Table 4 (cont.)

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
CARDIOVASCULAR	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
HYPOTENSION	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
NAUSEA	0 (0.0%)	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
DIMINISHED APPETITE	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
NERVOUS SYSTEM	3 (10.7%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (10.7%)
VERTIGO/DIZZINESS	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
THOUGHT IMPAIRMENT	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
TREMOR	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
CONJUNCTIVITIS	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
PERSONS WITH COMPLAINTS	7 (25.0%)	2 (7.1%)	3 (10.7%)	0 (0.0%)	1 (3.6%)	0 (0.0%)		8 (28.6%)
PERSONS WITH NO COMPLAINTS	21 (75.0%)	26 (92.9%)	25 (89.3%)	28 (100.0%)	27 (96.4%)	28 (100.0%)		20 (71.4%)

Table 4 (cont.)

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						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 4 (cont.)

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 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
SORENESS	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
SYSTEMIC	2 (7.1%)	2 (7.1%)	1 (3.6%)	2 (7.1%)	1 (3.7%)	1 (3.7%)	5 (17.9%)
WHOLE BODY/GENERAL	2 (7.1%)	1 (3.6%)	1 (3.6%)	2 (7.1%)	1 (3.7%)	1 (3.7%)	4 (14.3%)
SWEATING	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
FATIGUE/WEAKNESS	1 (3.6%)	0 (0.0%)	0 (0.0%)	2 (7.1%)	1 (3.7%)	1 (3.7%)	4 (14.3%)
MALAISE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	1 (3.7%)	0 (0.0%)	1 (3.6%)
HEADACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
HOT AND COLD FLASHES	0 (0.0%)	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
HOT FLASHES	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)
RESPIRATORY	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	2 (7.1%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (3.6%)

00560

Table 4 (cont.)

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 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
CARDIOVASCULAR	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
PALLOR	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.6%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (3.6%)	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)		2 (7.1%)
NAUSEA	0 (0.0%)	1 (3.6%)	1 (3.6%)	1 (3.6%)	0 (0.0%)	0 (0.0%)		2 (7.1%)
PERSONS WITH COMPLAINTS	3 (10.7%)	2 (7.1%)	1 (3.6%)	2 (7.1%)	1 (3.7%)	1 (3.7%)		5 (17.9%)
PERSONS WITH NO COMPLAINTS	25 (89.3%)	26 (92.9%)	27 (96.4%)	26 (92.9%)	26 (96.3%)	26 (96.3%)		23 (82.1%)
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 4 (cont.)

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 (27 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (3.7%)	1 (3.7%)	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
SORENESS	1 (3.7%)	1 (3.7%)	0 (0.0%)	1 (3.7%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
SYSTEMIC	4 (14.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	4 (14.8%)
WHOLE BODY/GENERAL	4 (14.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (14.8%)
FEVER (TEMP. NOT REPORTED)	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
FATIGUE/WEAKNESS	3 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (11.1%)
ACHINESS	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
CARDIOVASCULAR	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
PALLOR	1 (3.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (3.7%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	1 (3.7%)
PERSONS WITH COMPLAINTS	4 (14.8%)	1 (3.7%)	0 (0.0%)	1 (3.7%)	0 (0.0%)	1 (3.7%)	4 (14.8%)

00562

Table 4 (cont.)

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 (27 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PERSONS WITH NO COMPLAINTS	23 (85.2%)	26 (96.3%)	27 (100.0%)	26 (96.3%)	27 (100.0%)	26 (96.3%)		23 (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 5

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

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

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (28 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	17 (60.7%)	27 (96.4%)	24 (85.7%)	26 (96.3%)	24 (88.9%)	22 (81.5%)			15 (53.6%)
99 - 99.9	11 (39.3%)	1 (3.6%)	4 (14.3%)	1 (3.7%)	3 (11.1%)	5 (18.5%)			13 (46.4%)
TEMPERATURE TAKEN	28 (100.0%)	28 (100.0%)	28 (100.0%)	27 (96.4%)	27 (96.4%)	27 (96.4%)			28 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	1 (3.6%)	1 (3.6%)			0 (0.0%)

00564

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

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

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (28 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	24 (85.7%)	27 (96.4%)	27 (96.4%)	26 (92.9%)	26 (96.3%)	25 (92.6%)			21 (75.0%)
99 - 99.9	4 (14.3%)	1 (3.6%)	1 (3.6%)	2 (7.1%)	1 (3.7%)	2 (7.4%)			7 (25.0%)
TEMPERATURE TAKEN	28 (100.0%)	28 (100.0%)	28 (100.0%)	28 (100.0%)	27 (96.4%)	27 (96.4%)			28 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.6%)	1 (3.6%)			0 (0.0%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

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

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (27 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	19 (76.0%)	23 (85.2%)	25 (92.6%)	26 (96.3%)	25 (92.6%)	24 (88.9%)			18 (66.7%)
99 - 99.9	6 (24.0%)	4 (14.8%)	2 (7.4%)	1 (3.7%)	2 (7.4%)	3 (11.1%)			9 (33.3%)
TEMPERATURE TAKEN	25 (92.6%)	27 (100.0%)	27 (100.0%)	27 (100.0%)	27 (100.0%)	27 (100.0%)			27 (100.0%)
TEMPERATURE NOT TAKEN	2 (7.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

STUDY 885

PROGRAM:	Yeast Recombinant Hepatitis B Vaccine, Study 885
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 81990D/18066/C-L215 81766B/18067/C-L216 81991D/18068/C-L217 81992A/18070/C-L219 81954I/18071/C-L220
PRIMARY INVESTIGATOR:	Alan I. Leibowitz, M.D. Associate Professor of Medicine University of South Florida School of Medicine Tampa, Florida 33612
SECONDARY INVESTIGATOR:	John T. Sinnott, M.D. Ben G. Yango, M.D. University of South Florida School of Medicine Tampa, Florida, 33612
STUDY LOCATION:	University of South Florida Medical Center Tampa, Florida 33612 Affiliated hospitals and other area health facilities.
DATE INITIATED:	July, 1985
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population will consist of approximately 250 healthy adults of either sex (excluding pregnant women), who are negative for hepatitis B virus serologic markers, have normal liver function tests and have not prebiously received any hepatitis B vaccine.

Study 885

PROCEDURE:

Participants are assigned to one of five lots of vaccine, stratified by sex and age (50 persons per lot). All study subjects receive a 10 mcg dose intramuscular injection of vaccine at 0, 1 and 6 months. Participants are asked to record their temperatures and any local or systemic complaints for five days after each injection.

Blood samples are obtained prior to vaccination and at 1, 2, 3, 6, 8, 12 and 24 months post initial injection. All specimens are assayed for HBsAg, anti-HBs, and anti-HBc by MSDRL. ALT levels will be tested pre-vaccination and at two and eight months post initial injection at the University of South Florida. Samples with an anti-HBs titer ≥25 mIU/ml may be tested for anti-a and anti-d activity. Samples may also be assayed for yeast antibody at MSDRL.

RESULTS:

HEALTHY ADULTS

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

1. Number Vaccinated:

Lot	Injection No. 1	2	3
81990D/18066/C-L215	0	0	0
81766B/18067/C-L216	0	0	0
81991D/18068/C-L217	50	0	0
81992A/18070/C-L219	50	50	0
81954I/18071/C-L220	50	50	0

2. Serologic Results:

No serologic results are currently available.

3. Clinical Complaints:

There have been no serious or alarming adverse reactions attributable to vaccine.

STUDY 889

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 889
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant 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:	Yeast Recombinant Hepatitis B Vaccine Lot 993/C-K937 (20 mcg/HBsAg/ml)
PRIMARY INVESTIGATOR:	Robert P. Perrillo, M.D. Director, Gastroenterology Veterans Administration Medical Center St. Louis, Missouri 63125
SECONDARY INVESTIGATOR:	Oliver H. Lowry, M.D. Department of Pharmacology Washington Univ. School of Medicine St. Louis, Missouri 63110
STUDY LOCATION:	Beverly Farms Foundation Godfrey, Illinois 62035 Veterans Administration Medical Center St. Louis, Missouri 63125
DATE STUDY INITIATED:	June 19, 1985
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of approximately 250 mentally retarded individuals, above 5 years of age, and 50 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 889

STUDY PROCEDURE:

Mentally retarded individuals are randomly assigned to one of two groups, stratified by sex and age. Health care personnel constitute a third group.

Mentally retarded individuals receive a 0.5 ml (10 mcg HBsAg) or a 1.0 ml (20 mcg HBsAg) intramuscular injection of vaccine at 0, 1, and 6 months. Health care personnel receive a 0.5 ml (10 mcg HBsAg) intramuscular injection of vaccine according to the same regimen.

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 two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 3, 6, 10 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc and anti-HBs. The pre-vaccination and 3 month post-vaccination samples are also tested for 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:

HEALTH CARE PERSONNEL

10 mcg Lot 993/C-K937 at 0, 1, and 6 months

1. Number Vaccinated:

Injection No.		
1	2	3
88	82	74

One person with an initial ALT level approximately 1.5 times normal (69) received vaccine. A post-vaccination ALT level is not yet available. Three month post-vaccination samples will be tested for ALT.

2394I/2
1/3/86

Study 889

RESULTS: (Contd)

2. Serologic Results:

Serologic data at 1 month are available for 82 health care personnel.

At 1 month 17% (14/82) of vaccine recipients seroconverted (S/N ≥2.1) and 6% (5/82) developed protective levels of antibody (mIU/ml ≥10). The GMT for all vaccinees was 0.5 mIU/ml at that time. Among responders with a titer of S/N ≥2.1, the GMT at 1 month was 6.3 mIU/ml, while for responders with a titer of mIU/ml ≥10 the GMT was 25 mIU/ml.

3. Clinical Results:

Clinical follow-up data are available for 82 health care personnel following two injections of vaccine. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 1 and 2. In summary:

Clinical Complaint	% Frequency by Injection No. 1	2	3
Injection Site	1 (1/82)	0 (0/82)	NA
Systemic	5 (4/82)	6 (5/82)	NA

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

Events Reported to OoBRR

A 37 year-old female noted facial warmth and flushing 14 hours after receiving the first injection of vaccine. Within the next 3 hours she developed facial urticaria. She was treated with cold packs. All symptoms subsided within 12 hours. The subject was treated with Benadryl prior to the second and third injections, and had no post-vaccination reactions.

