	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	2 (1.6%)
URINARY TRACT INFECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
DYSURIA	0 (0.0%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
OTHER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
ORGANS OF SPECIAL SENSE	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

Table 4 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (132 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
BLURRED VISION	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
PERSONS WITH COMPLAINTS	32 (24.8%)	26 (20.2%)	17 (13.2%)	9 (7.0%)	5 (3.9%)	5 (3.9%)	49 (38.0%)
PERSONS WITH NO COMPLAINTS	97 (75.2%)	103 (79.8%)	112 (86.8%)	120 (93.0%)	124 (96.1%)	124 (96.1%)	80 (62.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

00400

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (125 PATIENTS) - DOSE 2						NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION						
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	13 (10.9%)	10 (8.4%)	7 (5.9%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	18 (15.1%)
PAIN	1 (0.8%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	3 (2.5%)
SORENESS	5 (4.2%)	4 (3.4%)	3 (2.5%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	6 (5.0%)
TENDERNESS	7 (5.9%)	4 (3.4%)	3 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (7.6%)
STIFFNESS/TIGHTNESS	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
SYSTEMIC	5 (4.2%)	9 (7.6%)	7 (5.9%)	5 (4.2%)	6 (5.0%)	6 (5.0%)	13 (10.9%)
WHOLE BODY/GENERAL	3 (2.5%)	5 (4.2%)	3 (2.5%)	2 (1.7%)	2 (1.7%)	2 (1.7%)	8 (6.7%)
FATIGUE/WEAKNESS	3 (2.5%)	2 (1.7%)	1 (0.8%)	2 (1.7%)	2 (1.7%)	2 (1.7%)	5 (4.2%)
MALAISE	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	3 (2.5%)
HEADACHE	0 (0.0%)	2 (1.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)
INTEGUMENTARY SYSTEM	0 (0.0%)	1 (0.8%)	2 (1.7%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	2 (1.7%)
URTICARIA/HIVES	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)

00401

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (125 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PRURITIS/ITCHING	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
RESPIRATORY	1 (0.8%)	2 (1.7%)	1 (0.8%)	2 (1.7%)	4 (3.4%)	4 (3.4%)		5 (4.2%)
PHARYNGITIS (SORE THROAT)	1 (0.8%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	2 (1.7%)	2 (1.7%)		3 (2.5%)
LARYNGITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
BRONCHITIS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)		1 (0.8%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
HEMIC AND LYMPHATIC	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
LYMPHADENOPATHY, GENERAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
LYMPHADENOPATHY, CERVICAL	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
MUSCULOSKELETAL	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
MYALGIA	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
DIGESTIVE SYSTEM	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)

00402

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (125 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
ABDOMINAL PAINS/CRAMPS	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
DIARRHEA	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.8%)
PERSONS WITH COMPLAINTS	16 (13.4%)	16 (13.4%)	14 (11.8%)	7 (5.9%)	7 (5.9%)	7 (5.9%)		27 (22.7%)
PERSONS WITH NO COMPLAINTS	103 (86.6%)	103 (86.6%)	105 (88.2%)	112 (94.1%)	112 (94.1%)	112 (94.1%)		92 (77.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00403

Table 4 (cont)
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (109 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	11 (14.3%)	10 (13.0%)	6 (7.8%)	6 (7.8%)	5 (6.5%)	5 (6.5%)	13 (16.9%)
PAIN	1 (1.3%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
SORENESS	8 (10.4%)	6 (7.8%)	3 (3.9%)	3 (3.9%)	2 (2.6%)	2 (2.6%)	9 (11.7%)
TENDERNESS	2 (2.6%)	2 (2.6%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	3 (3.9%)
ERYTHEMA (REDNESS)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	2 (2.6%)
INDURATION	0 (0.0%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)
PAPULE(S)	0 (0.0%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)
STIFFNESS/TIGHTNESS	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	1 (1.3%)
SYSTEMIC	1 (1.3%)	2 (2.6%)	2 (2.6%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	4 (5.2%)
WHOLE BODY/GENERAL	1 (1.3%)	2 (2.6%)	2 (2.6%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	4 (5.2%)
MALAISE	0 (0.0%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
HEADACHE	0 (0.0%)	1 (1.3%)	2 (2.6%)	1 (1.3%)	1 (1.3%)	0 (0.0%)	2 (2.6%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (109 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
ACHINESS	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)
PERSONS WITH COMPLAINTS	12 (15.6%)	12 (15.6%)	7 (9.1%)	6 (7.8%)	6 (7.8%)	5 (6.5%)	15 (19.5%)
PERSONS WITH NO COMPLAINTS	65 (84.4%)	65 (84.4%)	70 (90.9%)	71 (92.2%)	71 (92.2%)	72 (93.5%)	62 (80.5%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 5

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (7 PATIENTS) - DOSE 1						NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION						
	0	1	2	3	4	5	
SYSTEMIC	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
WHOLE BODY/GENERAL	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
SENSATION OF WARMTH, GENERAL	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
PERSONS WITH COMPLAINTS	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
PERSONS WITH NO COMPLAINTS	5 (83.3%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	5 (83.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 5 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0613
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (4 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (50.0%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (50.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (50.0%)
RESPIRATORY	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
EARACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
PERSONS WITH NO COMPLAINTS	2 (100.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)		1 (50.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00407

Table 6

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (61 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
NORMAL	60 (98.4%)	59 (96.7%)	60 (98.4%)	60 (98.4%)	60 (98.4%)	59 (98.3%)		59 (96.7%)
< 99	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.6%)	1 (1.7%)		1 (1.6%)
99 - 99.9	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
TEMPERATURE TAKEN	61 (100.0%)	61 (100.0%)	61 (100.0%)	61 (100.0%)	61 (100.0%)	60 (98.4%)		61 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.6%)		0 (0.0%)

Table 6 (cont)
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (61 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	60 (98.4%)	61 (100.0%)	60 (98.4%)	61 (100.0%)	61 (100.0%)	61 (100.0%)			59 (96.7%)
< 99	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (1.6%)
99 - 99.9	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (1.6%)
TEMPERATURE TAKEN	61 (100.0%)	61 (100.0%)	61 (100.0%)	61 (100.0%)	61 (100.0%)	61 (100.0%)			61 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

00409

Table 6 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (60 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)		60 (100.0%)
TEMPERATURE TAKEN	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)	60 (100.0%)		60 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (121 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	114 (94.2%)	117 (96.7%)	116 (96.7%)	115 (95.8%)	117 (98.3%)	116 (95.9%)		109 (90.1%)
< 99	2 (1.7%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)		2 (1.7%)
99 - 99.9	4 (3.3%)	2 (1.7%)	2 (1.7%)	5 (4.2%)	2 (1.7%)	4 (3.3%)		8 (6.6%)
100 - 100.9	1 (0.8%)	1 (0.8%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (1.7%)
TEMPERATURE TAKEN	121 (100.0%)	121 (100.0%)	120 (99.2%)	120 (99.2%)	119 (98.3%)	121 (100.0%)		121 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (0.8%)	2 (1.7%)	0 (0.0%)		0 (0.0%)

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (120 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	113 (95.0%)	114 (95.8%)	114 (95.8%)	116 (97.5%)	115 (96.6%)	116 (97.5%)			110 (92.4%)
< 99	4 (3.4%)	3 (2.5%)	4 (3.4%)	2 (1.7%)	2 (1.7%)	2 (1.7%)			5 (4.2%)
99 - 99.9	2 (1.7%)	2 (1.7%)	1 (0.8%)	1 (0.8%)	2 (1.7%)	1 (0.8%)			4 (3.4%)
TEMPERATURE TAKEN	119 (99.2%)	119 (99.2%)	119 (99.2%)	119 (99.2%)	119 (99.2%)	119 (99.2%)			119 (99.2%)
TEMPERATURE NOT TAKEN	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)			1 (0.8%)

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (115 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	78 (100.0%)	78 (100.0%)	78 (100.0%)	78 (100.0%)	78 (100.0%)	78 (100.0%)		78 (100.0%)
TEMPERATURE TAKEN	78 (67.8%)	78 (67.8%)	78 (67.8%)	78 (67.8%)	78 (67.8%)	78 (67.8%)		78 (67.8%)
TEMPERATURE NOT TAKEN	37 (32.2%)	37 (32.2%)	37 (32.2%)	37 (32.2%)	37 (32.2%)	37 (32.2%)		37 (32.2%)

00413

Table 8

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (132 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	114 (89.1%)	118 (91.5%)	119 (93.0%)	119 (93.0%)	118 (92.2%)	118 (92.2%)			111 (86.0%)
< 99	4 (3.1%)	7 (5.4%)	5 (3.9%)	2 (1.6%)	4 (3.1%)	5 (3.9%)			4 (3.1%)
99 - 99.9	10 (7.8%)	4 (3.1%)	4 (3.1%)	6 (4.7%)	6 (4.7%)	5 (3.9%)			13 (10.1%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)			1 (0.8%)
TEMPERATURE TAKEN	128 (97.0%)	129 (97.7%)	128 (97.0%)	128 (97.0%)	128 (97.0%)	128 (97.0%)			129 (97.7%)
TEMPERATURE NOT TAKEN	4 (3.0%)	3 (2.3%)	4 (3.0%)	4 (3.0%)	4 (3.0%)	4 (3.0%)			3 (2.3%)

Table 8 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (125 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	109 (92.4%)	112 (94.9%)	112 (94.9%)	113 (95.8%)	114 (96.6%)	111 (94.1%)		104 (88.1%)
< 99	4 (3.4%)	3 (2.5%)	4 (3.4%)	2 (1.7%)	2 (1.7%)	1 (0.8%)		3 (2.5%)
99 - 99.9	5 (4.2%)	3 (2.5%)	2 (1.7%)	3 (2.5%)	2 (1.7%)	5 (4.2%)		10 (8.5%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)		1 (0.8%)
TEMPERATURE TAKEN	118 (94.4%)	118 (94.4%)	118 (94.4%)	118 (94.4%)	118 (94.4%)	118 (94.4%)		118 (94.4%)
TEMPERATURE NOT TAKEN	7 (5.6%)	7 (5.6%)	7 (5.6%)	7 (5.6%)	7 (5.6%)	7 (5.6%)		7 (5.6%)

Table 8 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (109 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	71 (92.2%)	71 (93.4%)	72 (93.5%)	72 (94.7%)	72 (93.5%)	72 (93.5%)			71 (92.2%)
< 99	3 (3.9%)	2 (2.6%)	3 (3.9%)	2 (2.6%)	3 (3.9%)	3 (3.9%)			1 (1.3%)
99 - 99.9	2 (2.6%)	3 (3.9%)	2 (2.6%)	2 (2.6%)	2 (2.6%)	2 (2.6%)			4 (5.2%)
100 - 100.9	1 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (1.3%)
TEMPERATURE TAKEN	77 (70.6%)	76 (69.7%)	77 (70.6%)	76 (69.7%)	77 (70.6%)	77 (70.6%)			77 (70.6%)
TEMPERATURE NOT TAKEN	32 (29.4%)	33 (30.3%)	32 (29.4%)	33 (30.3%)	32 (29.4%)	32 (29.4%)			32 (29.4%)

Table 9
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (7 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	3 (50.0%)	3 (50.0%)	3 (50.0%)	3 (50.0%)	3 (50.0%)	3 (50.0%)		3 (50.0%)
< 99	2 (33.3%)	3 (50.0%)	3 (50.0%)	3 (50.0%)	2 (33.3%)	3 (50.0%)		1 (16.7%)
99 - 99.9	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)		2 (33.3%)
TEMPERATURE TAKEN	6 (85.7%)	6 (85.7%)	6 (85.7%)	6 (85.7%)	6 (85.7%)	6 (85.7%)		6 (85.7%)
TEMPERATURE NOT TAKEN	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)		1 (14.3%)

Table 9 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0813
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (4 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	1 (50.0%)	2 (100.0%)	2 (100.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)			0 (0.0%)
99 - 99.9	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (50.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)			1 (50.0%)
TEMPERATURE TAKEN	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)			2 (50.0%)
TEMPERATURE NOT TAKEN	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)			2 (50.0%)

IMMUNOGENICITY OF RECOMBINANT YEAST HEPATITIS B VACCINE

SIR,—In Dr Jilg and colleagues' study (Nov 24, p 1174) in thirty recipients of recombinant hepatitis B vaccine "the immune response in the recombinant vaccine group was less pronounced during the first months than in the plasma vaccine group, as shown by lower seroconversion rates and lower mean anti-HBs levels". They compared a 10 μg dose of recombinant vaccine with a 20 μg dose of plasma-derived vaccine.

As indicated in the table, our results in a similar study in one hundred and seven seronegative health professionals, 21–30 years of age, revealed essentially the same immune response in recipients of 5 μg and 10 μg doses of recombinant yeast hepatitis B vaccine when compared with a comparable group who received 20 μg doses of plasma-derived vaccine.

Valid conclusions cannot be drawn from studies in thirty or a hundred vaccinees. More extensive studies will be required to evaluate anti-HBs response and its persistence in recipients of recombinant hepatitis B vaccine. In the meantime, our initial results are encouraging.

NYU Medical Center,
New York, NY 10016, USA

MORTON DAVIDSON
SAUL KRUGMAN

THE LANCET, JANUARY 12, 1985

SEROCONVERSION RATES AND GEOMETRIC MEAN TITRES (GMT) OF SERONEGATIVE INDIVIDUALS, ADULTS GIVEN RECOMBINANT OR PLASMA-DERIVED HEPATITIS B VACCINE

	Recombinant vaccine†						Plasma derived (20 μg)‡	
	10 μg			5 μg				
Time* (mo)	Anti-HBs response	mIU/ml (GMT)	S/N ratio (GMT)	Anti-HBs response	mIU/ml (GMT)	S/N ratio (GMT)	Anti-HBs response	S/N ratio (GMT)
0	..	..	..	..	..	..	..	..
1	22/51 (43%)	42	10	21/56 (37%)	95	25	10/47 (21%)	20
2	48/51 (94%)	88	37	51/54 (94%)	60	10	34/47 (72%)	37
3	50/51 (98%)	105	52	53/56 (95%)	128	51	45/47 (96%)	70
6	49/50 (98%)	321	83	51/56 (91%)	104	42	44/47 (94%)	94
7/8	49/50 (98%)	1011	164	49/50 (98%)	830	124	46/47 (98%)	141

*Vaccine given at 0, 1, and 6 months. Follow-up to 7 months (plasma derived) or 8 months (recombinant). †Merck lot 972C-B-444. ‡Merck lot 731.

Davidson M, Krugman S. Immunogenicity of recombinant yeast hepatitis B vaccine. Lancet 1985; 1:108-9.

RECOMBINANT YEAST HEPATITIS B VACCINE: SIDE EFFECTS AND IMMUNOGENICITY COMPARED WITH PLASMA-DERIVED HEPATITIS B VACCINE.

Morton Davidson and Saul Krugman
NYU Medical Center, New York, N.Y.

A yeast recombinant hepatitis B vaccine (Merck Lot no. 972/C-K444) was evaluated in 107 seronegative health professionals, 21-30 years of age. The clinical and antibody responses were compared with the results of a previous similar study using a plasma-derived hepatitis B vaccine (Merck Lot no. 751).