Table 1

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (82 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
SORENESS	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
SYSTEMIC	1 (1.2%)	2 (2.4%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (4.9%)
WHOLE BODY/GENERAL	0 (0.0%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
FLUSH	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
HEADACHE	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
ITCHING, FACIAL	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
URTICARIA, FACIAL	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
DIGESTIVE SYSTEM	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
NAUSEA	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
VOMITING	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
NERVOUS SYSTEM	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (82 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PARESTHESIAS	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
PERSONS WITH COMPLAINTS	1 (1.2%)	3 (3.7%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (6.1%)
PERSONS WITH NO COMPLAINTS	81 (98.8%)	79 (96.3%)	80 (97.6%)	82 (100.0%)	82 (100.0%)	82 (100.0%)		77 (93.9%)
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%)

00573

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0689
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (82 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	0 (0.0%)	2 (2.4%)	2 (2.4%)	1 (1.2%)	2 (2.4%)	1 (1.2%)	5 (6.1%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	2 (2.4%)
HEADACHE	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	2 (2.4%)
INTEGUMENTARY SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.2%)
PRURITIS/ITCHING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.2%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.2%)
TONSILLITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.2%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
NAUSEA	0 (0.0%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
VOMITING	0 (0.0%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
PERSONS WITH COMPLAINTS	0 (0.0%)	2 (2.4%)	2 (2.4%)	1 (1.2%)	2 (2.4%)	1 (1.2%)	5 (6.1%)
PERSONS WITH NO COMPLAINTS	82 (100.0%)	80 (97.6%)	80 (97.6%)	81 (98.8%)	80 (97.6%)	81 (98.8%)	77 (93.9%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

CLINICAL COMPLAINTS	TOTAL VACCINEES (82 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%)

00575

Table 2

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (82 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	70 (87.5%)	67 (84.8%)	60 (80.0%)	68 (88.3%)	68 (89.5%)	69 (89.6%)		50 (61.7%)
99 - 99.9	7 (8.7%)	11 (13.9%)	12 (16.0%)	9 (11.7%)	7 (9.2%)	8 (10.4%)		25 (30.9%)
100 - 100.9	2 (2.5%)	1 (1.3%)	3 (4.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)		5 (6.2%)
101 - 101.9	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
TEMPERATURE TAKEN	80 (97.6%)	79 (96.3%)	75 (91.5%)	77 (93.9%)	76 (92.7%)	77 (93.9%)		81 (98.8%)
TEMPERATURE NOT TAKEN	2 (2.4%)	3 (3.7%)	7 (8.5%)	5 (6.1%)	6 (7.3%)	5 (6.1%)		1 (1.2%)

Table 2 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0689
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: HEALTH CARE PERSONNEL

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (82 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	69 (84.1%)	70 (85.4%)	76 (92.7%)	76 (92.7%)	73 (90.1%)	76 (92.7%)			61 (74.4%)
99 - 99.9	12 (14.6%)	9 (11.0%)	4 (4.9%)	4 (4.9%)	8 (9.9%)	6 (7.3%)			17 (20.7%)
100 - 100.9	1 (1.2%)	3 (3.7%)	2 (2.4%)	2 (2.4%)	0 (0.0%)	0 (0.0%)			4 (4.9%)
TEMPERATURE TAKEN	82 (100.0%)	82 (100.0%)	82 (100.0%)	82 (100.0%)	81 (98.8%)	82 (100.0%)			82 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)			0 (0.0%)

STUDY 891

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 891
PURPOSE:	To compare the antibody and clinical responses to recombinant hepatitis B vaccine and plasma-derived hepatitis B vaccine among healthy adults and children who are negative for hepatitis B virus serologic markers.
VACCINES:	1. Yeast Recombinant Hepatitis B Vaccine Lot 979/C-K564 (10 mcg HBsAg/ml) 2. Plasma-Derived Hepatitis B Vaccine Lot 0027L (20 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Dr. Hu Zong-Han Department of Biological Products Inspection Bureau of Pharmaceutical and Biological Inspection Ministry of Health Temple of Heaven, West Gate Beijing, People's Republic of China
SECONDARY INVESTIGATOR:	Dr. Shi Guiyong Director of Epidemic Department Chinese Medical University Shen Yang, People's Republic of China
STUDY LOCATION:	Shen Yang Municipal Anti-Epidemic Station Shen Yang, People's Republic of China
DATE STUDY INITIATED:	December, 1985
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 200 healthy adults and 200 healthy children of either sex (exluding pregnant women), who are negative for HBsAg, anti-HBc and HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 891

STUDY PROCEDURE: Participants are grouped by age and randomly assigned to receive the yeast recombinant or plasma-derived hepatitis B vaccine as follows:

Group	Population	Vaccine	Dose	Number	Regimen
1	Adults (≥30 years)	Recombinant	10 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
2	Adults (18-29 years)		10 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
3	Children (5-10 years)		5 mcg	100	0.5 ml intramuscular injection of vaccine at 0, 1, and 6 months
4	Adults (≥30 years)	Plasma	20 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
5	Adults (18-29 years)		20 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
6	Children (5-10 years)		10 mcg	100	0.5 ml intramuscular injection of vaccine at 0, 1, and 6 months

Study participants or the participant's parent or guardian record their temperature or that of their child, 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 to three weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 3, 6, 7, 8, 9, 12, and 24 months. All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT.

Study 891

RESULTS: (Contd) To date 100 adults and children have received one injection of yeast recombinant or plasma-derived hepatitis B vaccine. No serious or alarming reactions attributable to vaccination have been reported. Clinical follow-up data and serologic results are not yet available. The study continues in progress.

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 894
PURPOSE:	To compare immunologic responses to yeast recombinant versus plasma hepatitis B vaccine in homosexual males and to compare differences, if any, in adverse reactions to the two vaccines.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot 978/C-K563 Plasma-Derived Hepatitis B Vaccine (HEPTAVAX) Lot 1014/C-M252
PRIMARY INVESTIGATOR:	B. Frank Polk, M.D. Director, Infectious Disease Epidemiology Program Johns Hopkins Univ. School of Hygiene & Public Health Baltimore, MD
SECONDARY INVESTIGATORS:	Lois Eldred, P.A. Robin Fox, M.S. Edward Fuchs, P.A. Richard Kaslow, M.D. Nancy Odaka, M.H.S. Rachel Solomon, M.H.S.
STUDY LOCATION:	The Johns Hopkins Hospital Baltimore, MD
DATE INITIATED:	April, 1985
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population consists of 300-350 homosexual males who are negative for all hepatitis B markers and have not received any hepatitis B vaccine. The men are concurrently enrolled in a study to help the AIDS research effort (SHARE) at the Johns Hopkins University Hospital.

Study 894

PROCEDURE:

Eligible participants are randomized to receive an injection of either 20 mcg plasma or 10 mcg recombinant vaccine at 0, 1 and 6 months. Participants are asked to record their temperatures for 5 days after each injection and to note any local or systemic complaints.

Bloof specimens are obtained prior to vaccination and at 1, 6, 9 and 12 months post initial injection. After the first year of follow-up, serum samples are collected every 6 months for another two years. Baseline serum samples are assayed for HBsAg, anti-HBs and ALT. Follow-up serum samples are tested for development of anti-HBs antibodies.

RESULTS:

HOMOSEXUAL MALES:

10 mcg Lot 978/C-K563 yeast recombinant at 0, 1 and 6 months
20 mcg Lot 1014/C-M252 plasma at 0, 1 and 6 months

1. Number Vaccinated:

Vaccine	Injection No. 1	2	3
Yeast Recombinant	87	63	1
Plasma	88	70	0

2. Serologic Results:

No serological results are presently available.

Study 894

RESULTS: (Contd)

3. Clinical Complaints:

Clinical follow-up data are available for 83, 60, and 1 participants following injections one, two, and three of yeast recombinant vaccine, and for 88 and 67 participants following injections one and two of plasma vaccine. Specific complaints and maximum temperatures reported during the 5 days following each injection are provided in Tables 1 through 4.

There have been no serious or alarming adverse reactions attributable to either vaccine to date.

Type	Vaccine	Frequency in % by Injection No. 1	2	3
Injection Site	Recombinant	30(25/83)	35(21/60)	0(0/1)
	Plasma	42(37/88)	36(24/67)	
Systemic	Recombinant	29(24/83)	18(11/60)	0(0/1)
	Plasma	35(31/88)	25(17/67)	

Table 1

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (87 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	15 (18.5%)	14 (16.9%)	8 (9.6%)	4 (4.9%)	2 (2.5%)	0 (0.0%)	25 (30.1%)
SORENESS	14 (17.3%)	14 (16.9%)	8 (9.6%)	4 (4.9%)	1 (1.2%)	0 (0.0%)	23 (27.7%)
STIFFNESS/TIGHTNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	1 (1.2%)
HEMATOMA	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
SYSTEMIC	9 (11.1%)	11 (13.3%)	13 (15.7%)	11 (13.4%)	3 (3.7%)	4 (4.9%)	24 (28.9%)
WHOLE BODY/GENERAL	2 (2.5%)	5 (6.0%)	4 (4.8%)	2 (2.4%)	1 (1.2%)	2 (2.5%)	10 (12.0%)
CHILLS	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
FATIGUE/WEAKNESS	0 (0.0%)	5 (6.0%)	2 (2.4%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	6 (7.2%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	1 (1.2%)	2 (2.4%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
LIGHTHEADED	2 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
INTEGUMENTARY SYSTEM	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	2 (2.4%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (87 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
RASH, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
OTHER	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
RESPIRATORY	1 (1.2%)	1 (1.2%)	1 (1.2%)	2 (2.4%)	1 (1.2%)	1 (1.2%)		2 (2.4%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
UPPER RESPIRATORY INFECT., NOS	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)		1 (1.2%)
HEMIC AND LYMPHATIC	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)		1 (1.2%)
LYMPHADENOPATHY, GENERAL	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)		1 (1.2%)
MUSCULOSKELETAL	4 (4.9%)	3 (3.6%)	6 (7.2%)	4 (4.9%)	1 (1.2%)	0 (0.0%)		8 (9.6%)
ARTHRALGIA, MONOARTICULAR	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
ARTHRALGIA (OTHER)	2 (2.5%)	2 (2.4%)	4 (4.8%)	1 (1.2%)	1 (1.2%)	0 (0.0%)		5 (6.0%)
MYOSITIS	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
MYALGIA	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
MUSCLE STIFFNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (87 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
SORE CHEST	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
DIGESTIVE SYSTEM	1 (1.2%)	2 (2.4%)	2 (2.4%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		6 (7.2%)
DIARRHEA	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
NAUSEA	1 (1.2%)	2 (2.4%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		4 (4.8%)
VOMITING	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
OTHER	0 (0.0%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
UROGENITAL SYSTEM	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
KIDNEY PAIN	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.2%)
PERSONS WITH COMPLAINTS	21 (25.9%)	23 (27.7%)	19 (22.9%)	13 (15.9%)	5 (6.2%)	4 (4.9%)		42 (50.6%)
PERSONS WITH NO COMPLAINTS	60 (74.1%)	60 (72.3%)	64 (77.1%)	69 (84.1%)	76 (93.8%)	77 (95.1%)		41 (49.4%)
PERSONS WITH NO DATA	5 (5.8%)	4 (4.6%)	4 (4.6%)	5 (5.7%)	5 (5.8%)	5 (5.8%)		4 (4.6%)

00586

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (63 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	16 (26.7%)	11 (18.3%)	5 (8.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	21 (35.0%)
SORENESS	16 (26.7%)	11 (18.3%)	5 (8.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	21 (35.0%)
SYSTEMIC	5 (8.3%)	4 (6.7%)	6 (10.2%)	6 (10.2%)	5 (8.3%)	3 (5.1%)	11 (18.3%)
WHOLE BODY/GENERAL	2 (3.3%)	3 (5.0%)	3 (5.1%)	4 (6.8%)	2 (3.3%)	1 (1.7%)	5 (8.3%)
FATIGUE/WEAKNESS	1 (1.7%)	2 (3.3%)	2 (3.4%)	3 (5.1%)	2 (3.3%)	1 (1.7%)	3 (5.0%)
CHEST PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
LIGHTHEADED	1 (1.7%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
INTEGUMENTARY SYSTEM	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
OTHER	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (1.7%)
MUSCULOSKELETAL	1 (1.7%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	2 (3.3%)	1 (1.7%)	3 (5.0%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (63 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
ARTHRALGIA, MONOARTICULAR	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.7%)
ARTHRALGIA (OTHER)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	2 (3.3%)	1 (1.7%)		2 (3.3%)
DIGESTIVE SYSTEM	2 (3.3%)	0 (0.0%)	1 (1.7%)	2 (3.4%)	2 (3.3%)	1 (1.7%)		4 (6.7%)
DIARRHEA	2 (3.3%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		3 (5.0%)
NAUSEA	1 (1.7%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		2 (3.3%)
VOMITING	1 (1.7%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	1 (1.7%)		2 (3.3%)
ABDOMEN DISTENDED	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)		1 (1.7%)
UROGENITAL SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)		1 (1.7%)
KIDNEY PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.7%)	0 (0.0%)		1 (1.7%)
PSYCHIATRIC/BEHAVIORAL	1 (1.7%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.7%)
DREAMS, BIZARRE, UNUSUAL	1 (1.7%)	1 (1.7%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.7%)
PERSONS WITH COMPLAINTS	20 (33.3%)	15 (25.0%)	11 (18.6%)	6 (10.2%)	5 (8.3%)	3 (5.1%)		28 (46.7%)
PERSONS WITH NO COMPLAINTS	40 (66.7%)	45 (75.0%)	48 (81.4%)	53 (89.8%)	55 (91.7%)	56 (94.9%)		32 (53.3%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (63 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH NO DATA	2 (3.2%)	2 (3.2%)	2 (3.3%)	2 (3.3%)	2 (3.2%)	2 (3.3%)		2 (3.2%)

Table 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (1 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	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	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)		1 (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 2

PATIENT COUNT MAXIMUM TEMPERATURES

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE :
10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (87 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	2 (2.6%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.3%)			2 (2.4%)
< 99	64 (83.1%)	73 (91.2%)	76 (92.7%)	75 (93.8%)	74 (92.5%)	70 (90.9%)			61 (73.5%)
99 - 99.9	11 (14.3%)	4 (5.0%)	4 (4.9%)	4 (5.0%)	4 (5.0%)	5 (6.5%)			16 (19.3%)
100 - 100.9	0 (0.0%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	1 (1.2%)	1 (1.3%)			3 (3.6%)
101 - 101.9	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (1.2%)
TEMPERATURE TAKEN	77 (88.5%)	80 (92.0%)	82 (94.3%)	80 (92.0%)	80 (92.0%)	77 (88.5%)			83 (95.4%)
TEMPERATURE NOT TAKEN	10 (11.5%)	7 (8.0%)	5 (5.7%)	7 (8.0%)	7 (8.0%)	10 (11.5%)			4 (4.6%)

Table 2 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (63 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	3 (5.3%)	3 (5.3%)	3 (5.4%)	3 (5.4%)	3 (5.4%)	3 (5.5%)			3 (5.3%)
< 99	44 (77.2%)	49 (86.0%)	49 (87.5%)	44 (78.6%)	45 (80.4%)	46 (83.6%)			35 (61.4%)
99 - 99.9	9 (15.8%)	4 (7.0%)	2 (3.6%)	6 (10.7%)	8 (14.3%)	5 (9.1%)			15 (26.3%)
100 - 100.9	1 (1.8%)	1 (1.8%)	2 (3.6%)	3 (5.4%)	0 (0.0%)	1 (1.8%)			4 (7.0%)
TEMPERATURE TAKEN	57 (90.5%)	57 (90.5%)	56 (88.9%)	56 (88.9%)	56 (88.9%)	55 (87.3%)			57 (90.5%)
TEMPERATURE NOT TAKEN	6 (9.5%)	6 (9.5%)	7 (11.1%)	7 (11.1%)	7 (11.1%)	8 (12.7%)			6 (9.5%)

Table 2 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES

STUDY : 0894
TREATMENT :
LOT NUMBER : CK563
DOSE : 10 MCG

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

00593

Table 3

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CH252
DOSE : 20 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (88 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	23 (27.4%)	17 (19.3%)	9 (10.3%)	4 (4.7%)	1 (1.1%)	1 (1.2%)	37 (42.0%)
SORENESS	23 (27.4%)	17 (19.3%)	9 (10.3%)	4 (4.7%)	1 (1.1%)	1 (1.2%)	37 (42.0%)
SYSTEMIC	12 (14.3%)	22 (25.0%)	15 (17.2%)	9 (10.5%)	7 (8.0%)	7 (8.1%)	31 (35.2%)
WHOLE BODY/GENERAL	9 (10.7%)	15 (17.0%)	7 (8.0%)	7 (8.1%)	6 (6.9%)	4 (4.7%)	24 (27.3%)
CHILLS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	2 (2.3%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.3%)
FATIGUE/WEAKNESS	7 (8.3%)	10 (11.4%)	5 (5.7%)	5 (5.8%)	4 (4.6%)	3 (3.5%)	16 (18.2%)
HEADACHE	3 (3.6%)	4 (4.5%)	2 (2.3%)	2 (2.3%)	2 (2.3%)	1 (1.2%)	9 (10.2%)
LIGHTHEADED	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
PAIN	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
HERPES LABIALIS, RECURRENT	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE : 20 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (88 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
INTEGUMENTARY SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)		1 (1.1%)
RASH, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)		1 (1.1%)
MUSCULOSKELETAL	2 (2.4%)	6 (6.8%)	4 (4.6%)	4 (4.7%)	2 (2.3%)	3 (3.5%)		9 (10.2%)
ARTHRALGIA (OTHER)	1 (1.2%)	5 (5.7%)	3 (3.4%)	3 (3.5%)	1 (1.1%)	2 (2.3%)		8 (9.1%)
MYOSITIS	1 (1.2%)	1 (1.1%)	1 (1.1%)	1 (1.2%)	1 (1.1%)	1 (1.2%)		1 (1.1%)
DIGESTIVE SYSTEM	1 (1.2%)	5 (5.7%)	6 (6.9%)	2 (2.3%)	0 (0.0%)	1 (1.2%)		10 (11.4%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.1%)
DIARRHEA	0 (0.0%)	3 (3.4%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (3.4%)
NAUSEA	1 (1.2%)	2 (2.3%)	3 (3.4%)	2 (2.3%)	0 (0.0%)	1 (1.2%)		6 (6.8%)
VOMITING	0 (0.0%)	1 (1.1%)	2 (2.3%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		2 (2.3%)
OTHER	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.1%)
PSYCHIATRIC/BEHAVIORAL	2 (2.4%)	1 (1.1%)	1 (1.1%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		2 (2.3%)
EMOTIONAL LABILITY	1 (1.2%)	1 (1.1%)	1 (1.1%)	1 (1.2%)	0 (0.0%)	0 (0.0%)		1 (1.1%)

00595

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE : 20 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (88 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
IRRITABILITY	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.1%)
PERSONS WITH COMPLAINTS	31 (36.9%)	33 (37.5%)	21 (24.1%)	12 (14.0%)	8 (9.2%)	8 (9.3%)		54 (61.4%)
PERSONS WITH NO COMPLAINTS	53 (63.1%)	55 (62.5%)	66 (75.9%)	74 (86.0%)	79 (90.8%)	78 (90.7%)		34 (38.6%)
PERSONS WITH NO DATA	1 (1.2%)	0 (0.0%)	1 (1.1%)	1 (1.1%)	1 (1.1%)	2 (2.3%)		0 (0.0%)