The vaccine was administered at 0, 1 and 6 months to the following three groups: 1) 51 adults who received a 10 mcg dose of recombinant vaccine; 2) 56 adults who received a 5 mcg dose of recombinant vaccine, and 3) 47 adults who received a 20 mcg dose of plasma-derived vaccine. The three groups included medical students, house staff, and nurses who were of comparable age and sex.

Results

Side effects were negligible in all three groups. They consisted of transient, local soreness at the site of the inoculation in about 25% of the vaccinees in each group. No systemic reactions were observed.

The seroconversion rates and geometric mean titers are summarized in the Table. The results are essentially the same for all three groups. Under the conditions of this study the 5 mcg and 10 mcg doses of recombinant hepatitis B vaccine were just as immunogenic as a 20 mcg dose of plasma-derived hepatitis B vaccine.

Comment

A recent report by Jilg et al (Lancet 1984; 2:1174-75) described a similar study in 30 seronegative medical students and laboratory workers whose age and sex were comparable to those in our groups. They stated that "the immune response in the recombinant vaccine group was less pronounced during the first months than in the plasma vaccine group, as shown by lower seroconversion rates and lower mean anti-HBs levels." Our results in 107 similar recipients of the recombinant hepatitis B vaccine do not support this conclusion.

It is obvious that valid conclusions cannot be drawn from studies involving either 30 or 100 vaccinees. More extensive studies will be required to determine anti-HBs response and its persistence in recipients of recombinant hepatitis B vaccines.

Davidson M, Krugman S. Recombinant yeast hepatitis B vaccine: Side effects and immunogenicity compared with plasma-derived hepatitis B vaccine. Submitted for publication to Hepatitis Scientific Memoranda.

TABLE

Seroconversion Rates and Geometric Mean Titers of Seronegative Adults Who Received Recombinant Yeast Hepatitis B Vaccine (Merck Lot No. 972/C-K444) or Plasma-Derived Hepatitis B Vaccine (Merck Lot No. 751).

Time Interval (Months)	Recombinant Hepatitis B Vaccine					
	10 mcg dose			5 mcg dose		
	anti-HBs response	mIU/ml GMT	S/N Ratio GMT	anti-HBs response	mIU/ml GMT	S/N Ratio GMT
0	-	-	-	-	-	-
1	22/51 (43%)	42	19	21/56 (37%)	55	25
2	48/51 (94%)	88	37	51/56 (91%)	69	38
3	50/51 (98%)	145	52	52/56 (93%)	128	51
6	49/50 (98%)	321	63	53/56 (95%)	184	42
8	45/46 (98%)	1911	164	49/50 (98%)	839	124

Vaccine given at 0, 1 and 6 months.
Age Range: 21 - 30 years

Time Interval (Months)	Plasma-Derived Hepatitis B Vaccine 20 mcg dose	
	anti-HBs response	S/N Ratio GMT
0	-	-
1	18/47 (38%)	20
2	34/47 (79%)	37
3	45/47 (96%)	79
6	44/47 (94%)	94
7	46/47 (98%)	141

Vaccine given at 0, 1 and 6 months.
Age range: 21 - 30 years

Janurary 1986

REPORT NO. 3
in Support for a License Application for

RECOMBIVAX
(Yeast Recombinant Hepatitis B Vaccine, MSD)
CLINICAL DATA*
VOLUME 2 OF 3

Merck Sharp & Dohme Research Laboratories

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 815
PURPOSE:	To compare antibody and clinical responses to yeast recombinant and plasma-derived hepatitis B vaccine among: 1 Mentally retarded individuals who are negative for hepatitis B virus serologic markers. 2. Health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	1. Yeast Recombinant Hepatitis B Vaccine Lot 993/C-K937 (20 mcg/HBsAg/ml) 2. Plasma-Derived Hepatitis B Vaccine Lot 2277K (20 mcg HBsAg/ml
PRIMARY INVESTIGATOR:	Solko W. Schalm, M.D. Department of Internal Medicine and Gastroenterology University Hospital Dijkzigt Rotterdam, The Netherlands
SECONDARY INVESTIGATORS:	Dr. Rudolf A. Heijtink Department of Virology Erasmus University Rotterdam, The Netherlands Dr. Maria Alida van de Velde Dr. Mr. Willem van den Bergh - Stichting Noordwijk, The Netherlands
STUDY LOCATION:	Dr. Mr. Willem van den Bergh-Stichting Noordwijk, The Netherlands University Hospital Dijkzigt Rotterdam, The Netherlands
DATE STUDY INITIATED:	December, 1985
DATE STUDY COMPLETED:	In progress

Study 815

STUDY POPULATION: The study population consists of approximately 90 mentally retarded individuals. and 90 health care personnel, who are negative for HBsAg, anti-HBc, anti-HBs, have a normal ALT and have not previously received any hepatitis B vaccine.

STUDY PROCEDURE: Mentally retarded individuals and health care personnel are randomly assigned to receive either yeast recombinant or plasma-derived hepatitis B vaccine, stratified by sex and age.

Mentally retarded individuals and health care personnel receive a 0.5 ml (10 mcg HBsAg) or a 1.0 ml (20 mcg HBsAg) intramuscular injection of yeast recombinant vaccine or a 1.0 ml (20 mcg HBsAg) intramuscular injection of plasma-derived vaccine at 0, 1, and 6 months.

The temperature of each vaccine recipient and any local or systemic complaints are recorded for five days after each injection of vaccine.

A blood sample is obtained from each study participant approximately three weeks before the first injection of vaccine. Post-vaccination blood samples are obtained from mentally retarded individuals at 3, 7, and 12 months and from health care personnel at 1, 2, 3, 6, 7, 9 and 12 months. Blood samples are obtained at 24 months from those participants who have seroconverted.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs and ALT. Samples may be assayed for yeast antibody. In addition, samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested for anti-a and anti-d subtype specificity.

RESULTS: Clinical follow-up data and serologic results are not yet available. The study continues in progress.

3234I/2
1/21/86

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 816
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among: 1. adult dialysis patients negative for hepatitis B serologic markers. 2. health care personnel negative for hepatitis B serologic markers. 3. adult dialysis patients negative for hepatitis B serologic markers, who previously received plasma-derived hepatitis B vaccine and were nonresponders (anti-HBs negative).
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 974/C-K446 (20 mcg HBsAg/ml) Lot 986/C-K733 (20 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Stanley Plotkin, M.D./Stuart Starr, M.D. Division of Preventive Medicine Joseph Stokes, Jr. Research Institute Children's Hospital of Philadelphia 34 Street and Civic Center Boulevard Philadelphia, Pennsylvania 19104
STUDY LOCATION:	Biomedical Applications of Lehigh Valley 2015 Hamilton Avenue Allentown, Pennsylvania 18104 Dialysis, Inc. 1230 Burmont Road Drexel Hill, Pennsylvania The Kidney Center of Delaware Count 15th Street and Upland Avenue Chester, Pennsylvania 19013 The Kidney Center of Chester County 960 East Lincoln Highway Downington, Pennsylvania 19335

Study 816

DATE STUDY INITIATED: May 14, 1984

DATE STUDY COMPLETED: In progress

STUDY POPULATION: The study population consists of 40-50 adult dialysis patients (including previous nonresponders to plasma-derived vaccine), and 20-25 health care personnel, of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, and have a normal ALT level. Dialysis patients (excluding nonresponders to plasma-derived vaccine) and health care personnel have not previously received any hepatitis B vaccine.

STUDY PROCEDURE: Dialysis patients are assigned to one of two groups, stratified by sex and age, to assure that patients in the two groups are similar. Health care personnel constitute a third group.

Dialysis patients receive 1.0 ml (20 mcg HBsAg) or 2 x 1.0 ml (40 mcg HBsAg) intramuscular injections of vaccine at 0, 1, and 6 months. Health care personnel receive 0.5 ml (10 mcg HBsAg) intramuscular injections of vaccine according to the same regimen. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

A blood sample is obtained from each study participant approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 3, 6, 8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBs, anti-HBc, and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested to determine anti-a and anti-d subtype specificity.

RESULTS: HEALTH CARE PERSONNEL

10 mcg Lot 974/C-K446 at 0, 1, and 6 months

Study 816

RESULTS: (Contd)

1. Number Vaccinated:

Injection No.		
1	2	3
8	8	6

2. Serologic Results:

Serologic data at 7/8 months are available for 5 health care personnel. At 7/8 months, 80% (4/5) of health care personnel seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 37.9 mIU/ml at that time. Among responders with a titer of S/N ≥2.1 and mIU/ml ≥10 the GMT was 127.2 mIU/ml.

By 12 months, 60% (3/5) of health care personnel retained an anti-HBs titer of mIU/ml ≥10. The GMT for all vaccinees was 16.4 mIU/ml at that time.

Anti-HBs responses at 1 through 12 months are included in Table 1.

3. Clinical Results:

Clinical follow-up data are available for 8 health care personnel following the first two injections and for 6 health care personnel following the third injection of vaccine. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 2 and 3. In summary:

Clinical Complaint	% Frequency by Injection No.		
	1	2	3
Injection Site	25 (2/8)	25 (2/8)	17 (1/6)
Systemic	38 (3/8)	25 (2/8)	17 (1/6)

Study 816

RESULTS: (Contd) No serious or alarming adverse reactions attributable to vaccination have been reported.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK446
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	RESPONDERS	
						S/N >= 2.1	MIU/ML >= 10
1 MONTH	25%	(2/8)	13%	(1/8)	1.2	13.2	86.5
3 MONTHS	40%	(2/5)	40%	(2/5)	7.1	355.5	355.5
6 MONTHS	75%	(3/4)	50%	(2/4)	6.6	18.4	30.6
7/8 MONTHS	80%	(4/5)	80%	(4/5)	37.9	127.2	127.2
12 MONTHS	80%	(4/5)	60%	(3/5)	16.4	44.7	88.9

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (8 PATIENTS) - DOSE 1 — DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (25.0%)
PAIN	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)
SORENESS	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)
SYSTEMIC	1 (12.5%)	1 (12.5%)	1 (12.5%)	3 (37.5%)	2 (25.0%)	2 (25.0%)	3 (37.5%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
HEADACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (25.0%)	1 (12.5%)	1 (12.5%)	2 (25.0%)
RESPIRATORY	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	1 (12.5%)
UPPER RESPIRATORY INFECT., NOS	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	1 (12.5%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)
WRIST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)
HIP PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	1 (12.5%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (8 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	1 (12.5%)
PERSONS WITH COMPLAINTS	3 (37.5%)	1 (12.5%)	1 (12.5%)	3 (37.5%)	2 (25.0%)	2 (25.0%)	4 (50.0%)
PERSONS WITH NO COMPLAINTS	5 (62.5%)	7 (87.5%)	7 (87.5%)	5 (62.5%)	6 (75.0%)	6 (75.0%)	4 (50.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (8 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	2 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (25.0%)
SORENESS	2 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (25.0%)
SYSTEMIC	1 (12.5%)	0 (0.0%)	2 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)		2 (25.0%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (25.0%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
NECK PAIN	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
NAUSEA	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
NERVOUS SYSTEM	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)
VERTIGO/DIZZINESS	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (12.5%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (8 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	2 (25.0%)	1 (12.5%)	2 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	2 (25.0%)
PERSONS WITH NO COMPLAINTS	6 (75.0%)	7 (87.5%)	6 (75.0%)	7 (87.5%)	8 (100.0%)	8 (100.0%)	6 (75.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (6 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
SORENESS	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
SYSTEMIC	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)
DIGESTIVE SYSTEM	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)
NAUSEA	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)
PERSONS WITH COMPLAINTS	2 (33.3%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	2 (33.3%)
PERSONS WITH NO COMPLAINTS	4 (66.7%)	5 (83.3%)	5 (83.3%)	5 (83.3%)	5 (83.3%)	5 (83.3%)	4 (66.7%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (8 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	7 (87.5%)	8 (100.0%)	8 (100.0%)	8 (100.0%)	7 (87.5%)	8 (100.0%)			7 (87.5%)
99 - 99.9	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)			1 (12.5%)
TEMPERATURE TAKEN	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)			8 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (8 PATIENTS) - DOSE 2 DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH MAX TEMP
NORMAL	3 (37.5%)	3 (37.5%)	3 (37.5%)	3 (37.5%)	3 (37.5%)	3 (37.5%)		3 (37.5%)
< 99	5 (62.5%)	5 (62.5%)	5 (62.5%)	5 (62.5%)	5 (62.5%)	5 (62.5%)		5 (62.5%)
TEMPERATURE TAKEN	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)	8 (100.0%)		8 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00435

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (6 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	2 (33.3%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	2 (33.3%)		2 (33.3%)
< 99	4 (66.7%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	4 (66.7%)		4 (66.7%)
TEMPERATURE TAKEN	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)		6 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 834
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 979/C-K564 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Mario Rizzetto, M.D. Division of Gastroenterology Molinette Hospital Turin, ITALY
SECONDARY INVESTIGATORS:	Caterina Canavese, M.D. Piero Stratta, M.D. Ferruccio Bonino, M.D. Molinette Hospital Turin, ITALY
STUDY LOCATION:	Molinette Hospital Turin, ITALY
DATE STUDY INITIATED:	August, 1985
DATE STUDY COMPLETED:	In progress.
STUDY POPULATION:	The study population consists of 25-30 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.
STUDY PROCEDURE:	Eligible study participants receive a 1.0 ml (10 mcg HBsAg) intramuscular injection of vaccine at 0, 1, and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

STUDY PROCEDURE: (Cont.)

A blood sample is obtained from each study participant approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer ≥25 mIU/ml may be tested to determine anti-a and anti-d subtype specificity.

RESULTS:

HEALTH CARE PERSONNEL

10 mcg Lot 979/C-K564 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
25	0	0

2. Serologic Results:

Serologic data are not presently available.

3. Clinical Results:

Clinical follow-up data are not yet available. No serious or alarming adverse experiences attributable to vaccine have been reported.

REACTION POSSIBLY RELATED TO VACCINE

A 40 year-old female developed a "few ecchymotic flat lesions on the lateral aspect of her breasts, bilaterally" four days after the first injection of vaccine. Over the following two days, the lesions increased, the next day vomiting occurred. All symptoms disappeared over the next 36 hours and the subject has remained well. There was no fever. WBC, hemoglobin, platelets, and coagulation profile were normal. The patient has no history of allergies to exogenous substances. No further vaccine was administered to this patient.

STUDY 835

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 835
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 979/C-K564
PRIMARY INVESTIGATOR:	Stanley M. Lemon, M.D. Division of Infectious Disease Department of Medicine 547 Burnett-Womack Clinical Sciences Bldg. 229H University of North Carolina School of Medicine Chapel Hill, North Carolina 27514
SECONDARY INVESTIGATOR:	Jack T. Stapleton, M.D. Division of Infectious Diseases Department of Medicine 547 Burnett-Womack Clinical Sciences Bldg. 229H University of North Carolina School of Medicine Chapel Hill, North Carolina 27514
STUDY LOCATION:	The University of North Carolina School of Medicine North Carolina Memorial Hospital Chapel Hill, North Carolina 27514
DATE STUDY INITIATED:	October 26, 1984
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 25-30 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 835

STUDY PROCEDURE:

Eligible study participants receive a 1.0 ml (10 mcg HBsAg) intramuscular injection of vaccine at 0, 1 and 6 months. Vaccine recipients record their temperatures and any local or systemic complaints for five days after each injection of vaccine.