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE : 20 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (70 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	20 (30.3%)	13 (19.4%)	3 (4.5%)	2 (3.0%)	1 (1.5%)	0 (0.0%)		24 (35.8%)
SORENESS	20 (30.3%)	13 (19.4%)	3 (4.5%)	2 (3.0%)	0 (0.0%)	0 (0.0%)		23 (34.3%)
HEMATOMA	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)		2 (3.0%)
SYSTEMIC	7 (10.6%)	10 (14.9%)	6 (9.1%)	7 (10.4%)	6 (9.1%)	6 (9.1%)		17 (25.4%)
WHOLE BODY/GENERAL	3 (4.5%)	5 (7.5%)	5 (7.6%)	5 (7.5%)	4 (6.1%)	4 (6.1%)		10 (14.9%)
FATIGUE/WEAKNESS	2 (3.0%)	5 (7.5%)	5 (7.6%)	5 (7.5%)	4 (6.1%)	4 (6.1%)		9 (13.4%)
HEADACHE	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
INFECTIOUS SYNDROMES	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
HERPES GENITALIS, RECURRENT	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
INTEGUMENTARY SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.5%)		1 (1.5%)
RASH, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.5%)		1 (1.5%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.5%)	0 (0.0%)	0 (0.0%)		1 (1.5%)

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE : 20 MCG

CLINICAL COMPLAINTS	TOTAL VACCINEES (70 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.5%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
MUSCULOSKELETAL	2 (3.0%)	2 (3.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)		4 (6.0%)
ARTHRALGIA, MONOARTICULAR	1 (1.5%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
ARTHRALGIA (OTHER)	1 (1.5%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.0%)
MYALGIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
DIGESTIVE SYSTEM	2 (3.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (4.5%)
NAUSEA	2 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.0%)
LOOSE STOOL	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.5%)
PSYCHIATRIC/BEHAVIORAL	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)		1 (1.5%)
INSOMNIA/DISTURBED SLEEP	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)		1 (1.5%)
PERSONS WITH COMPLAINTS	23 (34.8%)	21 (31.3%)	9 (13.6%)	9 (13.4%)	7 (10.6%)	6 (9.1%)		34 (50.7%)
PERSONS WITH NO COMPLAINTS	43 (65.2%)	46 (68.7%)	57 (86.4%)	58 (86.6%)	59 (89.4%)	60 (90.9%)		33 (49.3%)
PERSONS WITH NO DATA	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)	1 (1.5%)		1 (1.5%)

Table 4

PATIENT COUNT MAXIMUM TEMPERATURES

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE : 20 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (66 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (1.3%)	3 (3.6%)	3 (3.7%)	4 (5.0%)	4 (4.9%)	4 (5.0%)			2 (2.4%)
< 99	62 (80.5%)	70 (84.3%)	67 (81.7%)	66 (82.5%)	70 (86.4%)	70 (87.5%)			56 (66.7%)
99 - 99.9	14 (18.2%)	10 (12.0%)	11 (13.4%)	9 (11.2%)	6 (7.4%)	4 (5.0%)			24 (28.6%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	2 (2.5%)			2 (2.4%)
TEMPERATURE TAKEN	77 (87.5%)	83 (94.3%)	82 (93.2%)	80 (90.9%)	81 (92.0%)	80 (90.9%)			84 (95.5%)
TEMPERATURE NOT TAKEN	11 (12.5%)	5 (5.7%)	6 (6.8%)	8 (9.1%)	7 (8.0%)	8 (9.1%)			4 (4.5%)

Table 4 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES

STUDY : 0894
TREATMENT :
LOT NUMBER : CM252
DOSE :
20 MCG

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (70 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	3 (4.8%)	4 (6.2%)	3 (4.6%)	4 (6.3%)	4 (6.3%)	4 (6.3%)			2 (3.0%)
< 99	54 (87.1%)	57 (87.7%)	57 (87.7%)	56 (87.5%)	56 (87.5%)	55 (85.9%)			52 (77.6%)
99 - 99.9	5 (8.1%)	4 (6.2%)	5 (7.7%)	4 (6.3%)	4 (6.3%)	5 (7.8%)			13 (19.4%)
TEMPERATURE TAKEN	62 (88.6%)	65 (92.9%)	65 (92.9%)	64 (91.4%)	64 (91.4%)	64 (91.4%)			67 (95.7%)
TEMPERATURE NOT TAKEN	8 (11.4%)	5 (7.1%)	5 (7.1%)	6 (8.6%)	6 (8.6%)	6 (8.6%)			3 (4.3%)

00600

PROTOCOL:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 898.
PURPOSE:	To evaluate antibody and clinical responses of initially seronegative healthy adults to 10 and 20 mcg injections of yeast recombinant hepatitis B vaccine.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #85860/22123/C-M125 (20 mcg HBsAg/ml) Lot #85861/22124/C-M126 (10 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	Robert Bishop, M.D. Health Services WP38-4 Merck Sharp and Dohme West Point, PA 19486
SECONDARY INVESTIGATOR:	E. P. Avencena, M.D. Health Services WP38-4 Merck Sharp and Dohme West Point, PA 19486
STUDY LOCATION:	Merck Sharp and Dohme West Point, PA 19486
DATE INITIATED:	November 18, 1985
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population will consist of approximately 40 employees of Merck & Co., Inc. of either sex (excluding pregnant women) who are 40 years of age or older, 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 participants receive a 1.0 ml (10 mcg or 20 mcg HBsAg) intramuscular injection of vaccine in the deltoid muscle on day 0, and at 1 and 6 months. Vaccine recipients are asked to record their temperature daily for five days after each injection of the vaccine and also to record any local or systemic complaints that they may have during this period.

A blood specimen (10-15 ml) is obtained from each participant 1-2 weeks before the first injection of vaccine is given. Post-vaccination blood samples are taken at 1, 2, 3, 6, and 8 months following the first injection from all vaccine recipients and at 12 and 24 months from those who develop antibody by 8 months. All samples will be tested for HBsAg, anti-HBc, and anti-HBs. The prevaccination sample and the two month post-vaccination sample will also be tested for ALT.

Subjects who fail to develop antibody following three injections of vaccine and those who have a transient antibody response that becomes negative by 12 months after the first injection may receive a fourth injection of vaccine. An additional blood sample will be taken one month after the fourth injection of vaccine.

RESULTS:

One person has received a single 10 mcg injection of vaccine, while two persons have received single 20 mcg injections of vaccine. None had any complaints. Post-vaccination serologic results are not yet available.

STUDY 900

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 900.
PURPOSE:	To evaluate antibody and clinical responses to the vaccine among healthy male homosexuals who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #85861/22124/CM126 (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:	August 1985.
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population will consist of approximately 200 healthy male homosexuals who are negative for HBsAg, anti-HBc and anti-HBs, and have not previously received any hepatitis B vaccine.

Study 900

PROCEDURE:

Prior to enrollment in the study, all prospective participants will receive a full medical examination. Any evidence of possible immune deficiency will eliminate a candidate from receiving vaccine. A blood sample will also be obtained prior to vaccination and assayed for hepatitis B serologic markers and for antibodies to HTLV III.

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.

Follow-up blood samples will be obtained at 1, 2, 3, 6, 8, 12, and 24 months following the first injection of vaccine. All samples will be assayed for HBsAg, anti-HBc and anti-HBs. The 12 and 24 month samples will also be tested for antibodies to HTLV III. Assays will be performed in Dr. Zuckerman's laboratory. In addition, samples may be assayed for yeast antibodies and anti-HBs subtype specificity by MSDRL.

Subjects who fail to develop anti-HBs following three doses of vaccine (nonresponders) and those who have a transient antibody response (transient responders) that becomes negative by 12 months after the first dose, may receive a fourth injection of vaccine. An additional blood sample will be taken one month after the fourth dose.

A complete physical examination will be repeated at 6, 12, and 24 months.

RESULTS:

Serologic and clinical follow-up data are not currently 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 904
PURPOSE:	To evaluate clinical and antibody responses among initially seronegative healthy adults 20 years of age or older to 10 mcg doses of yeast recombinant hepatitis B vaccine
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #89426/22930/C-M178 (10 mcg HBsAg/0.5 ml) Lot #81991D/18068/C-L217 (10 mcg HBsAg/0.5 ml)
PRIMARY INVESTIGATOR:	Harold A. Kessler, M.D. Assistant Professor of Medicine and Immunology/Microbiology Section of Infectious Diseases Department of Medicine Rush-Presbyterian-St. Luke's Medical Center 1753 West Congress Parkway Chicago, IL 60612
SECONDARY INVESTIGATORS:	Constance Ann Benson, M.D. Rush-Presbyterian-St. Luke's Medical Center Section of Infectious Diseases 1753 West Congress Parkway Chicago, IL 60612 Alan A. Harris, M.D. Rush-Presbyterian-St. Luke's Medical Center Section of Infectious Diseases 1753 West Congress Parkway Chicago, IL 60612
STUDY LOCATION:	Rush-Presbyterian-St. Luke's Medical Center 1753 West Congress Parkway Chicago, IL 60612
DATE INITIATED:	October, 1985
DATE COMPLETED:	In progress.

Study 904

STUDY POPULATION:

The study population will consist of approximately 100 healthy adults of either sex (excluding pregnant women) who are 20 years of age or older, are negative for HBsAg, anti-HBc and anti-HBs, have a normal ALT level, and have not previously received any hepatitis B vaccine.

PROCEDURE:

Participants will be assigned to one of two groups as defined below:

Group	Number of Participants	Vaccine Lot	Dose Volume (HBsAg)
1	50	89426/22930/C-M718	0.5 ml (10 mcg)
2	50	81991D/18068/C-L217	0.5 ml (10 mcg)

Participation in either group 1 or 2 will be determined by a randomization schedule provided by Merck Sharp & Dohme.

Eligible participants receive a 0.5 ml injection of vaccine in the deltoid muscle at 0, 1, and 6 months. Study subjects are asked to take and record their temperatures for five days after each injection of vaccine and to record any local or systemic complaints.

A blood sample will be obtained at 1-2 weeks prior to the first injection of vaccine. Post-vaccination blood samples (10-15 ml) will be obtained at 1, 2, 3, 6, and 8 months following the first dose of vaccine from all vaccinees and at 12 and 24 months from those who have developed antibody by 8 months. All samples will be tested for HBsAg, anti-HBc, and anti-HBs. The sample taken 2 months after the first dose of vaccine will also be tested for ALT.

Subjects who fail to develop antibody following three doses of vaccine (nonresponders) and those who have a transient antibody response (transient responders) that becomes negative by 12 months after the first dose, may receive a fourth dose of vaccine. An additional blood sample will be taken one month after the fourth dose.

Sera may also be assayed for yeast antibodies and anti-HBs subtype specificity.

All assays will be done at Rush-Presbyterian-St. Luke's Medical Center.

Study 904

RESULTS:

HEALTHY ADULTS:

10 mcg Lot #89426/22930/C-M178 at 0, 1, and 6 months
10 mcg Lot 81991D/18068/C-L217 at 0, 1, and 6 months

1. Number Vaccinated:

	Injection No.		
	1	2	3
Lot C-M178	50	50	0
Lot C-L217	50	50	0

2. Serologic Results:

Serologic data are not yet available.

3. Clinical Complaints:

Clinical follow-up data are not yet available. No serious or alarming advierse experiences have been reported.

The study continues in progress.

STUDY 907

PROGRAM: Yeast Recombinant Hepatitis B Vaccine, Study 907

PURPOSE: To evaluate antibody and clinical responses to 10 mcg doses of yeast recombinant hepatitis B vaccine following intramuscular or subcutaneous administration.

VACCINE: Yeast Recombinant Hepatitis B Vaccine Lot C-L215 (10 mcg HBsAg/0.5 ml)

PRIMARY INVESTIGATOR:
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SECONDARY INVESTIGATORS:
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STUDY LOCATION: Tokyo and Osaka
Japan

DATE INITIATED: May 7, 1985

DATE COMPLETED: In progress.

STUDY POPULATION:

Population	Number of Subjects	Regimen
Healthy adults	124	10 mcg (0.5 ml) at 0, 1, and 6 months I.M. or S.C.

Study 907

PROCEDURE:

Participants received intramuscular or subcutaneous injections of vaccine according to the regimen outlined above under STUDY POPULATION. Participants were asked to record their temperature daily for three days after each injection and to note any local or systemic complaints.

Serum samples were obtained before vaccination. Follow- up blood specimens have been or will be obtained 1, 2, 4, 6, 7, 9 and 12 months after the initial dose of vaccine. Serum samples have been or will be assayed for HBsAg, anti-HBs, anti-HBc and several other laboratory exami- nations by the (b) (4) Samples may also be assayed at the (b) (4) for yeast antibody.

RESULTS:

1. Number Vaccinated:

Injection No.		
1	2	3
124	124	121

2. Serologic Results:

The anti-HBs seroconversion proportions were 28% (16/57) and 28% (17/61) at one month after the first dose, 93% (52/56) and 87% (53/61) at 6 months and 98% (54/55) and 97% (56/58) at 7 months with intramuscular and subcutaneous injections, respectively.

3. Clinical Complaints:

Route of Injection	Type of Complaints	Frequency in % by Injection No. 1	2	3
I.M.	Injection Site	19.4% (12/62)	11.3% (7/62)	*
	Systemic	9.7% (6/62)	14.5% (9/62)	*
S.C.	Injection Site	16.1% (10/62)	11.3% (7/62)	*
	Systemic	16.1% (10/62)	8.1% (5/62)	*

There were no serious or alarming reactions attributed to vaccination.

* not yet analyzed

Study 907

RESULTS: (Contd)

TABLE 1

Antibody Responses Among Healthy 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 (S/N)											
	Before		1 mo.		2 mos.		4 mos.		6 mos.		7 mos.	
	I.M.	S.C.	I.M.	S.C.	I.M.	S.C.	I.M.	S.C.	I.M.	S.C.	I.M.	S.C.
<2.1	57	61	41	44	13	18	6	10	4	8	1	2
2.1- 21			14	16	31	38	24	30	25	36	0	7
21-103			2	1	12	5	26	20	25	16	6	12
105-208					1		1	1	2	1	31	32
100-											17	5
Seroconversion %			28.1	27.9	77.2	70.1	89.5	83.6	92.9	86.9	98.2	96.6

PROGRAM: Yeast Recombinant Hepatitis B Vaccine, Study 912

PURPOSE: To evaluate antibody and clinical responses to 10 mcg doses of yeast recombinant hepatitis B vaccine following intramuscular or subcutaneous administration.

VACCINE: Yeast Recombinant Hepatitis B Vaccine Lot C-L220 (10 mcg HBsAg/0.5 ml)

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Study 912

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	Dr. Tetsuzo Koda, M.D. Division of Internal Medicine Ashiya Municipal Hospital
	Dr. Eiji Komori, M.D. Division of Internal Medicine Kobe Central Municipal Hospital
STUDY LOCATION:	Osaka, Domyoji, Ashiya and Kobe Japan
DATE INITIATED:	September 2, 1985
DATE COMPLETED:	In progress.

STUDY POPULATION:

Population	Number of Subjects	Regimen
Healthy health care personnel	175	10 mcg (0.5 ml) at 0, 1, and 6 months I.M. or S.C.

Study 912

PROCEDURE:

Participants received intramuscular or subcutaneous injections of vaccine according to the regimen outlined above under STUDY POPULATION. Participants were asked to record their temperature daily for three days after each injection and to note any local or systemic complaints.

Serum samples were obtained before vaccination. Follow-up blood specimens have been or will be obtained 1, 2, 4, 6, 7, 9 and 12 months after the initial dose of vaccine. Serum samples have been or will be assayed for HBsAg, anti-HBs, anti-HBc and several other laboratory examinations by the (b) (4). Samples may also be assayed at the for yeast antibody.

RESULTS:

1. Number Vaccinated:

Injection Number		
1	2	3
124	124	*

* not yet vaccinated

2. Serologic Results:

The anti-HBs seroconversion proportions were 45% (38/84) and 22% (19/85) at one month after the first dose and 75% (56/75) and 59% (43/83) at one month after the second dose with intramuscular and subcutaneous injections, respectively.

3. Clinical Complaints:

Route of Injection	Type of Complaints	Frequency in % by Injection No. 1	2	3
I.M.	Injection Site	3.4% (3/87)	0 % (0/85)	
	Systemic	23.0% (20/87)	10.6% (9/85)	
S.C.	Injection Site	6.8% (6/88)	9.1% (9/88)	
	Systemic	27.3% (24/88)	12.5% (11/88)	

There were no serious or alarming reactions attributed to vaccination.

Study 912

RESULTS: (Contd)

TABLE 1

Antibody Responses Among Healthy Adults Following Vaccination with 10 mcg Doses of Recombinant Vaccine Lot C-L220 at 0 and 1 Month

RIA Cut-Off Index	Anti-HBs Response (S/N)					
	Before		1 mo.		2 mos.	
	I.M.	S.C.	I.M.	S.C.	I.M.	S.C.
<2.1	84	85	46	66	19	30
2.1- 21			39	18	36	32
21-103			9	1	19	11
105-208					1	
100-						
Seroconversion %			45.2	22.4	74.7	58.9

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 914
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 #85861/22124/C-M126 (10 mcg HBsAg/ml)
PRIMARY INVESTIGATORS:	Alain Burette, M.D. venue 1' Echevinage 19-1180 Bruxelles Belgiu, Michel Deltenre, M.D. rue des Hippocampes 20-1080 Bruxelles Belgium
STUDY LOCATION:	Hospital Brugman Bruxelles Belgium
DATE INITIATED:	November 21, 1985
DATE COMPLETED:	In progress.
STUDY POPULATION:	The study population will consist of approximately 20 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.
PROCEDURE:	Eligible participants receive a 1.0 ml (10 mcg HBsAg) injection of vaccine into the deltoid muscle at 0, 1, and 6 months. Study participants are asked to take and record their temperatures for five days after each injection of vaccine and to record any local or systemic complaints. They are also asked to notify the study physician immediately if any unexpected or serious reaction occurs.

Study 914

PROCEDURE: (Contd)

A blood sample (10-15 ml) will be obtained from each participant approximately 2 weeks prior to the first injection of vaccine. Follow-up blood samples will be obtained at 1, 2, 3, 6, and 8 months following the first injection of vaccine from all vaccinees and at 12 and 24 months from those who have developed antibody by 8 months. All serum samples will be tested for HBsAg, Anti-HBc and anti-HBs. The 2 month post-vaccination sample will also be tested for ALT. If any subject experiences clinical symptoms compatible with hepatitis, blood samples drawn at that time will also be tested for ALT.

Subjects who fail to develop antibody following three doses of vaccine and those who have only a transient antibody response that becomes negative by 12 months after the first dose may receive a fourth dose of vaccine. An additional blood sample will be taken one month after the fourth dose.

Assays for HBsAg, anti-HBs and anti-HBc on the pre-vaccination serum samples and all ALT assays will be performed in Belgium. The Merck Sharp & Dohme Research Laboratories in West Point, Pennsylvania will perform post-vaccination assays for HBsAg, anti-HBc, and anti-HBs. Assays also may be done for yeast antibodies and anti-HBs subtype specificity.

RESULTS:

HEALTH CARE PERSONNEL:

10 mcg Lot #85861/22124/C-M126 at 0, 1, and 6 months

1. Number Vaccinated:

Dose Level	Injection No. 1	2	3
10 mcg	20	20	0

2. Serologic Results:

Serologic data are not yet available.

3. Clinical Complaints:

Clinical follow-up data are not yet available. However, the study investigator states that no local or general sign of intolerance has been observed. The study continues in progress.