A blood sample is obtained from each study participant approximately two weeks before and on the day of the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested to determine anti-a and anti-d type specificity.

RESULTS:

HEALTH CARE PERSONNEL

10 mcg Lot 979/C-K564 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
29	29	23

Two persons initially anti-HBs positive received vaccine. One subject displayed a marked boost in titer after one injection of vaccine. The other subject developed a protective level of antibody ($\geq$10 mIU/ml) by 10 months post-vaccination.

2. Serologic Results:

Serologic data at 7-9 months are available for 19 study participants. At 7-9 months, 100% (19/19) of vaccine recipients seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT for all vaccinees and responders (S/N $\geq$2.1 and $\geq$10 mIU/ml) was 560.9 mIU/ml at that time. Anti-HBs responses at 1 through 7-9 months are included in Table 1.

Study 835

RESULTS: (Cont.)

3. Clinical Results:

Clinical follow-up data are available for 26 study participants following the first injection, 25 participants following the second, and for 23 participants following the third injection of vaccine. Clinical complaints and maximum temperatures are provided in Tables 2 and 3. In summary:

Clinical Complaint	% Frequency by Injection No. 1	2	3
Injection Site	27(7/26)	28(7/25)	30(7/23)
Systemic	23(6/26)	16(4/25)	13(3/23)

No serious or alarming adverse reactions attributable to vaccination have been reported.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK564
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	30%	(8/27)	15%	(4/27)	0.9	13.9	77.2
2 MONTHS	73%	(19/26)	42%	(11/26)	7.2	23.2	89.1
3 MONTHS	83%	(5/6)	67%	(4/6)	25.3	61.5	103.6
6 MONTHS	95%	(18/19)	89%	(17/19)	38.4	50.2	57.1
7/9 MONTHS	100%	(19/19)	100%	(19/19)	560.9	560.9	560.9

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (29 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	6 (23.1%)	3 (11.5%)	3 (11.5%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	7 (26.9%)
SORENESS	5 (19.2%)	3 (11.5%)	3 (11.5%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	7 (26.9%)
NUMBNESS	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
SYSTEMIC	3 (11.5%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	2 (7.7%)	2 (7.7%)	6 (23.1%)
WHOLE BODY/GENERAL	1 (3.8%)	1 (3.8%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	4 (15.4%)
CHILLS	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
HEADACHE	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	3 (11.5%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)
MUSCULOSKELETAL	2 (7.7%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	2 (7.7%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (29 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
ARTHRALGIA, MONOARTICULAR	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
MYALGIA	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
NECK PAIN	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
EARACHE	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
IRRITABILITY	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.8%)
PERSONS WITH COMPLAINTS	8 (30.8%)	4 (15.4%)	4 (15.4%)	2 (7.7%)	2 (7.7%)	2 (7.7%)		12 (46.2%)
PERSONS WITH NO COMPLAINTS	18 (69.2%)	22 (84.6%)	22 (84.6%)	24 (92.3%)	24 (92.3%)	24 (92.3%)		14 (53.8%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (29 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	4 (16.0%)	4 (16.0%)	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		7 (28.0%)
PAIN	2 (8.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (12.0%)
SORENESS	2 (8.0%)	4 (16.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (20.0%)
TENDERNESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
ERYTHEMA (REDNESS)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
PRURITIS (ITCHING)	0 (0.0%)	2 (8.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (8.0%)
SYSTEMIC	0 (0.0%)	2 (8.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	2 (8.0%)		4 (16.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)		2 (8.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
MALAISE	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)		2 (8.0%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)		1 (4.0%)
VIRAL INFECTION, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)		1 (4.0%)

00444

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (29 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
INTEGUMENTARY SYSTEM	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
RASH, NOS	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)		1 (4.0%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)		1 (4.0%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)		1 (4.0%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)		1 (4.0%)
MYALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)		1 (4.0%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
DIARRHEA	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
NAUSEA	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
PERSONS WITH COMPLAINTS	4 (16.0%)	6 (24.0%)	2 (8.0%)	0 (0.0%)	1 (4.0%)	2 (8.0%)		9 (36.0%)
PERSONS WITH NO COMPLAINTS	21 (84.0%)	19 (76.0%)	23 (92.0%)	25 (100.0%)	24 (96.0%)	23 (92.0%)		16 (64.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (29 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH NO DATA	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)		1 (3.8%)

00446

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (23 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	6 (26.1%)	4 (17.4%)	2 (8.7%)	1 (4.3%)	1 (4.3%)	0 (0.0%)	7 (30.4%)
PAIN ON INJECTION	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SORENESS	6 (26.1%)	3 (13.0%)	2 (8.7%)	1 (4.3%)	1 (4.3%)	0 (0.0%)	6 (26.1%)
ERYTHEMA (REDNESS)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SWELLING	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
PRURITIS (ITCHING)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SYSTEMIC	0 (0.0%)	2 (8.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	3 (13.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
CHILLS	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
FLUSH	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	1 (4.3%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	1 (4.3%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (23 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)		1 (4.3%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.3%)
DIARRHEA	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.3%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.3%)
EYES, BURNING	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.3%)
PERSONS WITH COMPLAINTS	6 (26.1%)	5 (21.7%)	2 (8.7%)	1 (4.3%)	1 (4.3%)	1 (4.3%)		7 (30.4%)
PERSONS WITH NO COMPLAINTS	17 (73.9%)	18 (78.3%)	21 (91.3%)	22 (95.7%)	22 (95.7%)	22 (95.7%)		16 (69.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (29 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	2 (8.0%)	2 (8.0%)	2 (8.0%)	2 (8.0%)	2 (8.3%)	2 (8.7%)			2 (8.0%)
< 99	19 (76.0%)	21 (84.0%)	20 (80.0%)	20 (80.0%)	19 (79.2%)	19 (82.6%)			15 (60.0%)
99 - 99.9	4 (16.0%)	2 (8.0%)	3 (12.0%)	1 (4.0%)	1 (4.2%)	2 (8.7%)			5 (20.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)	2 (8.3%)	0 (0.0%)			3 (12.0%)
TEMPERATURE TAKEN	25 (86.2%)	25 (86.2%)	25 (86.2%)	25 (86.2%)	24 (82.8%)	23 (79.3%)			25 (86.2%)
TEMPERATURE NOT TAKEN	4 (13.8%)	4 (13.8%)	4 (13.8%)	4 (13.8%)	5 (17.2%)	6 (20.7%)			4 (13.8%)

00449

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (29 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (4.0%)	1 (4.0%)	1 (4.3%)	1 (4.2%)	1 (4.2%)	1 (4.3%)			1 (4.0%)
< 99	20 (80.0%)	19 (76.0%)	18 (78.3%)	20 (83.3%)	21 (87.5%)	19 (82.6%)			15 (60.0%)
99 - 99.9	4 (16.0%)	4 (16.0%)	4 (17.4%)	3 (12.5%)	2 (8.3%)	3 (13.0%)			8 (32.0%)
103 - 103.9	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (4.0%)
TEMPERATURE TAKEN	25 (86.2%)	25 (86.2%)	23 (79.3%)	24 (82.8%)	24 (82.8%)	23 (79.3%)			25 (86.2%)
TEMPERATURE NOT TAKEN	4 (13.8%)	4 (13.8%)	6 (20.7%)	5 (17.2%)	5 (17.2%)	6 (20.7%)			4 (13.8%)

00450

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0835
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (23 PATIENTS) - DOSE 3								
	DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	1 (5.0%)	1 (5.0%)	1 (4.8%)	1 (5.3%)	1 (5.3%)	1 (5.3%)			1 (4.8%)
< 99	17 (85.0%)	16 (80.0%)	17 (81.0%)	17 (89.5%)	16 (84.2%)	16 (84.2%)			16 (76.2%)
99 - 99.9	2 (10.0%)	3 (15.0%)	3 (14.3%)	1 (5.3%)	2 (10.5%)	2 (10.5%)			4 (19.0%)
TEMPERATURE TAKEN	20 (87.0%)	20 (87.0%)	21 (91.3%)	19 (82.6%)	19 (82.6%)	19 (82.6%)			21 (91.3%)
TEMPERATURE NOT TAKEN	3 (13.0%)	3 (13.0%)	2 (8.7%)	4 (17.4%)	4 (17.4%)	4 (17.4%)			2 (8.7%)

00451

STUDY 838

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 838.
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine in the following, initially seronegative, adult populations: 1. Dialysis Patients 2. Predialysis Patients 3. Health Care Personnel
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #986/C-K733 (20 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Professor Dr. Friedrich Deinhardt Director Max v. Pettenkofer Institute Pettenkoferstr. 9a 8000 Muenchen 2 West Germany
SECONDARY INVESTIGATORS:	Dr. Wolfgang Jilg Max v. Pettenkofer Institute Pettenkoferstr. 9a 8000 Muenchen 2 West Germany Professor Dr. Juergen Bommer Medizinische Universitatsklinik Bergheimer Str. 56 6900 Heidelberg 1 West Germany Professor Dr. R. Mueller Medizinische Hochschule Hannover Abt. f. Innere Medizin Karl-Wiechert-Allee 9 D-3000 Hannover-Kleefeld West Germany Professor Dr. Horst Braas Staedtische Krankenanstalten Medizinische Klinik II Bremserstr. 79 D-6700 Ludwigshafen West Germany

Study 838

SECONDARY INVESTIGATORS: (Cont.)

Dr. Bernhard Weinel
Staedtische Krankenanstalten
Medizinische Klinik II
Bremserstr. 79
D-6700 Ludwigshafen
West Germany

STUDY LOCATIONS: Munich, Heidelberg, Hannover, and Ludwigshafen, West Germany

DATE INITIATED: June 7, 1984

DATE COMPLETED: In progress

STUDY POPULATIONS: Under the original protocol and subsequent addenda, the following groups are enrolled in the study. Participants may be of either sex, but pregnant women are excluded. Prospective vaccine recipients must be negative for hepatitis B serologic markers, have a normal ALT level and may not have received any hepatitis B vaccine (except as noted under addendum #2).

Protocol/ Addendum #	Population	Approx. Number	Regimen
Initial protocol	Health Care Personnel	25	10 mcg (0.5 ml) at 0, 1, and 6 months
Initial protocol	Dialysis Patients	50	40 mcg (2 x 1.0 ml) at 0, 1 and 6 months
Add. #1	Dialysis Patients	20	20 mcg (1.0 ml) at 0, 1, 2, 3, 4, and 6 months
Add. #1	Dialysis Patients	20	40 mcg (2 x 1.0 ml) at 0, 1, 2, 3, 4, and 6 months

Study 838

STUDY POPULATIONS: (Cont.)

Protocol/ Addendum #	Population	Approx. Number	Regimen
Add. #2	Initial protocol subjects who do not form anti-HBs after 3 doses of vaccine		10 mcg (0.5 ml) for health care personnel; 40 mcg (2 x 1.0 ml) for dialysis patients
Add. #3	Predialysis patients	10	40 mcg (2 x 1.0 ml) at 0, 1, and 6 months

PROCEDURE:

Participants receive intramuscular injections of vaccine according to the regimens outlined above under STUDY POPULATIONS.

Study participants will be asked to record their temperature for five days after each injection and to note any local or systemic complaints.

Serum samples will be obtained prior to and on the day of vaccination. Follow-up blood specimens will be obtained 1, 2, 3, 6, 8, 12 and 24 months post the initial injection of vaccine. Nonresponders who receive a fourth injection of vaccine under addendum #2 will have a blood sample taken one month after this injection. Serum samples will be assayed for HBsAg, anti-HBs, anti-HBc and ALT by Dr. Deinhardt's laboratory. Samples may also be assayed at MSDRL for yeast antibody. Those that are positive for anti-HBs with a titer of $\geq$25 mIU/ml may be assayed for anti-a and anti-d subtype specificity.

Study 838

RESULTS:

HEALTH CARE PERSONNEL:

10 mcg Lot #986/C-K733 at 0, 1, and 6 months.

1. Number Vaccinated:

Injection No.		
1	2	3
22	19	17

2. Serologic Results:

Serologic data are available for 17 participants at 7/8 months of follow-up. Ninety-four percent (16/17) of the subjects seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10) at that time. The GMT at 7/8 months for all vaccinees was 284.8 mIU/ml and 437.1 for responders (mIU/ml ≥10).

Refer to Table 1 for anti-HBs responses and GMTs through 10 months of follow-up.

3. Clinical Complaints:

Clinical follow-up data are available for 22 and 13 participants after injections 1 and 2, respectively. The overall frequencies of complaints are presented below.

Type of Complaint	Frequency in % by Injection No.		
	1	2	3
Injection Site	18(4/22)	8(1/13)	---
Systemic	27(6/22)	8(1/13)	---

Refer to Table 2 for listings of specific clinical complaints by injection number. Maximum temperature data are provided in Table 3.

There were no serious or alarming adverse experiences attributable to vaccine.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK733
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% [illegible] ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	19%	(4/21)	9.5%	(2/21)	0.6	13.6	43.0
2 MONTHS	58%	(11/19)	47%	(9/19)	4.1	27.0	39.2
3 MONTHS	82%	(14/17)	71%	(12/17)	15.7	36.5	46.9
6 MONTHS	83%	(10/12)	83%	(10/12)	26.9	66.2	66.2
7/8 MONTHS	94%	(16/17)	94%	(16/17)	284.8	437.1	437.1
10 MONTHS	100%	(9/9)	100%	(9/9)	509.4	509.4	509.4

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	4 (18.2%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (18.2%)
PAIN	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
SORENESS	3 (13.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (13.6%)
SWELLING	0 (0.0%)	0 (0.0%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.5%)
SYSTEMIC	2 (9.1%)	4 (18.2%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		6 (27.3%)
WHOLE BODY/GENERAL	2 (9.1%)	4 (18.2%)	2 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		6 (27.3%)
FATIGUE/WEAKNESS	2 (9.1%)	3 (13.6%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (22.7%)
HEADACHE	0 (0.0%)	1 (4.5%)	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (9.1%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		1 (4.5%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		1 (4.5%)
PERSONS WITH COMPLAINTS	6 (27.3%)	4 (18.2%)	3 (13.6%)	0 (0.0%)	0 (0.0%)	1 (4.5%)		9 (40.9%)
PERSONS WITH NO COMPLAINTS	16 (72.7%)	18 (81.8%)	19 (86.4%)	22 (100.0%)	22 (100.0%)	21 (95.5%)		13 (59.1%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (13 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (7.7%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.7%)
PAIN	1 (7.7%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.7%)
SYSTEMIC	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.7%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.7%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.7%)
PERSONS WITH COMPLAINTS	1 (7.7%)	2 (15.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (15.4%)
PERSONS WITH NO COMPLAINTS	12 (92.3%)	11 (84.6%)	13 (100.0%)	13 (100.0%)	13 (100.0%)	13 (100.0%)		11 (84.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00459

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (22 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	10 (90.9%)	11 (91.7%)	10 (90.9%)	11 (100.0%)	9 (90.0%)	8 (88.9%)			9 (75.0%)
99 - 99.9	1 (9.1%)	1 (8.3%)	1 (9.1%)	0 (0.0%)	1 (10.0%)	1 (11.1%)			3 (25.0%)
TEMPERATURE TAKEN	11 (50.0%)	12 (54.5%)	11 (50.0%)	11 (50.0%)	10 (45.5%)	9 (40.9%)			12 (54.5%)
TEMPERATURE NOT TAKEN	11 (50.0%)	10 (45.5%)	11 (50.0%)	11 (50.0%)	12 (54.5%)	13 (59.1%)			10 (45.5%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (13 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	7 (100.0%)	7 (100.0%)	7 (100.0%)	6 (100.0%)	6 (100.0%)	6 (100.0%)			7 (100.0%)
TEMPERATURE TAKEN	7 (53.8%)	7 (53.8%)	7 (53.8%)	6 (46.2%)	6 (46.2%)	6 (46.2%)			7 (53.8%)
TEMPERATURE NOT TAKEN	6 (46.2%)	6 (46.2%)	6 (46.2%)	7 (53.8%)	7 (53.8%)	7 (53.8%)			6 (46.2%)

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 841.
PURPOSE:	To evaluate antibody and clinical responses to the vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #978/C-K 563 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATORS:	Arie J. Zuckerman, M.D. Professor of Microbiology Director, Department of Medical Microbiology London School of Hygiene and Tropical Medicine Keppel Street London WC1E 7HT United Kingdom Iain Murray-Lyon, M.D. Consultant Physician Charing Cross Hospital London W.6. United Kingdom
SECONDARY INVESTIGATORS:	Dr. John Coleman Charing Cross Hospital London W.6. United Kingdom Dr. Michael Anderson Charing Cross Hospital London W.6. United Kingdom
STUDY LOCATION:	Charing Cross Hospital London W.6. United Kingdom
DATE INITIATED:	May 1985.
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population will consist of 80-100 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, and have not previously received any hepatitis B vaccine.