HEALTHY TEENAGERS

SUMMARY - HEALTHY TEENAGERS

To date, 165 healthy male teenagers, 15-20 years old, have been immunized with yeast recombinant hepatitis B vaccine. Antibody and clinical responses to 10, 5 and 2.5 mcg doses of the vaccine administered at 0, 1 and 6 months in the deltoid muscle were evaluated in armed forces recruits who were negative for hepatitis B markers. Fifty-five recruits received each dose level. The vaccine was highly immunogenic and well tolerated in this population. Clinical complaints were mild and transient. Protective levels of antibody (mIU/ml $\geq$10) were induced in greater than 94% of vaccine recipients after 3 injections regardless of dose level administered. Ninety-eight to 100% of vaccine recipients developed protective levels of antibody after 2 injections of either 5 or 10 mcg doses of vaccine.

Immunogenicity

Antibody to hepatitis B surface antigen was measured at 1, 3, 6, 7 and 12 months postvaccination. At 7 months serologic data were available for 52, 54 and 53 vaccinees who received 10, 5 and 2.5 mcg doses, respectively.The seroconversion rate at 7 months was 100% for all dose levels when the cutoff was S/N $\geq$2.1. When the cutoff was mIU/ml $\geq$10, the seroconversion rates were 100% for 5 and 10 mcg and 94% for 2.5 mcg. At 12 months, 100% of those who received 5 or 10 mcg doses of vaccine continue to have protective levels of antibody, while 91% (48/53) of those who received 2.5 mcg doses continue to have protective levels of anti-BHs. Table 1 shows seroconversion rates for up to 12 months of follow-up. A significant effect of log dose level on seroconversion rates was seen at 3 months ($p = 0.006$) and 6 months ($p = 0.030$) when the cutoff was S/N $\geq$2.1, although the minimum seroconversion rates at these times were 91% and 94%, respectively (see Appendix 1 for methods used in statistical analysis). When the cutoff was mIU/ml $\geq$10 a significant effect was seen at 3 ($p < 0.001$), 6 ($p < 0.001$) and 7 months ($p = 0.033$). Seroconversion rates increased with log dose level.

Statistical analysis showed that log titers increased significantly with dose level at all time points ($p < 0.01$). Figure 1 illustrates this dose-response relationship at 7 months. Geometric mean titers for all vaccinees at 7 months were 3056.9 mIU/ml, 2553.4 mIU/ml and 846.3 mIU/ml for 10, 5 and 2.5 mcg doses, respectively (Table 1). Figure 1 gives confidence intervals on the predicted GMT at 7 months by dose in healthy teenagers. At 12 months geometric mean titers for all vaccinees were 583.1 mIU/ml, 498.1 mIU/ml and 324.7 mIU/ml for 10, 5 and 2.5 mcg doses respectively.

Safety

Clinical data following the first two injections of vaccine in 165 vaccinees were available for statistical analysis. Clinical data following the third injection in 164 vaccinees was summarized but not analyzed (Table 2). The incidences of local (injection site) complaints, of systemic complaints, of either local or systemic complaints, and of fever (oral temperature of 100°F or more) were analyzed. The incidence following the first, second, or third injection respectively, was defined as the number of subjects with the complaint

at any time during the 5 day period following vaccination divided by the number reporting while the total incidence was the sum of complaints over the three injections divided by the number with follow-up. In general, the vaccine was well tolerated in this population. Clinical complaints were mild and transient. The incidences of local complaints, of systemic complaints, of either injection site or systemic complaint, and of fever were evaluated as a function of log dose level. No significant trend was found after the first or second injection. Almost no fever was reported after either injection or at any dose level. The only local complaint reported was soreness (13%) and the only systemic complaints were malaise (6%) and headache (2%). The incidence of each complaint tended to be lower after the second injection. Clinical complaints following the third injection were minimal. The only complaint reported was injection site soreness (2-6%).

Study #819

Table 1

Antibody Responses Among Initially Seronegative Healthy Teenagers Following Vaccination with 10, 5, or 2.5 mcg Doses of Yeast Recombinant Hepatitis Vaccine B Lot 979/C-K564 or Lot 985/C-K732 at 0, 1 and 6 Months in Study 819

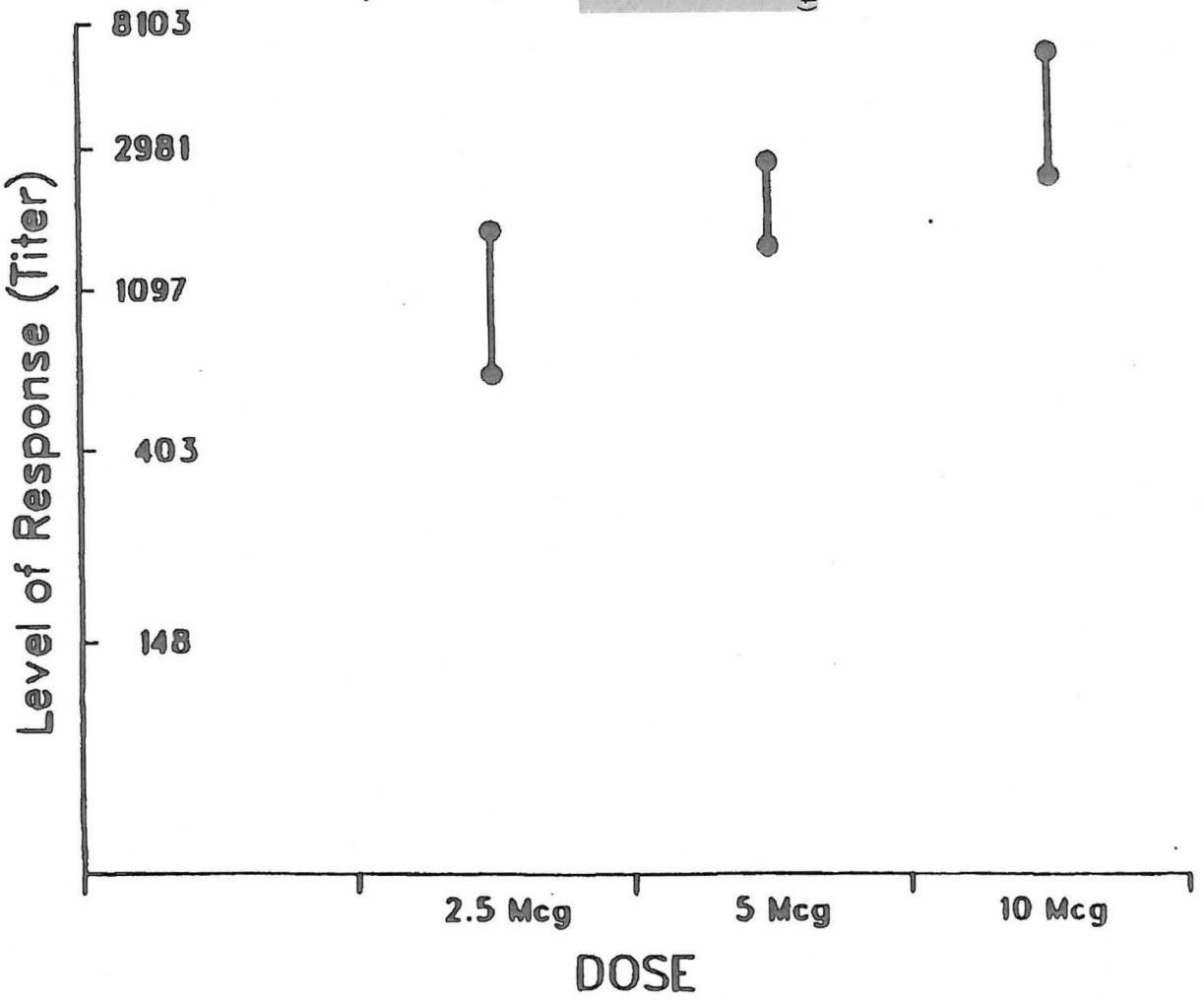
	10 mcg (Lot C-K564)					5 mcg (Lot C-K732)					2.5 mcg (Lot C-K732)				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
				Responders					Responders					Responders	
Time Mos.	S/N ≥ 2.1	mIU/ml ≥10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10	S/N ≥ 2.1	mIU/ml ≥10	All Vaccinees	S/N ≥ 2.1	mIU/ml 10	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10
1	67(36/54)	39(21/54)	10.7	32.8	116.6	59(32/54)	19(10/54)	4.0	10.5	58.5	59(32/54)	26(14/54)	4.3	9.90	24.5
3	100(53/53)	95(51/53)	213.3	213.3	245.8	100(54/54)	94(51/54)	107.9	107.9	127.4	91(49/54)	67(36/54)	23.7	31.8	63.3
6	100(53/53)	98(52/53)	199.0	199.0	211.0	100(54/54)	100(54/54)	107.5	107.5	107.5	94(48/51)	71(36/51)	24.7	31.3	59.4
7	100(52/52)	100(52/52)	3056.9	3056.9	3056.9	100(54/54)	100(54/54)	2553.3	2553.3	2553.3	100(53/53)	94(50/53)	846.3	846.3	1131.8
12	100(54/54)	100(54/54)	583.1	583.1	583.1	100(54/54)	100(54/54)	498.1	498.1	498.1	92(49/53)	91(48/53)	324.7	498.8	547.1

2477I/5
12/31/85

00619

FIGURE 1

Confidence Intervals on the Predicted Mean at 7 Months
By Dose in Healthy Teenagers
Who Received Yeast Recombinant Hepatitis B Vaccine
Prepared by the [redacted] (b) (4) Method



00620

Table 2

Percent (Proportion) of Healthy Teenagers (Ages 15-20) with Clinical Complaints During a 5-Day Period Following Vaccination With Yeast Recombinant Hepatitis B Vaccine

Study 819

Type of Complaint	First Injection	Second Injection	Third Injection	Total
	2.5 mcg of Vaccine			
Local (Injection Site)	12.7 (7/55)	1.8 (1/55)	1.9 (1/54)	4.8 (8/164)
Systemic	5.5 (3/55)	0 (0/55)	0 (0/54)	1.8 (3/164)
Any Local or Systemic	12.7 (7/55)	1.8 (1/55)	1.9 (1/54)	4.8 (8/164)
Fever ≥100° F (Oral)	0 (0/55)	0 (0/55)	0 (0/54)	(0) (0/164)
	5 mcg of Vaccine			
Local (Injection Site)	5.5 (3/55)	9.1 (5/55)	5.5 (3/55)	4.8 (8/165)
Systemic	3.6 (2/55)	3.6 (2/55)	0 (0/55)	2.4 (4/165)
Any Local or Systemic	9.1 (5/55)	9.1 (5/55)	5.5 (3/55)	6.1 (10/165)
Fever ≥100° F (Oral)	1.8 (1/55)	0 (0/55)	0 (0/55)	0.6 (1/165)
	10 mcg of Vaccine			
Local (Injection Site)	9.1 (5/55)	5.5 (3/55)	0 (0/55)	4.8 (8/165)
Systemic	5.5 (3/55)	0 (0/55)	0 (0/55)	1.8 (3/165)
Any Local or Systemic	12.7 (7/55)	5.5 (3/55)	0 (0/55)	6.1 (10/165)
Fever ≥ 100°F (Oral)	0 (0/55)	0 (0/55)	0 (0/55)	0 (0/165)

APPENDIX 1

STATISTICAL METHODS

All tests of significance were two-sided at 0.05 significance level.