Study 841

PROCEDURE:

Eligible participants will receive a 1.0 ml injection of vaccine in the deltoid muscle at 0, 1, and 6 months. Study participants will be asked to take and record their temperatures for five days after each injection of vaccine and to record any local or systemic complaints that they may have. They will be asked to notify the study physician immediately if any unexpected or serious reaction occurs.

Blood specimens will be obtained prior to and 1, 2, 3, 6, 8, 12, and 24 months following the first injection. All samples will be assayed in Dr. Zuckerman's laboratory for HBsAg, anti-HBc and anti-HBs. Samples may also be assayed for yeast antibody and subtype specificity.

RESULTS:

Serologic and clinical follow-up data are not presently available. No serious or alarming adverse experiences attributable to vaccine have been reported. The study continues in progress.

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 859
PURPOSE:	This study is designed to evaluate antibody and clinical responses to hepatitis B yeast recombinant vaccine among health care personnel who are negative for hepatitis B serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #978/C-K563 (10 mcg HBsAg)
PRINCIPAL INVESTIGATOR:	Nathan Clumeck, M.D. Assistant Department Head Section of Infectious Diseases Hospital of St. Pierre Rue Haute, 322 Brussels, BELGIUM
SECONDARY INVESTIGATOR:	Pierre Reding, M.D. Gastroenterology Service Hospital St. Pierre Rue Haute, 322 Brussels, BELGIUM
STUDY LOCATION:	Hospital of St. Pierre Section of Infectious Disease Department of Internal Medicine Rue Haute, 322 Brussels, BELGIUM
DATE INITIATED:	March 12, 1985
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population will consist of 30 to 50 health care personnel of either sex (excluding pregnant women), who are negative for anti-HBc, anti-HBs, HBsAg, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 859

STUDY PROCEDURE:

Participants receive a 1.0 ml intramuscular injection of vaccine on Day 0, 1, and 6 months. Prior to receipt of the vaccine, a serum sample is obtained from participants to screen for HBsAg, anti-HBc, yeast antibody and ALT levels. The vaccinees are asked to record their temperature for five days after each injection and note any local or systemic complaints. If any unexpected or serious reaction occurs, they are asked to notify the study physician immediately.

Follow-up blood samples will be obtained 1, 2, 3, 6, 8, 12, and 24 months after the first injection of vaccine. The samples will be assayed for HBsAg, anti-HBc, anti-HBs, ALT and yeast antibody. Samples with an anti-HBs titer $\geq$25 mIU/ml will be assayed for anti-a and anti-d sub-type specificity. Assays for ALT will be done by Dr. Clumeck in Belgium. All other assays on post-vaccination sera will be performed at MSDRL in West Point.

RESULTS:

HEALTH CARE PERSONNEL

10 mcg lot #978/C-K563 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
31	31	0

2. Serologic Results:

Serologic data are available for 30 participants. At three months, 80% (24/30) of the vaccinees seroconverted for anti-HBs (S/N $\geq$2.1). Fifty-three percent (16/30) of the subjects developed protective levels of anti-HBs (mIU/ml $\geq$10).

The GMT at three months for all vaccinees was 11.8 mIU/ml while it was 60.0 mIU/ml for responders with a titer of mIU/ml $\geq$10.

Refer to Table 1 for anti-HBs responses and GMTs through three months of follow-up.

RESULTS (CONT.):

One subject (case (b) (6) was found to be anti-HBs positive on the day of the first injection. There was no rise in antibody level after the first injection and a >4-fold rise in anti-HBs after the second injection.

3. Clinical Complaints:

A summary of frequencies of clinical complaints are not yet available. However, no serious or alarming events attributable to vaccine have been reported. Vaccination and follow-up continues in progress.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0859
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK563
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS		GMT (MIU/ML)		
				RESPONDERS	
	S/N >= 2.1	MIU/ML >= 10	ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	33% (10/30)	10% (3/30)	1.1	9.2	31.4
2 MONTHS	63% (19/30)	53% (16/30)	8.2	38.3	58.1
3 MONTHS	80% (24/30)	53% (16/30)	11.8	27.5	60.0

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 860.
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #978/C-K563 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Professor Dr. R. Laufs Director, Institute for Medical Microbiology and Immunology at the University of Hamburg Martinistrasse 52 2000 Hamburg 20 WEST GERMANY
SECONDARY INVESTIGATORS:	K. Katzner, M.D. S. Gaterman, M.D. Institute for Medical Microbiology and Immunology at the University of Hamburg Martinistrasse 52 2000 Hamburg 20 WEST GERMANY
STUDY LOCATION:	Institute for Medical Microbiology and Immunology at the University of Hamburg Martinistrasse 52 2000 Hamburg 20 WEST GERMANY
DATE INITIATED:	December 28, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 60 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 860

PROCEDURE:

Participants receive a 1.0 ml intramuscular injection of vaccine on Day 0, 1, and 6 months. Prior to receipt of the vaccine, a serum sample is obtained from participants to screen for HBsAg, anti-HBc, and anti-HBc, yeast antibody and ALT levels. The vaccine recipients are asked to record their temperature for 5 days after each injection and note any local or systemic complaints. If any unexpected or serious reaction occurs, they are asked to notify the study physician immediately.

Follow-up blood samples will be obtained 1, 2, 3, 6, 8, 12, and 24 hours post the first injection of vaccine. The samples will be assayed for HBsAg, anti-HBc, anti-HBs, and ALT in Dr. Laufs' laboratory and may be assayed for yeast antibody at MSDRL. In addition, an aliquot of serum from participants with an anti-HBs titer ≥25 mIU/ml will be sent to MSDRL to be assayed for anti-a and anti-d sub-type specificity of anti-HBs antibody.

RESULTS:

HEALTH CARE PERSONNEL:

10 mcg of Lot #978/C-K563 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
60	59	59

2. Serologic Results:

Serologic data are available for 56 participants at 7/8 months. One hundred percent (56/56) of the subjects seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT at 7/8 months was 2421.1 mIU/ml (all vaccinees and responders by either cutoff).

Refer to Table 1 for GMTs and anti-HBs responses for other time intervals.

Study 860

RESULTS (CONT.):

One subject was found to be seropositive for anti-HBs on the day of her first injection. At one month post the first injection of vaccine, she had a >4-fold boost in anti-HBs titer.

3. Clinical Complaints:

Clinical follow-up data are available for at least 47 participants after each injection. The overall frequencies of complaints are presented below.

Type of Complaint	Frequency in % by Injection No. 1	2	3
Injection Site	20(11/55)	28(15/54)	28(13/47)
Systemic	20(11/55)	11(6/54)	11(5/47)

Refer to Table 2 for listings of specific clinical complaints by injection number. Maximum temperature data are provided in Table 3.

There were no serious or alarming reactions attributable to vaccine.

ALT Elevations

Four subjects had ALT elevations 1.5 to 3.5 times the upper limit of normal day 0 through 5 months, 3 months after the second injection, one month after the second injection, and four months after the second injection, respectively. In all cases, the elevated ALT level(s) have returned to normal. None of the subjects was positive for HBsAg or anti-HBc.

One subject (case (b)(6)) who had an elevated ALT level 1.5 times the upper limit of normal prior to the first injection of vaccine, continued to have ALT elevations at each subsequent bleed (1, 2, 3, 5 and 7 months post the first injection). The ALT elevations range from 2.0 to 3.5 times the upper limit of normal. The subject is HBsAg and anti-HBc negative. Further serum samples and laboratory evaluation are pending.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
POPULATION : HEALTH CARE PERSONNEL
DOSE : 10 MCG
LOT : CK563
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (MIU/ML)		
						RESPONDERS	
	S/N >= 2.1		MIU/ML >= 10		ALL VACCINEES	S/N >= 2.1	MIU/ML >= 10
1 MONTH	43%	(25/58)	21%	(12/58)	1.3	8.6	19.4
2 MONTHS	90%	(52/58)	83%	(48/58)	60.7	60.7	74.8
3 MONTHS	96%	(54/56)	95%	(53/56)	127.1	127.1	135.0
6 MONTHS	100%	(58/58)	98%	(57/58)	217.0	217.0	229.7
7/8 MONTHS	100%	(56/56)	100%	(56/56)	2421.1	2421.1	2421.1

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (60 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	10 (18.2%)	3 (5.5%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		11 (20.0%)
PAIN	9 (16.4%)	3 (5.5%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		10 (18.2%)
TENDERNESS	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
SWELLING	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
SYSTEMIC	3 (5.5%)	4 (7.3%)	5 (9.1%)	4 (7.3%)	3 (5.5%)	0 (0.0%)		11 (20.0%)
WHOLE BODY/GENERAL	3 (5.5%)	2 (3.6%)	4 (7.3%)	2 (3.6%)	2 (3.6%)	0 (0.0%)		8 (14.5%)
FLUSH	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
FATIGUE/WEAKNESS	1 (1.8%)	0 (0.0%)	2 (3.6%)	1 (1.8%)	1 (1.8%)	0 (0.0%)		4 (7.3%)
HEADACHE	1 (1.8%)	2 (3.6%)	2 (3.6%)	2 (3.6%)	2 (3.6%)	0 (0.0%)		5 (9.1%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
MUSCULOSKELETAL	0 (0.0%)	2 (3.6%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (60 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
ARTHRALGIA (OTHER)	0 (0.0%)	1 (1.8%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
SHOULDER PAIN	0 (0.0%)	1 (1.8%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
DIGESTIVE SYSTEM	1 (1.8%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	1 (1.8%)	0 (0.0%)		2 (3.6%)
NAUSEA	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
GASTROENTERITIS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)	1 (1.8%)	0 (0.0%)		1 (1.8%)
UROGENITAL SYSTEM	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
OTHER	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
PERSONS WITH COMPLAINTS	12 (21.8%)	7 (12.7%)	8 (14.5%)	4 (7.3%)	3 (5.5%)	0 (0.0%)		17 (30.9%)
PERSONS WITH NO COMPLAINTS	43 (78.2%)	48 (87.3%)	47 (85.5%)	51 (92.7%)	52 (94.5%)	55 (100.0%)		38 (69.1%)
PERSONS WITH NO DATA	5 (8.3%)	5 (8.3%)	5 (8.3%)	5 (8.3%)	5 (8.3%)	5 (8.3%)		5 (8.3%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (59 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	13 (24.1%)	6 (11.1%)	4 (7.4%)	2 (3.7%)	1 (1.9%)	1 (1.9%)	15 (27.8%)
PAIN	10 (18.5%)	4 (7.4%)	2 (3.7%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	12 (22.2%)
TENDERNESS	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)
SWELLING	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)
PRURITIS (ITCHING)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)
ECCHYMOSIS	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)
SYSTEMIC	3 (5.6%)	3 (5.6%)	3 (5.6%)	5 (9.3%)	3 (5.6%)	3 (5.6%)	6 (11.1%)
WHOLE BODY/GENERAL	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	2 (3.7%)
HEADACHE	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	2 (3.7%)
INFECTIOUS SYNDROMES	1 (1.9%)	1 (1.9%)	1 (1.9%)	2 (3.7%)	1 (1.9%)	1 (1.9%)	2 (3.7%)
INFLUENZA, NOS	1 (1.9%)	1 (1.9%)	1 (1.9%)	2 (3.7%)	1 (1.9%)	1 (1.9%)	2 (3.7%)
RESPIRATORY	1 (1.9%)	1 (1.9%)	1 (1.9%)	2 (3.7%)	2 (3.7%)	2 (3.7%)	2 (3.7%)

00474

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (59 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
RHINITIS	1 (1.9%)	1 (1.9%)	1 (1.9%)	2 (3.7%)	2 (3.7%)	2 (3.7%)	2 (3.7%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)
PERSONS WITH COMPLAINTS	16 (29.6%)	9 (16.7%)	7 (13.0%)	7 (13.0%)	4 (7.4%)	4 (7.4%)	20 (37.0%)
PERSONS WITH NO COMPLAINTS	38 (70.4%)	45 (83.3%)	47 (87.0%)	47 (87.0%)	50 (92.6%)	50 (92.6%)	34 (63.0%)
PERSONS WITH NO DATA	5 (8.5%)	5 (8.5%)	5 (8.5%)	5 (8.5%)	5 (8.5%)	5 (8.5%)	5 (8.5%)

00475

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (59 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	9 (19.6%)	8 (17.0%)	3 (6.4%)	2 (4.3%)	1 (2.1%)	0 (0.0%)		13 (27.7%)
PAIN	8 (17.4%)	4 (8.5%)	2 (4.3%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		9 (19.1%)
SORENESS	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
PRURITIS (ITCHING)	1 (2.2%)	2 (4.3%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	0 (0.0%)		4 (8.5%)
HEMATOMA	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
SYSTEMIC	2 (4.3%)	1 (2.1%)	2 (4.3%)	2 (4.3%)	3 (6.4%)	1 (2.1%)		5 (10.6%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)		1 (2.1%)
INFLUENZA, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)		1 (2.1%)
RESPIRATORY	1 (2.2%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)		1 (2.1%)
RHINITIS	1 (2.2%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)		1 (2.1%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (59 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
DIGESTIVE SYSTEM	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.1%)	0 (0.0%)		2 (4.3%)
DIARRHEA	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
NAUSEA	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
GASTROENTERITIS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.1%)	0 (0.0%)		1 (2.1%)
ORGANS OF SPECIAL SENSE	1 (2.2%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)		1 (2.1%)
CONJUNCTIVITIS	1 (2.2%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)		1 (2.1%)
PERSONS WITH COMPLAINTS	11 (23.9%)	9 (19.1%)	5 (10.6%)	4 (8.5%)	4 (8.5%)	1 (2.1%)		17 (36.2%)
PERSONS WITH NO COMPLAINTS	35 (76.1%)	38 (80.9%)	42 (89.4%)	43 (91.5%)	43 (91.5%)	46 (97.9%)		30 (63.8%)
PERSONS WITH NO DATA	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	1 (2.1%)		1 (2.1%)

00877

Table 3
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (60 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	15 (37.5%)	30 (54.5%)	29 (52.7%)	25 (46.3%)	26 (47.3%)	24 (45.3%)		12 (21.8%)
99 - 99.9	23 (57.5%)	22 (40.0%)	25 (45.5%)	27 (50.0%)	27 (49.1%)	27 (50.9%)		35 (63.6%)
100 - 100.9	1 (2.5%)	2 (3.6%)	1 (1.8%)	2 (3.7%)	2 (3.6%)	2 (3.8%)		6 (10.9%)
101 - 101.9	1 (2.5%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
TEMPERATURE TAKEN	40 (66.7%)	55 (91.7%)	55 (91.7%)	54 (90.0%)	55 (91.7%)	53 (88.3%)		55 (91.7%)
TEMPERATURE NOT TAKEN	20 (33.3%)	5 (8.3%)	5 (8.3%)	6 (10.0%)	5 (8.3%)	7 (11.7%)		5 (8.3%)

Table 3 (cont)
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (59 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	17 (39.5%)	26 (48.1%)	29 (53.7%)	25 (47.2%)	27 (50.0%)	27 (55.1%)			15 (27.8%)
99 - 99.9	25 (58.1%)	24 (44.4%)	22 (40.7%)	27 (50.9%)	26 (48.1%)	21 (42.9%)			33 (61.1%)
100 - 100.9	1 (2.3%)	4 (7.4%)	3 (5.6%)	1 (1.9%)	1 (1.9%)	1 (2.0%)			6 (11.1%)
TEMPERATURE TAKEN	43 (72.9%)	54 (91.5%)	54 (91.5%)	53 (89.8%)	54 (91.5%)	49 (83.1%)			54 (91.5%)
TEMPERATURE NOT TAKEN	16 (27.1%)	5 (8.5%)	5 (8.5%)	6 (10.2%)	5 (8.5%)	10 (16.9%)			5 (8.5%)

Table 3 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0860
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (59 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	15 (37.5%)	14 (31.1%)	19 (43.2%)	22 (47.8%)	23 (51.1%)	24 (54.5%)			11 (23.9%)
99 - 99.9	22 (55.0%)	28 (62.2%)	23 (52.3%)	21 (45.7%)	18 (40.0%)	18 (40.9%)			27 (58.7%)
100 - 100.9	3 (7.5%)	2 (4.4%)	2 (4.5%)	3 (6.5%)	3 (6.7%)	2 (4.5%)			6 (13.0%)
102 - 102.9	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)			2 (4.3%)
TEMPERATURE TAKEN	40 (67.8%)	45 (76.3%)	44 (74.6%)	46 (78.0%)	45 (76.3%)	44 (74.6%)			46 (78.0%)
TEMPERATURE NOT TAKEN	19 (32.2%)	14 (23.7%)	15 (25.4%)	13 (22.0%)	14 (23.7%)	15 (25.4%)			13 (22.0%)

00480

STUDY 869

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 869
PURPOSE:	To evaluate immunological and clinical responses to yeast recombinant hepatitis B vaccine in health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #819910/18068/C-L217
PRIMARY INVESTIGATORS:	James G. Rankin, MB, BS, FRACP, FRCP(C) Director, Canadian Liver Foundation Epidemiology Unit and Professor Faculty of Medicine University of Toronto 12 Queen's Park Crescent West Toronto, Ontario M5S 1A8, Canada Randall A. Coates, MD, MHSc Assistant Professor Canadian Liver Foundation Epidemiology Unit University of Toronto 12 Queen's Park Crescent West Toronto, Ontario M5S 1A8, Canada
SECONDARY INVESTIGATORS:	David Stewart, MD, DECH, CCFP Medical Director, Department of Occupational Health and Safety 2075 Bayview Avenue Sunnybrook Medical Centre Toronto, Ontario M4N 3M5, Canada Mabel L. Halliday, MD, DPH, MSc Assistant Professor Canadian Liver Foundation Epidemiology Unit 12 Queen's Park Crescent West University of Toronto Toronto, Ontario M5S 1A8, Canada
STUDY LOCATION:	Sunnybrook Medical Centre 2075 Bayview Avenue Toronto, Ontario M4N 3M5, Canada

Study 869

DATE INITIATED: May 1985

DATE COMPLETED: In progress.

STUDY POPULATION: The study population will consist of health care personnel of either sex (excluding pregnant women) who are negative for hepatitis B virus serologic markers, have a normal ALT level and have not previously received any hepatitis B vaccine.

PROCEDURE: The study will be conducted in two stages. Stage I will include 30 participants and Stage II 120 participants. Participants will receive a 0.5 ml (10µg HBsAg) intramuscular injection of vaccine at 0, 1 and 6 months. Study subjects will be asked to record their temperatures and any local or systemic complaints for five days after each injection.

Blood samples will be obtained prior to vaccination, on Day 0, and at 1, 2, 3, 6, 8, 12 and 24 months post the initial injection. The pre and two-month sample will be tested for ALT. All samples will be assayed for HBsAg, anti-HBs and anti-HBc. Pre-vaccination tests will be performed in Toronto and post vaccination tests will be completed by MSDRL. Assays may also be done for yeast antibodies and anti-HBs subtype specificity.

RESULTS: HEALTH CARE PERSONNEL:

10 mcg lot #81991D/18068/C-L217 at 0, 1, and 6 months

1. Number Vaccinated:

Dose Level	Injection No. 1	2	3
10 mcg	71	71	0

Study 869

RESULTS: (Cont.)

2. Serologic Response:

Serologic data are available for 68 participants who received two injections of vaccine. At one month, 32% (22/68) of the participants seroconverted for anti-HBs S/N $\geq$ 2.1. Twelve percent (8/68) developed protective levels of anti-HBs (mIU/ml $\geq$ 10).

The GMT at one month for all vaccinees was 1.2 mIU/ml and 44.8 mIU/ml for responders with a titer of mIU/ml $\geq$10.

Serologic follow-up continues in progress.

3. Clinical Complaints:

Clinical follow-up data are available for 71 participants after injections one and two. The overall frequencies of complaints are presented below:

Type of Complaint	Frequency in % by Injection No. 1	2
Injection site	24 (17/71)	10 (7/71)
Systemic	30 (21/71)	17 (12/71)

Refer to Table 1 for listings of specific clinical complaints by injection number. Maximum temperature data are provided in Table 2.

There were no serious or alarming reactions attributable to vaccine.

Study 869

Reactions Reported to the OoBRR

One subject, a 46 year-old female health care worker, reported the onset of generalized pruritis 9 hours after administration of vaccine. Pruritis continued during the following 24 hours accompanied by irritability, nausea and parasthesias under the left breast. These symptoms resolved on the second and third days post vaccination. However, the participant reported that her extremities felt stiff and heavy. Her past medical history is significant for parasthesias which occurred 1 year prior to vaccination when a mass was surgically removed from her left breast. The investigator felt the subjects reaction had an emotional component and was probably not related to administration of vaccine.

Table 1

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	14 (19.7%)	7 (9.9%)	3 (4.2%)	1 (1.4%)	1 (1.4%)	1 (1.4%)		17 (23.9%)
INFLAMMATION	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
PAIN	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.8%)
SORENESS	9 (12.7%)	3 (4.2%)	2 (2.8%)	1 (1.4%)	1 (1.4%)	1 (1.4%)		10 (14.1%)
TENDERNESS	2 (2.8%)	2 (2.8%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (5.6%)
PRURITIS (ITCHING)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.8%)
SYSTEMIC	12 (16.9%)	6 (8.5%)	7 (9.9%)	6 (8.5%)	7 (9.9%)	2 (2.8%)		21 (29.6%)
WHOLE BODY/GENERAL	7 (9.9%)	0 (0.0%)	2 (2.8%)	1 (1.4%)	1 (1.4%)	0 (0.0%)		10 (14.1%)
FEVER (TEMP. NOT REPORTED)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
CHILLS	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
SWEATING	2 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.8%)
SENSATION OF WARMTH, GENERAL	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)

00485

Table 1 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
MALAISE	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
HEADACHE	2 (2.8%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)		5 (7.0%)
LIGHTHEADED	2 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.8%)
ACHINESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
HOT AND COLD FLASHES	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
RESPIRATORY	2 (2.8%)	2 (2.8%)	2 (2.8%)	3 (4.2%)	4 (5.6%)	1 (1.4%)		5 (7.0%)
RHINITIS	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)		2 (2.8%)
PHARYNGITIS (SORE THROAT)	2 (2.8%)	1 (1.4%)	2 (2.8%)	3 (4.2%)	4 (5.6%)	1 (1.4%)		5 (7.0%)
MUSCULOSKELETAL	2 (2.8%)	2 (2.8%)	2 (2.8%)	1 (1.4%)	1 (1.4%)	0 (0.0%)		5 (7.0%)
ARTHRALGIA (OTHER)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
SHOULDER PAIN	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	1 (1.4%)	0 (0.0%)		2 (2.8%)
NECK STIFFNESS	0 (0.0%)	2 (2.8%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)		2 (2.8%)

Table 1 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
ARM PAIN	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)		1 (1.4%)
OTHER	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
DIGESTIVE SYSTEM	3 (4.2%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)		5 (7.0%)
DIARRHEA	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
NAUSEA	3 (4.2%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (5.6%)
VOMITING	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	1 (1.4%)	0 (0.0%)		2 (2.8%)
NERVOUS SYSTEM	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)		3 (4.2%)
PARESTHESIAS	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)		1 (1.4%)
TWITCH/LOCAL SPASMS	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (2.8%)
PERSONS WITH COMPLAINTS	23 (32.4%)	12 (16.9%)	9 (12.7%)	7 (9.9%)	8 (11.3%)	3 (4.2%)		32 (45.1%)
PERSONS WITH NO COMPLAINTS	48 (67.6%)	59 (83.1%)	62 (87.3%)	64 (90.1%)	63 (88.7%)	68 (95.8%)		39 (54.9%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00487

Table 1 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	7 (9.9%)	3 (4.2%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (9.9%)
SORENESS	3 (4.2%)	2 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (4.2%)
TENDERNESS	2 (2.8%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.8%)
STIFFNESS/TIGHTNESS	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
PRURITIS (ITCHING)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
SYSTEMIC	7 (9.9%)	6 (8.5%)	5 (7.0%)	3 (4.2%)	4 (5.6%)	3 (4.2%)	12 (16.9%)
WHOLE BODY/GENERAL	5 (7.0%)	3 (4.2%)	3 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (12.7%)
FATIGUE/WEAKNESS	2 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.8%)
MALAISE	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.8%)
HEADACHE	3 (4.2%)	2 (2.8%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (7.0%)
LIGHTHEADED	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
HOT FLASHES	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)

00488

Table 1 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
RESPIRATORY	0 (0.0%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	2 (2.8%)
RHINITIS	0 (0.0%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
HEMIC AND LYMPHATIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
LYMPHADENOPATHY, CERVICAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
DIGESTIVE SYSTEM	2 (2.8%)	3 (4.2%)	2 (2.8%)	2 (2.8%)	2 (2.8%)	1 (1.4%)	4 (5.6%)
DIARRHEA	0 (0.0%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
NAUSEA	2 (2.8%)	2 (2.8%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	3 (4.2%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
DIMINISHED APPETITE	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.4%)
OTHER	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	0 (0.0%)	1 (1.4%)
NERVOUS SYSTEM	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.4%)

Table 1 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (71 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PARESTHESIAS	0 (0.0%)	1 (1.4%)	1 (1.4%)	1 (1.4%)	0 (0.0%)	0 (0.0%)		1 (1.4%)
PERSONS WITH COMPLAINTS	13 (18.3%)	9 (12.7%)	6 (8.5%)	3 (4.2%)	4 (5.6%)	3 (4.2%)		18 (25.4%)
PERSONS WITH NO COMPLAINTS	58 (81.7%)	62 (87.3%)	65 (91.5%)	68 (95.8%)	67 (94.4%)	68 (95.8%)		53 (74.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00490

Table 2

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (71 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (1.4%)	1 (1.4%)	1 (1.5%)	1 (1.4%)	1 (1.4%)	1 (1.4%)			1 (1.4%)
< 99	66 (94.3%)	66 (94.3%)	63 (92.6%)	62 (89.9%)	64 (92.8%)	68 (95.8%)			54 (76.1%)
99 - 99.9	2 (2.9%)	3 (4.3%)	4 (5.9%)	5 (7.2%)	3 (4.3%)	2 (2.8%)			13 (18.3%)
100 - 100.9	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	1 (1.4%)	0 (0.0%)			3 (4.2%)
TEMPERATURE TAKEN	70 (98.6%)	70 (98.6%)	68 (95.8%)	69 (97.2%)	69 (97.2%)	71 (100.0%)			71 (100.0%)
TEMPERATURE NOT TAKEN	1 (1.4%)	1 (1.4%)	3 (4.2%)	2 (2.8%)	2 (2.8%)	0 (0.0%)			0 (0.0%)

Table 2 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0869
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (71 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (1.4%)	1 (1.4%)	1 (1.5%)	1 (1.5%)	1 (1.4%)	1 (1.5%)			1 (1.4%)
< 99	63 (90.0%)	64 (92.8%)	58 (86.6%)	63 (92.6%)	65 (92.9%)	59 (89.4%)			57 (80.3%)
99 - 99.9	5 (7.1%)	3 (4.3%)	7 (10.4%)	3 (4.4%)	3 (4.3%)	5 (7.6%)			11 (15.5%)
100 - 100.9	1 (1.4%)	1 (1.4%)	1 (1.5%)	1 (1.5%)	1 (1.4%)	1 (1.5%)			2 (2.8%)
TEMPERATURE TAKEN	70 (98.6%)	69 (97.2%)	67 (94.4%)	68 (95.8%)	70 (98.6%)	66 (93.0%)			71 (100.0%)
TEMPERATURE NOT TAKEN	1 (1.4%)	2 (2.8%)	4 (5.6%)	3 (4.2%)	1 (1.4%)	5 (7.0%)			0 (0.0%)

STUDY 877

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 877
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among healthy adults who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 979/C-K564 (10 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Professor Oon Chong Jin University Department of Medicine I Singapore General Hospital Singapore 0316 Republic of Singapore
SECONDARY INVESTIGATOR:	Dr. Richard Guan University Department of Medicine I Singapore General Hospital Singapore 0316 Republic of Singapore
STUDY LOCATION:	Singapore General Hospital Singapore 0316 Republic of Singapore
DATE STUDY INITIATED:	January 26, 1985
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 25-30 healthy adults of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 877

STUDY PROCEDURE:

Eligible study participants receive a 1.0 ml (10 mcg HBsAg) intramuscular injection of vaccine at 0, 1, and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

A blood sample is obtained from each study participant approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may be assayed for yeast antibody. In addition, samples with an anti-HBs titer ≥25 mIU/ml may be tested to determine anti-a and anti-d subtype specificity.

RESULTS:

HEALTHY ADULTS

10 mcg Lot 979/C-K564 at 0, 1, and 6 months.