A. Clinical Complaints

1. The incidence of the various clinical complaints in dialysis patients on the three dose regimen, healthy teenagers and healthy children were evaluated as a function of log dose level using the Mantel-Haenszel Test[1] for trend.

2. All other differences in the incidences of the various clinical complaints in dialysis patients due to dose level or regimen and in health care personnel receiving vaccine from consistency lots were assessed by the Likelihood Ratio Chi-Square.

B. Seroconversion Rates

1. The effect of dose level on seroconversion rates in healthy adults, healthy teenagers and healthy children was analyzed over studies using the Mantel Haenszel Test[1] for trend.

2. Differences in seroconversion rates in healthy adults due to age or sex were evaluated over studies using the Mantel Haenszel Test[1] for heterogeneity.

3. Differences in seroconversion rates due to age in healthy children, dose level in dialysis patients, and vaccine lot in health care personnel were assessed by the Likelihood Ratio Chi-Square.

C. Level of Response (Titers)

The effect of age, sex, lot (consistency lots only in Study 880), or dose level (all other studies) in health care personnel and other healthy adults, of dose level in healthy teenagers, of dose level and age in healthy children, and of dose level and regimen in dialysis patients were analyzed by fitting these variables to a regression model. Subjects who were negative for antibody to hepatitis B surface antigen were assigned a titer of 0.3 mIU/ml in the analysis.

REFERENCE

1. Tarone RE, Ware J: On Distribution-Free Tests for Equality of Survival Distributions. Biometrika 64: 156-160, 1977.

STUDY 819

PROGRAM:	Yeast Recombinant Hepatitis B Vaccine, Study 819
PURPOSE:	To compare antibody and clinical responses to 5 and 10 mcg doses of the vaccine among teenagers who are negative for hepatitis B virus serologic markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #979/C-K564 - 10 mcg HBsAg/ml Lot #985/C-K732 - 5 mcg HBsAg/ml
PRIMARY INVESTIGATOR:	George Papaevangelou, M.D. Professor of Epidemiology & Medical Statistics National Center for Viral Hepatitis Athens School of Hygiene P. O. Box 14085 Athens 11522, Greece
SECONDARY INVESTIGATOR:	Charalambos Vissoulis, M.D. Associate Professor of Medicine University of Athens Medical School 47 Skoufa Street Athens 10672, Greece
STUDY LOCATION:	Greek Naval Base Poros, Greece
DATE INITIATED:	May 12, 1984
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 165 teenagers (15 - 20 years of age) who are armed forces recruits, 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 819

PROCEDURE:

Eligible participants are allocated by means of a prearranged balanced randomization list with code numbers to receive a 1.0 ml (10 mcg or 5 mcg) intramuscular injection of vaccine at 0, 1 and 6 months. Fifty-five receive 10 mcg doses and 55 receive 5 mcg doses.

As per an addendum to this study, 55 recruits receive a 0.5 ml (2.5 mcg) injection of vaccine at 0, 1 and 6 months.

Vaccinees are asked to record their temperature daily for 5 days after each injection and also to record any local or systemic complaints they may have during this period.

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, 3, 6, 7, 12 and 24 months. The samples are assayed for HBsAg, anti-HBc, anti-HBs and ALT. These assays are completed by Dr. Papaevangelou.

RESULTS:

HEALTHY TEENAGERS:

10 mcg Lot 979/C-K564 at 0, 1 and 6 months
5 mcg Lot 985/C-K732 at 0, 1 and 6 months
2.5 mcg Lot 985/C-K732 at 0, 1 and 6 months

1. Number Vaccinated:

Dose Level	Injection Number 1	2	3
10 mcg	55	55	55
5 mcg	55	55	55
2.5 mcg	55	55	54

Three individuals, one from each group, were seropositive at the time of immunization and are excluded from the serologic analysis.

Study 819

RESULTS: (CONT'D) 2. Serologic Results:

At 7 months serologic data are available for 52, 54, and 53 study participants who received 10, 5, and 2.5 mcg doses, respectively. The seroconversion rates at 7 months were 100% for all dose levels when the cutoff was S/N ≥2.1. When the cutoff was mIU/ml ≥10. The rates were 100% for 5 and 10 mcg and 94% for 2.5 mcg. At 7 and 12 months the following anti-HBs responses were noted. Table 1 shows seroconversion rates and GMT's through 12 months of follow-up.

Time (Months)	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
7	10 mcg	100(52/52)	100(52/52)	3056.9	3056.9	3056.9
12	10 mcg	100(54/54)	100(54/54)	583.1	583.1	583.1
7	5 mcg	100(54/54)	100(54/54)	2553.3	2553.3	2553.3
12	5 mcg	100(54/54)	100(54/54)	498.1	498.1	498.1
7	2.5 mcg	100(53/53)	94(50/53)	846.3	846.3	1131.8
12	2.5 mcg	92(49/53)	91(48/53)	324.7	498.8	547.1

3. Clinical Complaints

Clinical follow-up data are available for 55, 55, and 54 participants following each injection of 10, 5 and 2.5 mcg doses, respectively. Data following the third injection has not yet been entered into the data base. Specific complaints and maximum temperatures reported during the five days following the first two injections are provided in Tables 2 through 7.

Type of Complaint	Dose Level	Frequency in % by Injection No. 1	2	3
Injection Site	10 mcg	9(5/55)	6(3/55)	0(0/55)
	5 mcg	6(3/55)	9(5/55)	6(3/55)
	2.5 mcg	13(7/55)	2(1/55)	2(1/54)
Systemic	10 mcg	6(3/55)	0(0/55)	0(0/55)
	5 mcg	4(2/55)	4(2/55)	0(0/55)
	2.5 mcg	6(3/55)	0(0/55)	0(0/54)

Study 819

RESULTS (CONT'D):

The vaccine was well tolerated. All complaints were mild and transient. There were no serious or alarming adverse reactions attributable to vaccine.

HBsAg

One recipient (Case (b) (6) of 5 mcg doses became borderline positive for HBsAg at 3 months (S/N=2.11). His ALT level at this time was within normal limits and he was negative for anti-HBc. His pre-bleed and 1, 6 and 7 and 12 month bleedings were negative for HBsAg and anti-HBc. There is no evidence to suggest that this individual has become infected. It appears likely that the low positive test for HBsAg was spurious.

PUBLICATIONS:

Dandolos E, Roumeliotou-Karayannis A, Richardson SC, Papaevaneglou G. Safety and immunogenicity of a recombinant hepatitis B vaccine. Accepted for publication in J Med Virology 1985.

Papaevangelou G, Dandolos E, Roumeliotou-Karayannis A, Richardson SC. Immunogenicity of recombinant hepatitis B vaccine. Lancet 1985; 1:455-6.

Study #819

Table 1

Antibody Responses Among Initially Seronegative Healthy Teenagers Following Vaccination with 10, 5, or 2.5 mcg Doses of Yeast Recombinant Hepatitis Vaccine B Lot 979/C-K564 or Lot 985/C-K732 at 0, 1 and 6 Months in Study 819

	10 mcg (Lot C-K564)					5 mcg (Lot C-K732)					2.5 mcg (Lot C-K732)				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
				Responders					Responders					Responders	
Time Mos.	S/N ≥ 2.1	mIU/ml ≥10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10	S/N ≥ 2.1	mIU/ml ≥10	All Vaccinees	S/N ≥ 2.1	mIU/ml 10	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10
1	67(36/54)	39(21/54)	10.7	32.8	116.6	59(32/54)	19(10/54)	4.0	10.5	58.5	59(32/54)	26(14/54)	4.3	9.90	24.5
3	100(53/53)	95(51/53)	213.3	213.3	245.8	100(54/54)	94(51/54)	107.9	107.9	127.4	91(49/54)	67(36/54)	23.7	31.8	63.3
6	100(53/53)	98(52/53)	199.0	199.0	211.0	100(54/54)	100(54/54)	107.5	107.5	107.5	94(48/51)	71(36/51)	24.7	31.3	59.4
7	100(52/52)	100(52/52)	3056.9	3056.9	3056.9	100(54/54)	100(54/54)	2553.3	2553.3	2553.3	100(53/53)	94(50/53)	846.3	846.3	1131.8
12	100(54/54)	100(54/54)	583.1	583.1	583.1	100(54/54)	100(54/54)	498.1	498.1	498.1	92(49/53)	91(48/53)	324.7	498.8	547.1

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Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	0 (0.0%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
SORENESS	0 (0.0%)	0 (0.0%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
SYSTEMIC	0 (0.0%)	1 (1.8%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (1.8%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
MALAISE	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
HEADACHE	0 (0.0%)	1 (1.8%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (1.8%)	6 (10.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		7 (12.7%)
PERSONS WITH NO COMPLAINTS	0 (0.0%)	54 (98.2%)	49 (89.1%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		48 (87.3%)
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 : 0819
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	2 (3.6%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
SORENESS	2 (3.6%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
PERSONS WITH COMPLAINTS	2 (3.6%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
PERSONS WITH NO COMPLAINTS	53 (96.4%)	52 (94.5%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		52 (94.5%)
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%)