1. Number Vaccinated:

Injection No.		
1	2	3
31	31	31

2. Serologic Results:

Serologic data at 7-8 months are available for 29 study participants. Immune responses to vaccine were measured using an enzyme-linked immunosorbent assay (ELISA) to detect anti-HBs antibody. At 7-8 months 97% (28/29) of vaccine recipients seroconverted (mIU/ml ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 508.9 mIU/ml. Among responders with a titer of mIU/ml ≥10 the GMT was 663.7 mIU/ml. Anti-HBs responses at 1 through 7-8 months are included in Table 1.

Study 877

RESULTS: (Contd)

3. Clinical Complaints:

No serious or alarming adverse reactions attributable to vaccination have been reported.

Study 877

Table 1

Antibody Responses* Among Initially Seronegative Healthy Adults
Following Vaccination with 10 mcg Doses of
Yeast Recombinant Hepatitis B Vaccine
Lot 979/C-K564 at 0, 1, and 6 Months in Study 877

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
	mIU/ml ≥2.1	mIU/ml ≥10	All Vaccinees	Responders mIU/ml ≥2.1	Responders mIU/ml ≥10
1	0 (0/31)	0 (0/31)	0.3	--	--
2	48 (15/31)	32 (10/31)	2.1	16.4	26.9
3	71 (22/31)	55 (17/31)	6.1	21.0	28.7
6	77 (24/31)	65 (20/31)	12.1	35.5	49.4
7-8	97 (28/29)	97 (28/29)	508.9	663.7	663.7

* ELISA

STUDY 880

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 880
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 81990D/18066/C-L215 (10 mcg HBsAg/.5 ml) Lot 81766B/18067/C-L216 (10 mcg HBsAg/.5 ml) Lot 81991D/18068/C-L217 (10 mcg HBsAg/.5 ml) Lot 81992A/18070/C-L219 (10 mcg HBsAg/.5 ml) Lot 81954I/18071/C-L220 (10 mcg HBsAg/.5 ml)
PRIMARY INVESTIGATOR:	Gary P. Wormser, M.D. Department of Infectious Diseases West Chester County Medical Center Macy Pavilion 208 S.E. Valhalla, New York 10595
SECONDARY INVESTIGATOR:	Katherine Small, M.D. Robert L. Yarrish, M.D. West Chester County Medical Center Macy Pavilion 208 S.E. Valhalla, New York 10595
STUDY LOCATION:	West Chester County Medical Center Macy Pavilion 207 S.E. Valhalla, New York 10595
DATE STUDY INITIATED:	April 1, 1985
DATE STUDY COMPLETED:	In progress

Study 880

STUDY POPULATION: The study population consists of approximately 250 health care personnel of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

STUDY PROCEDURE: Health care personnel are assigned to one of the five lots of vaccine, stratified by sex and age, to assure that recipients of each lot are similar. Approximately fifty persons are assigned to each lot of vaccine.

Eligible study participants receive a 0.5 ml (10 mcg HBsAg) intramuscular injection of one of the five lots of vaccine at 0, 1 and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

Blood samples are obtained from each study participant approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 2, 3, 6, 7/8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc, and anti-HBs. ALT testing is performed on all pre-vaccination and 2 month post-vaccination samples. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested for anti-a and anti-d subtype specificity.

RESULTS: HEALTH CARE PERSONNEL

10 mcg Lot 81990D/18066/C-L215 at 0, 1, and 6 months
10 mcg Lot 81766B/18067/C-L216 at 0, 1, and 6 months
10 mcg Lot 81991D/18068/C-L217 at 0, 1, and 6 months
10 mcg Lot 81992A/18070/C-L219 at 0, 1, and 6 months
10 mcg Lot 81954I/18071/C-L220 at 0, 1, and 6 months

Study 880

RESULTS: (Cont.)

1. Number Vaccinated:

Lot	Injection No. 1	2	3
C-L215	48	48	40
C-L216	43	43	24
C-L217	53	53	26
C-L219	46	46	25
C-L220	43	43	38

2. Serologic Results:

Serologic data at 7/8 months are available for 33 (lot C-L215), 24 (lot C-L216), 23(lot C-L217), 25 (lot C-L219) and 34 (lot C-L220) study participants. At 7/8 months anti-HBs responses are as follows:

Lot	% Anti-HBs Positive S/N ≥2.1	mIU/ml ≥10	GMT (mIU/ml) All Vaccinees	Responders S/N ≥2.1	mIU/ml ≥10
C-L215	100(33/33)	94(31/33)	591.2	591.2	799.3
C-L216	100(24/24)	100(24/24)	1187.6	1187.6	1187.6
C-L217	96(22/23)	91(21/23)	345.8	476.4	593.6
C-L219	92(23/25)	92(23/25)	332.6	612.0	612.0
C-L220	100(34/34)	100(34/34)	1012.0	1012.0	1012.0

Anti-HBs responses at 1 through 7/8 months are included in Tables 1-5.

RESULTS: (Cont.)

3. Clinical Results:

Clinical follow-up data are available for 233, 221, and 99 study participants following the first, second and third injections of vaccine, respectively. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 6-15.

Clinical Complaint	Lot	% Frequency By Injection No. 1	2	3
Injection Site	C-L215	8(4/48)	13(6/46)	4(1/24)
	C-L216	9(4/43)	5(2/43)	9(1/11)
	C-L217	11(6/53)	4(2/53)	0(0/17)
	C-L219	17(8/46)	9(4/46)	6(1/17)
	C-L220	0(0/43)	9(4/43)	7(2/30)
Systemic	C-L215	2(1/48)	2(1/46)	4(1/24)
	C-L216	17(8/43)	2(1/43)	0(0/11)
	C-L217	13(7/53)	4(2/53)	0(0/17)
	C-L219	9(4/46)	0(0/46)	6(1/17)
	C-L220	7(3/43)	5(2/43)	3(1/30)

No serious or alarming adverse reactions attributable to vaccination have been reported.

ALT Elevations

One subject whose pre-vaccination ALT level was normal had a transient elevated level of this enzyme at 2 months post-vaccination. A follow-up serum sample obtained 1 week later showed a decreasing ALT. A reason for the ALT elevation was not ascertained. The subject has not developed anti-HBs after two injections of vaccine and has not been reported to show any clinical or serologic signs (HBsAg or anti-HBc) of hepatitis B through 6 months of follow-up.

Study 880

RESULTS: (Cont.)

HBV Markers (Anti-HBc)

In two subjects, the 6 (C-L219) and 8 (C-L220) month post-vaccination serum samples, respectively, were borderline positive for anti-HBc. All previous serum samples were negative for anti-HBc. The two subjects developed anti-HBs at 1 and 2 months, respectively. Both subjects have remained HBsAg negative and there has been no report of clinical illness.

Events Reported to OoBRR

A 25 year-old female subject recorded a temperature of 100.1°F several days after administration of a second injection of vaccine (lot C-L215). A CBC completed at that time revealed a normal WBC with a normal differential but a platelet count greater than 1 x $10^6/mm^3$ was noted. Bone marrow examination revealed numerous megakaryocytes. A pre-existing myeloproliferative disorder is considered the most likely diagnosis.

Table 1

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 81990D/18066/C-L215 at 0, 1, and 6 Months in Study 880

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1 Month	24 (11/46)	13 (6/46)	0.9	12.5	33.0
2 Months	76 (32/42)	50 (21/42)	11.1	30.0	77.5
3 Months	86 (32/37)	73 (27/37)	31.9	58.7	95.4
6 Months	86 (31/36)	64 (23/36)	23.0	36.8	71.8
7/8 Months	100 (33/33)	94 (31/33)	591.2	591.2	799.3

Table 2

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 81766B/18067/C-L216 at 0, 1, and 6 Months in Study 880

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1 Month	20 (8/41)	7 (3/41)	0.7	9.3	39.6
2 Months	86 (32/37)	65 (24/37)	14.4	25.2	45.4
3 Months	86 (25/29)	76 (22/29)	18.7	34.2	45.7
6 Months	100 (22/22)	100 (22/22)	51.5	51.5	51.5
7/8 Months	100 (24/24)	100 (24/24)	1187.6	1187.6	1187.6

2398I/9
1/28/86

00503

Table 3

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 819910/18068/C-L217 at 0, 1, and 6 Months in Study 880

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1 Month	19 (10/52)	8 (4/52)	0.8	14.5	91.2
2 Months	75 (36/48)	58 (28/48)	12.1	33.6	58.8
3 Months	84 (32/38)	68 (26/38)	23.6	48.7	77.4
6 Months	87 (26/30)	77 (23/30)	27.5	53.5	69.7
7/8 Months	96 (22/23)	91 (21/23)	345.8	476.4	593.6

2398I/10
1/28/86

00504

Table 4

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 81992A/18070/C-L219 at 0, 1, and 6 Months in Study 880

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1 Month	22 (10/45)	9 (4/45)	0.7	10.7	36.7
2 Months	64 (27/42)	40 (17/42)	6.3	27.2	69.1
3 Months	66 (21/32)	59 (19/32)	9.5	51.7	63.9
6 Months	90 (27/30)	73 (22/30)	29.7	48.0	77.2
7/8 Months	92 (23/25)	92 (23/25)	332.6	612.0	612.0

23981/11
1/28/86

Table 5

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 81954I/18071/C-L220 at 0, 1, and 6 Months in Study 880

Time (Months)	% with Anti-HBs		GMT (mIU/ml)		
			All Vaccinees	Responders	
	S/N ≥ 2.1	mIU/ml ≥ 10		S/N ≥ 2.1	mIU/ml ≥ 10
1 Month	40 (17/43)	21 (9/43)	1.7	14.6	63.8
2 Months	84 (36/43)	60 (26/43)	16.6	30.6	60.8
3 Months	97 (34/35)	83 (29/36)	50.5	55.6	84.8
6 Months	97 (37/38)	89 (34/38)	39.5	43.2	53.1
7/8 Months	100 (34/34)	100 (34/34)	1012.0	1012.0	1012.0

Table 6

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (48 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
[illegible]ON, LOCAL (INJECT. SITE)	1 (2.1%)	3 (6.3%)	1 (2.1%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		4 (8.3%)
[illegible]GRENESS	1 (2.1%)	2 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (6.3%)
[illegible]TENDERNESS	0 (0.0%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
[illegible]MIC	0 (0.0%)	1 (2.1%)	1 (2.1%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
[illegible] BODY/GENERAL	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
ILLNESS, NOS	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
RHINITIS	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.1%)	0 (0.0%)	0 (0.0%)		1 (2.1%)
PERSONS WITH COMPLAINTS	1 (2.1%)	4 (8.3%)	2 (4.2%)	2 (4.2%)	0 (0.0%)	0 (0.0%)		5 (10.4%)
PERSONS WITH NO COMPLAINTS	47 (97.9%)	44 (91.7%)	46 (95.8%)	46 (95.8%)	48 (100.0%)	48 (100.0%)		43 (89.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00507

Table 6 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (48 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
ION, LOCAL (INJECT. SITE)	4 (8.7%)	3 (6.5%)	2 (4.3%)	1 (2.2%)	1 (2.2%)	0 (0.0%)		6 (13.0%)
RENESS	4 (8.7%)	3 (6.5%)	2 (4.3%)	1 (2.2%)	1 (2.2%)	0 (0.0%)		6 (13.0%)
C	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
TORY	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
PPER RESPIRATORY INFECT., NOS	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
PERSONS WITH COMPLAINTS	5 (10.9%)	3 (6.5%)	2 (4.3%)	1 (2.2%)	1 (2.2%)	0 (0.0%)		6 (13.0%)
PERSONS WITH NO COMPLAINTS	41 (89.1%)	43 (93.5%)	44 (95.7%)	45 (97.8%)	45 (97.8%)	46 (100.0%)		40 (87.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 6 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (40 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
...ON, LOCAL (INJECT. SITE)	0 (0.0%)	1 (4.2%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
...ENESS	0 (0.0%)	1 (4.2%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
...	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
...ODY/GENERAL	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
...ALAISE	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
PERSONS WITH COMPLAINTS	1 (4.2%)	1 (4.2%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.2%)
PERSONS WITH NO COMPLAINTS	23 (95.8%)	23 (95.8%)	23 (95.8%)	24 (100.0%)	24 (100.0%)	24 (100.0%)		23 (95.8%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (48 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
< 99	36 (80.0%)	38 (84.4%)	35 (79.5%)	36 (81.8%)	37 (88.1%)	37 (92.5%)			25 (55.6%)
99 - 99.9	8 (17.8%)	7 (15.6%)	9 (20.5%)	8 (18.2%)	5 (11.9%)	3 (7.5%)			19 (42.2%)
100 - 100.9	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (2.2%)
TEMPERATURE TAKEN	45 (93.8%)	45 (93.8%)	44 (91.7%)	44 (91.7%)	42 (87.5%)	40 (83.3%)			45 (93.8%)
TEMPERATURE NOT TAKEN	3 (6.3%)	3 (6.3%)	4 (8.3%)	4 (8.3%)	6 (12.5%)	8 (16.7%)			3 (6.3%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (48 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	34 (89.5%)	35 (94.6%)	33 (86.8%)	35 (94.6%)	36 (97.3%)	32 (91.4%)			28 (73.7%)
99 - 99.9	4 (10.5%)	2 (5.4%)	5 (13.2%)	2 (5.4%)	1 (2.7%)	3 (8.6%)			10 (26.3%)
TEMPERATURE TAKEN	38 (79.2%)	37 (77.1%)	38 (79.2%)	37 (77.1%)	37 (77.1%)	35 (72.9%)			38 (79.2%)
TEMPERATURE NOT TAKEN	10 (20.8%)	11 (22.9%)	10 (20.8%)	11 (22.9%)	11 (22.9%)	13 (27.1%)			10 (20.8%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL215
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (40 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	11 (78.6%)	13 (92.9%)	13 (92.9%)	10 (76.9%)	13 (92.9%)	11 (91.7%)		8 (57.1%)
99 - 99.9	3 (21.4%)	1 (7.1%)	1 (7.1%)	3 (23.1%)	1 (7.1%)	1 (8.3%)		6 (42.9%)
TEMPERATURE TAKEN	14 (35.0%)	14 (35.0%)	14 (35.0%)	13 (32.5%)	14 (35.0%)	12 (30.0%)		14 (35.0%)
TEMPERATURE NOT TAKEN	26 (65.0%)	26 (65.0%)	26 (65.0%)	27 (67.5%)	26 (65.0%)	28 (70.0%)		26 (65.0%)

Table 8

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
INFECTION, LOCAL (INJECT. SITE)	2 (4.7%)	1 (2.3%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		4 (9.3%)
REDNESS	2 (4.7%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
WARMNESS	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
ERYTHEMA (REDNESS)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SWELLING	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SYSTEMIC	2 (4.7%)	3 (7.0%)	2 (4.7%)	3 (7.0%)	1 (2.3%)	0 (0.0%)		8 (18.6%)
WHOLE BODY/GENERAL	1 (2.3%)	2 (4.7%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
SWEATING	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
HEADACHE	0 (0.0%)	1 (2.3%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		2 (4.7%)
RESPIRATORY	0 (0.0%)	1 (2.3%)	1 (2.3%)	3 (7.0%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)		2 (4.7%)

Table 8 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
MUSCULOSKELETAL	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
ARTHRALGIA (OTHER)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
DIGESTIVE SYSTEM	0 (0.0%)	2 (4.7%)	2 (4.7%)	1 (2.3%)	1 (2.3%)	0 (0.0%)		4 (9.3%)
DIARRHEA	0 (0.0%)	2 (4.7%)	2 (4.7%)	1 (2.3%)	1 (2.3%)	0 (0.0%)		4 (9.3%)
NAUSEA	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
NERVOUS SYSTEM	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
VERTIGO/DIZZINESS	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
PERSONS WITH COMPLAINTS	4 (9.3%)	4 (9.3%)	2 (4.7%)	3 (7.0%)	1 (2.3%)	0 (0.0%)		9 (20.9%)
PERSONS WITH NO COMPLAINTS	39 (90.7%)	39 (90.7%)	41 (95.3%)	40 (93.0%)	42 (97.7%)	43 (100.0%)		34 (79.1%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 8 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		2 (4.7%)
INFLAMMATION	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SORENESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	1 (2.3%)		1 (2.3%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
HEADACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)		1 (2.3%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)		1 (2.3%)
PERSONS WITH COMPLAINTS	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)	1 (2.3%)		2 (4.7%)
PERSONS WITH NO COMPLAINTS	42 (97.7%)	43 (100.0%)	43 (100.0%)	43 (100.0%)	42 (97.7%)	42 (97.7%)		41 (95.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 8 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (18 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (9.1%)
SORENESS	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (9.1%)
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (9.1%)
PERSONS WITH NO COMPLAINTS	11 (100.0%)	11 (100.0%)	10 (90.9%)	11 (100.0%)	11 (100.0%)	11 (100.0%)		10 (90.9%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 9

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (43 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	33 (94.3%)	33 (94.3%)	33 (97.1%)	30 (93.8%)	33 (100.0%)	30 (100.0%)			29 (82.9%)
99 - 99.9	2 (5.7%)	2 (5.7%)	1 (2.9%)	2 (6.3%)	0 (0.0%)	0 (0.0%)			6 (17.1%)
TEMPERATURE TAKEN	35 (81.4%)	35 (81.4%)	34 (79.1%)	32 (74.4%)	33 (76.7%)	30 (69.8%)			35 (81.4%)
TEMPERATURE NOT TAKEN	8 (18.6%)	8 (18.6%)	9 (20.9%)	11 (25.6%)	10 (23.3%)	13 (30.2%)			8 (18.6%)

Table 9 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (43 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	23 (92.0%)	22 (100.0%)	22 (91.7%)	21 (95.5%)	21 (95.5%)	19 (90.5%)			20 (80.0%)
99 - 99.9	2 (8.0%)	0 (0.0%)	2 (8.3%)	1 (4.5%)	1 (4.5%)	2 (9.5%)			5 (20.0%)
TEMPERATURE TAKEN	25 (58.1%)	22 (51.2%)	24 (55.8%)	22 (51.2%)	22 (51.2%)	21 (48.8%)			25 (58.1%)
TEMPERATURE NOT TAKEN	18 (41.9%)	21 (48.8%)	19 (44.2%)	21 (48.8%)	21 (48.8%)	22 (51.2%)			18 (41.9%)

Table 9 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL216
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (18 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	5 (83.3%)	5 (83.3%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	5 (100.0%)			5 (83.3%)
99 - 99.9	1 (16.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (16.7%)
TEMPERATURE TAKEN	6 (33.3%)	6 (33.3%)	6 (33.3%)	6 (33.3%)	6 (33.3%)	5 (27.8%)			6 (33.3%)
TEMPERATURE NOT TAKEN	12 (66.7%)	12 (66.7%)	12 (66.7%)	12 (66.7%)	12 (66.7%)	13 (72.2%)			12 (66.7%)

Table 10

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (53 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	4 (7.5%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)		6 (11.3%)
PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)		1 (1.9%)
SORENESS	4 (7.5%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.4%)
SYSTEMIC	3 (5.7%)	3 (5.7%)	1 (1.9%)	1 (1.9%)	2 (3.8%)	0 (0.0%)		7 (13.2%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)		3 (5.7%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)		2 (3.8%)
HEADACHE	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)		2 (3.8%)
INFECTIOUS SYNDROMES	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
HERPES LABIALIS, RECURRENT	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
RHINORRHEA	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
PHARYNGITIS (SORE THROAT)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
MUSCULOSKELETAL	2 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.8%)

00520

Table 10 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (53 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
NECK PAIN	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
ARM PAIN	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)		2 (3.8%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)		1 (1.9%)
PERSONS WITH COMPLAINTS	6 (11.3%)	4 (7.5%)	1 (1.9%)	1 (1.9%)	3 (5.7%)	0 (0.0%)		12 (22.6%)
PERSONS WITH NO COMPLAINTS	47 (88.7%)	49 (92.5%)	52 (98.1%)	52 (98.1%)	50 (94.3%)	53 (100.0%)		41 (77.4%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 10 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

: 0880
:
: CL217
: 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (53 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	2 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)		2 (3.8%)
PAIN ON INJECTION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)		1 (1.9%)
SORENESS	2 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.8%)
SYSTEMIC	1 (1.9%)	1 (1.9%)	1 (1.9%)	2 (3.8%)	0 (0.0%)	0 (0.0%)		2 (3.8%)
WHOLE BODY/GENERAL	1 (1.9%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
FATIGUE/WEAKNESS	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
MALAISE	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
HEADACHE	0 (0.0%)	1 (1.9%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)		1 (1.9%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)		2 (3.8%)
NECK STIFFNESS	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (1.9%)	0 (0.0%)	0 (0.0%)		2 (3.8%)
PERSONS WITH COMPLAINTS	2 (3.8%)	1 (1.9%)	1 (1.9%)	2 (3.8%)	0 (0.0%)	1 (1.9%)		2 (3.8%)
PERSONS WITH NO COMPLAINTS	51 (96.2%)	52 (98.1%)	52 (98.1%)	51 (96.2%)	53 (100.0%)	52 (98.1%)		51 (96.2%)

Table 10 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

: 0880
:
NUMBER : CL217
: 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (53 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 10 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

: 0880
:
LOT NUMBER : CL217
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (26 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
PERSONS WITH NO COMPLAINTS	17 (100.0%)	17 (100.0%)	17 (100.0%)	17 (100.0%)	17 (100.0%)	17 (100.0%)		17 (100.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 11

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (53 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	34 (89.5%)	38 (100.0%)	33 (86.8%)	35 (92.1%)	35 (94.6%)	33 (94.3%)			29 (76.3%)
99 - 99.9	4 (10.5%)	0 (0.0%)	4 (10.5%)	3 (7.9%)	2 (5.4%)	2 (5.7%)			8 (21.1%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (2.6%)
TEMPERATURE TAKEN	38 (71.7%)	38 (71.7%)	38 (71.7%)	38 (71.7%)	37 (69.8%)	35 (66.0%)			38 (71.7%)
TEMPERATURE NOT TAKEN	15 (28.3%)	15 (28.3%)	15 (28.3%)	15 (28.3%)	16 (30.2%)	18 (34.0%)			15 (28.3%)

00525

Table 11 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (53 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	28 (87.5%)	27 (87.1%)	28 (96.6%)	27 (96.4%)	25 (89.3%)	23 (88.5%)			23 (71.9%)
99 - 99.9	4 (12.5%)	4 (12.9%)	1 (3.4%)	1 (3.6%)	3 (10.7%)	2 (7.7%)			8 (25.0%)
102 - 102.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)			1 (3.1%)
TEMPERATURE TAKEN	32 (60.4%)	31 (58.5%)	29 (54.7%)	28 (52.8%)	28 (52.8%)	26 (49.1%)			32 (60.4%)
TEMPERATURE NOT TAKEN	21 (39.6%)	22 (41.5%)	24 (45.3%)	25 (47.2%)	25 (47.2%)	27 (50.9%)			21 (39.6%)

00526

Table 11 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL217
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (26 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	5 (100.0%)	5 (100.0%)	5 (100.0%)	5 (100.0%)	5 (100.0%)	5 (100.0%)		5 (100.0%)
TEMPERATURE TAKEN	5 (19.2%)	5 (19.2%)	5 (19.2%)	5 (19.2%)	5 (19.2%)	5 (19.2%)		5 (19.2%)
TEMPERATURE NOT TAKEN	21 (80.8%)	21 (80.8%)	21 (80.8%)	21 (80.8%)	21 (80.8%)	21 (80.8%)		21 (80.8%)

Table 12

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (46 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	8 (17.4%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		8 (17.4%)
PAIN	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (4.3%)
SORENESS	5 (10.9%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (10.9%)
RASH, NOS	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
SYSTEMIC	1 (2.2%)	1 (2.2%)	2 (4.3%)	2 (4.3%)	1 (2.2%)	0 (0.0%)		4 (8.7%)
WHOLE BODY/GENERAL	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
SWEATING	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	2 (4.3%)	2 (4.3%)	1 (2.2%)	0 (0.0%)		2 (4.3%)
SINUSITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	2 (4.3%)	1 (2.2%)	1 (2.2%)	0 (0.0%)		2 (4.3%)
DIGESTIVE SYSTEM	1 (2.2%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (4.3%)

Table 12 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (46 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
DIARRHEA	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
NAUSEA	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
VOMITING	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
PERSONS WITH COMPLAINTS	8 (17.4%)	3 (6.5%)	2 (4.3%)	2 (4.3%)	1 (2.2%)	0 (0.0%)		10 (21.7%)
PERSONS WITH NO COMPLAINTS	38 (82.6%)	43 (93.5%)	44 (95.7%)	44 (95.7%)	45 (97.8%)	46 (100.0%)		36 (78.3%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00529

Table 12 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (46 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	3 (6.5%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (8.7%)
INFLAMMATION	3 (6.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (6.5%)
TENDERNESS	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.2%)
PATIENTS WITH COMPLAINTS	3 (6.5%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (8.7%)
PATIENTS WITH NO COMPLAINTS	43 (93.5%)	45 (97.8%)	46 (100.0%)	46 (100.0%)	46 (100.0%)	46 (100.0%)		42 (91.3%)
PATIENTS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 12 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
PAIN	0 (0.0%)	1 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.9%)
PRURITIC	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
WHOLE BODY/GENERAL	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
HEADACHE	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)
PERSONS WITH COMPLAINTS	1 (5.9%)	2 (11.8%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		2 (11.8%)
PERSONS WITH NO COMPLAINTS	16 (94.1%)	15 (88.2%)	16 (94.1%)	16 (94.1%)	16 (94.1%)	16 (94.1%)		15 (88.2%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00531

Table 13

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (46 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	33 (86.8%)	35 (94.6%)	34 (91.9%)	31 (86.1%)	34 (91.9%)	33 (97.1%)			26 (68.4%)
99 - 99.9	5 (13.2%)	2 (5.4%)	3 (8.1%)	5 (13.9%)	3 (8.1%)	1 (2.9%)			12 (31.6%)
TEMPERATURE TAKEN	38 (82.6%)	37 (80.4%)	37 (80.4%)	36 (78.3%)	37 (80.4%)	34 (73.9%)			38 (82.6%)
TEMPERATURE NOT TAKEN	8 (17.4%)	9 (19.6%)	9 (19.6%)	10 (21.7%)	9 (19.6%)	12 (26.1%)			8 (17.4%)

Table 13 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (46 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	23 (88.5%)	24 (92.3%)	21 (80.8%)	25 (96.2%)	19 (73.1%)	20 (87.0%)		17 (65.4%)
99 - 99.9	3 (11.5%)	2 (7.7%)	5 (19.2%)	1 (3.8%)	7 (26.9%)	3 (13.0%)		9 (34.6%)
TEMPERATURE TAKEN	26 (56.5%)	26 (56.5%)	26 (56.5%)	26 (56.5%)	26 (56.5%)	23 (50.0%)		26 (56.5%)
TEMPERATURE NOT TAKEN	20 (43.5%)	20 (43.5%)	20 (43.5%)	20 (43.5%)	20 (43.5%)	23 (50.0%)		20 (43.5%)

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Table 13 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL219
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (21 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	10 (83.3%)	8 (72.7%)	9 (81.8%)	10 (90.9%)	9 (81.8%)	9 (81.8%)		7 (58.3%)
99 - 99.9	2 (16.7%)	3 (27.3%)	2 (18.2%)	1 (9.1%)	2 (18.2%)	2 (18.2%)		5 (41.7%)
TEMPERATURE TAKEN	12 (57.1%)	11 (52.4%)	11 (52.4%)	11 (52.4%)	11 (52.4%)	11 (52.4%)		12 (57.1%)
TEMPERATURE NOT TAKEN	9 (42.9%)	10 (47.6%)	10 (47.6%)	10 (47.6%)	10 (47.6%)	10 (47.6%)		9 (42.9%)

00534

Table 14

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 1							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
[illegible]	0 (0.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
[illegible] BODY/GENERAL	0 (0.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
[illegible]TIGUE/WEAKNESS	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (4.7%)
HEADACHE	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
[illegible]NS WITH COMPLAINTS	0 (0.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (7.0%)
[illegible]NS WITH NO COMPLAINTS	43 (100.0%)	40 (93.0%)	43 (100.0%)	43 (100.0%)	43 (100.0%)	43 (100.0%)		40 (93.0%)
[illegible]NS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

00535

Table 14 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 2 DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
LOCATION, LOCAL (INJECT. SITE)	4 (9.3%)	3 (7.0%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		4 (9.3%)
PAIN	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SORENESS	2 (4.7%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (4.7%)
INDURATION	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
HEMATOMA	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SYSTEMIC	0 (0.0%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0 (0.0%)	0 (0.0%)		2 (4.7%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
HEADACHE	0 (0.0%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
RESPIRATORY	0 (0.0%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
PERSONS WITH COMPLAINTS	4 (9.3%)	5 (11.6%)	3 (7.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)		6 (14.0%)
PERSONS WITH NO COMPLAINTS	39 (90.7%)	38 (88.4%)	40 (93.0%)	40 (93.0%)	43 (100.0%)	43 (100.0%)		37 (86.0%)

Table 14 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (43 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 14 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (38 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	2 (6.7%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
SORENESS	0 (0.0%)	2 (6.7%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
SYSTEMIC	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
WHOLE BODY/GENERAL	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
MALAISE	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
N, WITH COMPLAINTS	1 (3.3%)	2 (6.7%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (10.0%)
N, WITH NO COMPLAINTS	29 (96.7%)	28 (93.3%)	28 (93.3%)	30 (100.0%)	30 (100.0%)	30 (100.0%)		27 (90.0%)
N, WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 15

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (43 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	36 (85.7%)	40 (95.2%)	38 (95.0%)	38 (95.0%)	36 (94.7%)	32 (100.0%)			31 (73.8%)
99 - 99.9	6 (14.3%)	2 (4.8%)	2 (5.0%)	2 (5.0%)	2 (5.3%)	0 (0.0%)			11 (26.2%)
TEMPERATURE TAKEN	42 (97.7%)	42 (97.7%)	40 (93.0%)	40 (93.0%)	38 (88.4%)	32 (74.4%)			42 (97.7%)
TEMPERATURE NOT TAKEN	1 (2.3%)	1 (2.3%)	3 (7.0%)	3 (7.0%)	5 (11.6%)	11 (25.6%)			1 (2.3%)

Table 15 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0880
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (43 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	37 (92.5%)	36 (90.0%)	37 (94.9%)	38 (97.4%)	37 (94.9%)	33 (94.3%)			31 (77.5%)
99 - 99.9	3 (7.5%)	4 (10.0%)	2 (5.1%)	1 (2.6%)	2 (5.1%)	2 (5.7%)			9 (22.5%)
TEMPERATURE TAKEN	40 (93.0%)	40 (93.0%)	39 (90.7%)	39 (90.7%)	39 (90.7%)	35 (81.4%)			40 (93.0%)
TEMPERATURE NOT TAKEN	3 (7.0%)	3 (7.0%)	4 (9.3%)	4 (9.3%)	4 (9.3%)	8 (18.6%)			3 (7.0%)

Table 15 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0080
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (38 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	17 (85.0%)	19 (95.0%)	18 (90.0%)	19 (95.0%)	18 (94.7%)	16 (94.1%)		16 (80.0%)
99 - 99.9	3 (15.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)	1 (5.3%)	1 (5.9%)		4 (20.0%)
TEMPERATURE TAKEN	20 (52.6%)	20 (52.6%)	20 (52.6%)	20 (52.6%)	19 (50.0%)	17 (44.7%)		20 (52.6%)
TEMPERATURE NOT TAKEN	18 (47.4%)	18 (47.4%)	18 (47.4%)	18 (47.4%)	19 (50.0%)	21 (55.3%)		18 (47.4%)

PROGRAM:	Alum-Adsorbed Recombinant Hepatitis B Vaccine, Study 882
PURPOSE:	To evaluate antibody and clinical responses to 10 mcg doses of recombinant hepatitis B vaccine in healthy adult male volunteers.
VACCINE:	Recombinant Hepatitis B Vaccine - Alum Adsorbed: Lot #81990D/18066/C-L215
PRIMARY INVESTIGATOR:	Shiro Iino, M.D. First Department of Internal Medicine Faculty of Medicine University of Tokyo Hongo, Bunkyo-ku, Tokyo Tokyo, Japan
STUDY LOCATION:	Tokyo and Osaka, Japan
DATE INITIATED:	February 26, 1985
DATE COMPLETED:	In progress
STUDY POPULATION:	The population consists of 40 healthy adults (20 to 59 years of age) who are negative for hepatitis B virus serologic markers, have normal liver function tests and have not previously received any hepatitis B vaccine.
STUDY PROCEDURE:	Each participant receives a 10 mcg intramuscular injection of vaccine on day 0, 1 and 6 months. Study subjects are asked to record their temperatures and any local or systemic complaints for five days after each injection. Serum samples are obtained prior to vaccination, and at 1, 2, 3, 4, 5, 6, 7, 9 and 12 months post initial injection. All specimens are assayed for HBsAg, anti-HBs, anti-HBc and several other laboratory examinations by the (b) (4) Samples may also be assayed at (b) (4) for yeast antibody.

2396I/86I/1
1/19/86

Study 882

RESULTS:

INITIALLY SERONEGATIVE HEALTHY ADULTS

10 mcg lot #819900/18066/C-L215 at 0, 1, and 6 months

1. Number Vaccinated:

Dose Level	Injection Number		
	1	2	3
10 mcg	40	40	40

2. Serologic Results:

When the cutoff was S/N ≥2.1, the anti-HBs seroconversion rate was 33% (13/40) one month after the first injection, and 100% (40/40) at 7 months. Table 1 lists antibody responses for up to nine months of follow-up.

3. Clinical Complaints:

Clinical follow-up data are available for 40 participants following each injection.

Type of Complaint	Dose Level	Frequency in % by Injection No.		
		1	2	3
Injection Site	10 mcg	10 (4/40)	13 (5/40)	10 (4/40)
Systemic	10 mcg	8 (3/40)	3 (1/40)	5 (2/40)

There have been serious or alarming adverse reactions attributable to vaccine reported.

Study 882

Table 1

Antibody Responses Among Healthy Male Adults Following Vaccination with 10 mcg Doses of Recombinant Vaccine Lot C-L215 at 0, 1, and 6 Months

RIA Cut-Off Index	Anti-HBs Response								
	Before	1 Mo.	2 Mos.	3 Mos.	4 Mos.	5 Mos.	6 Mos.	7 Mos.	9 Mos.
<2.1	40	27	12	8	4	4	4		
2.1-21		12	23	24	24	18	20	5	5
21-103		1	5	8	9	13	13	3	3
105-208					3	4	3	24	19
210-						1		8	12
Seroconversion %		32.5	70.0	80.0	90.0	90.0	90.0	100	100

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 883
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among health care personnel who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 819541/18071/C-L220 (10 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Stanley Plotkin, M.D./Stuart Starr, M.D. Division of Preventive Medicine Joseph Stokes, Jr. Research Institute Children's Hospital of Philadelphia Philadelphia, Pennsylvania 19104
SECONDARY INVESTIGATOR:	Vernon Brightman, DMD, DDS Univ. of Pennsylvania School of Dental Medicine Philadelphia, Pennsylvania 19104
STUDY LOCATION:	University of Pennsylvania School of Dental Medicine 4001 Spruce Street Philadelphia, Pennsylvania 19104
DATE STUDY INITIATED:	November 13, 1984
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of approximately 50 healthy dental students of either sex (excluding pregnant women), who are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 883

STUDY PROCEDURE:

Eligible study participants receive a 0.25 ml (5 mcg HBsAg) or 0.5 ml (10 mcg HBsAg) intramuscular injection of vaccine at 0, 1, and 6 months. Vaccine recipients record their temperature and any local or systemic complaints for five days after each injection of vaccine.

A blood sample is obtained approximately two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 2 weeks, 1, 2, 3, 6, 8, 12 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT. Samples may be tested for yeast antibody. In addition, samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested for anti-a and anti-d subtype specificity.

RESULTS:

HEALTH CARE PERSONNEL

5 mcg Lot 81954I/18071/C-L220 at 0, 1, and 6 months
10 mcg Lot 81954I/18071/C-L220 at 0, 1, and 6 months

1. Number Vaccinated:

Dose (mcg)	Injection No. 1	2	3
5	25	25	24
10	28	28	27

2. Serologic Results:

Serologic data at 7-8 months are available for 20 study participants who received a 5 mcg dose and 24 participants who received a 10 mcg dose of vaccine.

Study 883

RESULTS: (Cont.)

At 7-8 months, anti-HBs responses are as follows:

Dose (mcg)	% Anti-HBs Positive S/N ≥2.1	% Anti-HBs Positive mIU/ml ≥10	GMT (mIU/ml) All Vaccinees	GMT (mIU/ml) Responders S/N ≥2.1	GMT (mIU/ml) Responders mIU/ml ≥10
5	100(20/20)	95(19/20)	215.3	215.3	259.0
10	100(24/24)	96(23/24)	863.2	863.2	1084.9

3. Clinical Results:

Clinical follow-up data are available for 25 (5 mcg dose) and 28 (10 mcg dose) study participants following the first two injections and for 23 (5 mcg dose) and 27 (10 mcg dose) participants following the third injection of vaccine. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 2-5. In summary:

Clinical Complaint	Dose (mcg)	% Frequency by Injection No. 1	2	3
Injection Site	5	4(1/25)	0(0/25)	4(1/23)
	10	7(2/28)	4(1/28)	4(1/27)
Systemic	5	28(7/25)	4(1/25)	13(3/23)
	10	29(8/28)	18(5/28)	15(4/27)

No serious or alarming adverse reactions attributable to vaccination have been reported.

ALT Elevations

Alanine aminotransferase levels were normal in all vaccine recipients except for elevations at 8 months in two participants. Case Nos. (b) (6) had ALT levels of 116 and 122, respectively, at 8 months. However, the serum sample obtained from Case No. (b) (6) was hemolyzed. Subsequent serum samples have not been obtained from this individual.

Study 883

ALT Elevations (Contd)

Case No. (b) (6) had a normal ALT level at 12 months. Neither individual has shown any clinical or serologic signs (HBsAg or anti-HBc) of hepatitis B.

HBV Markers (HBsAg)

One initially seronegative vaccine recipient (5 mcg dose) had a 6-month post-vaccination serum sample marginally positive for HBsAg (S/N = 2.4). The same serum sample was reported negative on retest (S/N $\leq$2.1). All other post-vaccination samples, including the sample obtained at 8 months, were negative for HBsAg. All serum samples were negative for anti-HBc. Alanine aminotransferase levels were normal. The subject developed anti-HBs at 3 months.

Events Reported to OoBRR

A (b) (6) developed persistent cough and tiredness. He was seen by a physician approximately 4 months after his second injection (10 mcg dose) of vaccine and was tentatively diagnosed as having chronic lymphatic leukemia. The illness is felt not to be related to the vaccine.

Table 1

Antibody Responses Among Initially Seronegative Health Care Personnel Following Vaccination with 5 or 10 mcg Doses of Yeast Recombinant Hepatitis B Vaccine Lot 819541/18071/C-L220 at 0, 1, and 6 Months in Study 883

	5 mcg					10 mcg				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
Time (Months)	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	Responders S/N ≥ 2.1	Responders mIU/ml ≥ 10	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	Responders S/N ≥ 2.1	Responders mIU/ml ≥ 10
2 weeks	13 (3/24)	4 (1/24)	0.5	5.4	10.4	4 (1/28)	4(1/28)	0.4	22.2	22.2
1	12 (3/25)	8 (2/25)	0.6	12.4	16.7	14 (4/28)	7 (2/28)	0.6	15.5	50.9
2	59 (13/22)	41 (9/22)	5.3	23.5	40.2	65 (17/26)	31 (8/26)	4.3	12.2	31.8
3	79 (19/24)	54 (13/24)	10.1	21.1	40.3	86 (24/28)	64 (18/28)	11.9	21.9	34.3
6	81 (17/21)	57 (12/21)	10.8	20.4	36.0	85 (22/26)	85 (22/26)	30.3	46.7	54.4
7/8	100 (20/20)	95 (19/20)	215.3	215.3	259.0	100 (24/24)	96 (23/24)	863.2	863.2	1084.9

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SORENESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SYSTEMIC	6 (24.0%)	4 (16.0%)	3 (12.0%)	3 (12.0%)	3 (12.0%)	2 (8.0%)	7 (28.0%)
WHOLE BODY/GENERAL	3 (12.0%)	2 (8.0%)	1 (4.0%)	2 (8.0%)	2 (8.0%)	1 (4.0%)	3 (12.0%)
CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
SWEATING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
FATIGUE/WEAKNESS	3 (12.0%)	2 (8.0%)	1 (4.0%)	2 (8.0%)	2 (8.0%)	1 (4.0%)	3 (12.0%)
LIGHTHEADED	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
ACHINESS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
INTEGUMENTARY SYSTEM	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
PRURITIS/ITCHING	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PIMPLE	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)

00550

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
RESPIRATORY	2 (8.0%)	2 (8.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	3 (12.0%)
RHINITIS	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
UPPER RESPIRATORY INFECT., NOS	2 (8.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	2 (8.0%)
COUGH	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
DIGESTIVE SYSTEM	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	2 (8.0%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)
NAUSEA	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
DIMINISHED APPETITE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
NERVOUS SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)
VERTIGO/DIZZINESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)
PERSONS WITH COMPLAINTS	7 (28.0%)	4 (16.0%)	3 (12.0%)	3 (12.0%)	3 (12.0%)	2 (8.0%)	8 (32.0%)
PERSONS WITH NO COMPLAINTS	18 (72.0%)	21 (84.0%)	22 (88.0%)	22 (88.0%)	22 (88.0%)	23 (92.0%)	17 (68.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

00551

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
WHOLE BODY/GENERAL	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
HEADACHE	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PERSONS WITH COMPLAINTS	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)
PERSONS WITH NO COMPLAINTS	23 (95.8%)	24 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	24 (96.0%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (24 PATIENTS) - DOSE 3						NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION						
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SORENESS	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SYSTEMIC	3 (13.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	3 (13.0%)
WHOLE BODY/GENERAL	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
HEADACHE	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
RESPIRATORY	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
UPPER RESPIRATORY INFECT., NOS	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
DIGESTIVE SYSTEM	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
NAUSEA	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
PERSONS WITH COMPLAINTS	4 (17.4%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	4 (17.4%)
PERSONS WITH NO COMPLAINTS	19 (82.6%)	23 (100.0%)	23 (100.0%)	22 (95.7%)	23 (100.0%)	23 (100.0%)	19 (82.6%)
PERSONS WITH NO DATA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
< 99	22 (88.0%)	20 (80.0%)	22 (88.0%)	22 (88.0%)	24 (96.0%)	24 (96.0%)		17 (68.0%)
99 - 99.9	3 (12.0%)	4 (16.0%)	3 (12.0%)	3 (12.0%)	1 (4.0%)	1 (4.0%)		7 (28.0%)
100 - 100.9	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
TEMPERATURE TAKEN	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)	25 (100.0%)		25 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (25 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	19 (82.6%)	22 (95.7%)	23 (95.8%)	24 (100.0%)	23 (95.8%)	23 (100.0%)			18 (75.0%)
99 - 99.9	4 (17.4%)	1 (4.3%)	1 (4.2%)	0 (0.0%)	1 (4.2%)	0 (0.0%)			6 (25.0%)
TEMPERATURE TAKEN	23 (92.0%)	23 (92.0%)	24 (96.0%)	24 (96.0%)	24 (96.0%)	23 (92.0%)			24 (96.0%)
TEMPERATURE NOT TAKEN	2 (8.0%)	2 (8.0%)	1 (4.0%)	1 (4.0%)	1 (4.0%)	2 (8.0%)			1 (4.0%)

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Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 5 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (24 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	2 (8.7%)	2 (8.7%)	2 (8.7%)	2 (8.7%)	2 (8.7%)	2 (8.7%)			2 (8.7%)
< 99	19 (82.6%)	20 (87.0%)	21 (91.3%)	21 (91.3%)	19 (82.6%)	21 (91.3%)			18 (78.3%)
99 - 99.9	1 (4.3%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	2 (8.7%)	0 (0.0%)			2 (8.7%)
101 - 101.9	1 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (4.3%)
TEMPERATURE TAKEN	23 (95.8%)	23 (95.8%)	23 (95.8%)	23 (95.8%)	23 (95.8%)	23 (95.8%)			23 (95.8%)
TEMPERATURE NOT TAKEN	1 (4.2%)	1 (4.2%)	1 (4.2%)	1 (4.2%)	1 (4.2%)	1 (4.2%)			1 (4.2%)

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0883
TREATMENT :
LOT NUMBER : CL220
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (28 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	2 (7.1%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (7.1%)
SORENESS	2 (7.1%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (7.1%)
SYSTEMIC	7 (25.0%)	2 (7.1%)	3 (10.7%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	8 (28.6%)
WHOLE BODY/GENERAL	7 (25.0%)	1 (3.6%)	2 (7.1%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	7 (25.0%)
FEVER (TEMP. NOT REPORTED)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
SWEATING	1 (3.6%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
SENSATION OF WARMTH, GENERAL	2 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (7.1%)
FATIGUE/WEAKNESS	3 (10.7%)	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (10.7%)
MALAISE	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
HEADACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	1 (3.6%)
RESPIRATORY	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
UPPER RESPIRATORY INFECT., NOS	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)