00630

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
< 99	0 (0.0%)	54 (98.2%)	50 (90.9%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		49 (89.1%)
99 - 99.9	0 (0.0%)	1 (1.8%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		6 (10.9%)
TEMPERATURE TAKEN	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		55 (100.0%)
TEMPERATURE NOT TAKEN	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)		0 (0.0%)

00631

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK564
DOSE : 10 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	55 (100.0%)	53 (96.4%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			53 (96.4%)
99 - 99.9	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			2 (3.6%)
TEMPERATURE TAKEN	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			55 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)			0 (0.0%)

00632

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	0 (0.0%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
SORENESS	0 (0.0%)	0 (0.0%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (5.5%)
SYSTEMIC	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
MALAISE	0 (0.0%)	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
PERSONS WITH NO COMPLAINTS	0 (0.0%)	55 (100.0%)	50 (90.9%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		50 (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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	5 (9.1%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
SORENESS	5 (9.1%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
SYSTEMIC	2 (3.6%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
WHOLE BODY/GENERAL	2 (3.6%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
MALAISE	2 (3.6%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
HEADACHE	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
PERSONS WITH COMPLAINTS	5 (9.1%)	5 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (9.1%)
PERSONS WITH NO COMPLAINTS	50 (90.9%)	50 (90.9%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		50 (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 5

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
< 99	0 (0.0%)	54 (98.2%)	51 (92.7%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		50 (90.9%)
99 - 99.9	0 (0.0%)	1 (1.8%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (7.3%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.8%)
TEMPERATURE TAKEN	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)		55 (100.0%)
TEMPERATURE NOT TAKEN	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)		0 (0.0%)

00635

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	53 (96.4%)	53 (96.4%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		53 (96.4%)
99 - 99.9	2 (3.6%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (3.6%)
TEMPERATURE TAKEN	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		55 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)		0 (0.0%)

00636

Table 6

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	7 (12.7%)	7 (12.7%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (12.7%)
SORENESS	7 (12.7%)	7 (12.7%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (12.7%)
SYSTEMIC	3 (5.5%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (5.5%)
WHOLE BODY/GENERAL	3 (5.5%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (5.5%)
MALAISE	3 (5.5%)	3 (5.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (5.5%)
PERSONS WITH COMPLAINTS	7 (12.7%)	7 (12.7%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (12.7%)
PERSONS WITH NO COMPLAINTS	48 (87.3%)	48 (87.3%)	53 (96.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	48 (87.3%)
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 6 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

CLINICAL COMPLAINTS	TOTAL VACCINEES (55 PATIENTS) - DOSE 2						NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION						
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
SORENESS	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
PERSONS WITH COMPLAINTS	1 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.8%)
PERSONS WITH NO COMPLAINTS	54 (98.2%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	54 (98.2%)
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 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	55 (100.0%)	53 (96.4%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			53 (96.4%)
99 - 99.9	0 (0.0%)	2 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			2 (3.6%)
TEMPERATURE TAKEN	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			55 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)			0 (0.0%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0819
TREATMENT :
LOT NUMBER : CK732
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY TEENAGERS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (55 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		55 (100.0%)
TEMPERATURE TAKEN	55 (100.0%)	55 (100.0%)	55 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		55 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	55 (100.0%)	55 (100.0%)	55 (100.0%)		0 (0.0%)

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Safety and Immunogenicity of a Recombinant Hepatitis B Vaccine

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A hepatitis B vaccine produced in yeast by recombinant DNA technology was evaluated using 5-μg and 10-μg doses in a randomized trial lasting 7 months in 110 male armed forces recruits aged 17–19 years. Results were compared to those of an identical trial of a plasma-derived vaccine. No allergic reactions were observed, and the rate of mild side effects was similar to the plasma-derived vaccine. Seroconversion rates in the first month were 60% (33/55) and 67% (37/55) with the 5-μg and 10-μg doses of the recombinant vaccine, respectively. All participants seroconverted by 3 months, and none lost antibody. These results are very similar to those for plasma-derived vaccine. Comparison of titres of antibody to hepatitis B surface antigen (anti-HBs) showed a slightly higher level with the 10-μg than with the 5-μg dose of the recombinant vaccine. Geometric mean titres of anti-HBs after the booster dose were similar in the 5-μg and 10-μg dose recombinant vaccine groups (2,620 and 2,748 IU/l, respectively) and in the 5-μg plasma-derived vaccine group (3,591 IU/l) but significantly higher (9,227 IU/l) with the 10-μg dose of the plasma-derived vaccine. These results confirm the safety and immunogenicity of the recombinant vaccine, although further study is needed on the duration of immunity.

Key words: active immunoprophylaxis, hepatitis B, plasma-derived hepatitis B vaccine, recombinant hepatitis B vaccine

INTRODUCTION

The safety and immunogenicity of plasma-derived hepatitis B vaccines have been amply demonstrated by clinical trials in various high-risk groups in different parts of the world [Szmuness et al, 1980; Maupas et al, 1981; Beasley et al, 1983]. However, the high cost and limited availability have prevented widespread use of these vaccines, especially in the less developed areas where they are needed most. Vaccination programmes are at present generally limited to groups at high risk of infection, such as hospital personnel. Within these programmes, acceptance may have been affected by unfounded loss of confidence in the safety of the vaccine, following

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isons at each time point. All analyses were carried out after logarithmic transformation of anti-HBs titres.

RESULTS

The trial was completed in all but two recruits, both the losses being from the group receiving the 10-μg dose. One was lost from the study after receiving the second dose and the other after the booster dose. No participant developed either clinical or asymptomatic viral hepatitis, and neither anaphylactoid nor other allergic reactions were observed. Mild side effects were reported, but no case of fever above 37.5°C was noted, and no local discomfort or pain lasting for more than 1 day. The overall frequency of side effects was very similar to that reported for the plasma-derived vaccine in the earlier study (Table I).

The two groups receiving recombinant vaccine showed a similar and rapid immune response (Table II). Both of the recruits who did not complete follow-up had already seroconverted in the first month. All participants had seroconverted by 3 months, and none lost antibody. These rates are very similar to those recorded in the trial of the plasma-derived vaccine. Differences in seroconversion rates at 1 month between the four groups in Table II are not significant ($\chi^2_3 = 5.26$; $P = 0.15$).

Geometric mean titres (GMT) of anti-HBs are shown in Table III. Multivariate comparison between the two recombinant vaccine groups shows that they do not differ in rates of increase of anti-HBs ($F_{3,104} = 1.99$; $P > 0.1$). The 10-μg group had significantly higher GMT of antibody overall than the 5-μg group ($t_{105} = 2.08$; $P < 0.05$), although the difference appears to be small after the booster dose.

Multivariate comparisons of the anti-HBs profiles in the 5-μg and 10-μg recombinant vaccine groups against the corresponding plasma-derived vaccine groups show

TABLE I. Frequency of Side Effects by Type of Vaccine (Summed Over Administrations of Vaccine)

Side effect	Recombinant vaccine (%)	Plasma-derived vaccine (%)
Local pain	6.0	9.0
Fever <37.5°C	16.3	11.1
Other	2.3	2.3
Total	24.6	22.4

TABLE II. Number (%) of Seroconverted (anti-HBs > 2.1 IU/l) by Month and Type of Vaccine

	Recombinant vaccine		Plasma-derived vaccine	
Month	5 μg (N = 55)	10 μg (N = 55)	5 μg (N = 50)	10 μg (N = 50)
1	33 (60)	37 (67)	40 (80)	32 (64)
3	55 (100)	54 (100)[a]	49 (98)	49 (98)
6	55 (100)	54 (100)[a]	49 (98)	49 (98)
7	55 (100)	53 (100)[b]	49 (98)	50 (100)

[a]One person lost to follow-up.
[b]Two persons lost.

population, with all participants in both the trials of recombinant and plasma-derived vaccines being males of similar age living under exactly similar conditions.

Comparison of the 5-μg and 10-μg doses of recombinant vaccine shows a small advantage to the 10-μg dose overall in terms of GMT anti-HBs, although any final difference is slight. Davidson and Krugman [1985], with older vaccinees of both sexes, reported a final (8 months) GMT anti-HBs in the 10-μg group more than double that in the 5-μg group, although the statistical significance is not stated. Irrespective of dose, all participants in our trial reached the 10 IU/l generally regarded as protective. Only five (4.6%; two from the 5-μg group and three from the 10-μg group) had titres lower than 100 IU/l.

Our results confirm reports of the safety and immunogenicity of the Merck Sharp and Dohme recombinant yeast hepatitis B vaccine [Jilg et al, 1984b; Davidson and Krugman, 1985]. The minor differences observed in the immune response stress the need for more extensive studies in various population groups under consideration for vaccination, before the appropriate dose and vaccination scheme are decided. Similarly, further follow-up is required to establish the duration of protective levels of antibody [Jilg et al, 1984a; Davidson and Krugman, 1985]. Finally, in assessing the efficacy of the vaccine, information concerning the quality of the anti-HBs induced should complement the data on the anti-HBs levels achieved [Brown et al, 1984].

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IMMUNOGENICITY OF RECOMBINANT HEPATITIS B VACCINE

SIR,—Jilg et al[1] have compared the immunogenicity of recombinant[2] and plasma derived hepatitis B vaccines. We report for comparison the results of a similar trial of the recombinant vaccine in a younger age group. 55 male armed forces recruits, aged 17–19, all of whom were susceptible to hepatitis B virus were given

IMMUNE RESPONSES AFTER RECOMBINANT (n=55) OR PLASMA (n=50) HEPATITIS B VACCINATION

Month	Seroconversion		GMT anti-HBs (IU/l)	
	Recombinant	Plasma	Recombinant	Plasma
1	37 (67%)	32 (64%)	11	4
3	54 (100%)*	49 (98%)	198	278
6	54 (100%)*	49 (98%)	189	492
7	53 (100%)†	50 (100%)	2749	9227

*1 lost to follow-up. †2 lost.

10 μg of recombinant vaccine (lot 979/C-K 564, Merck Sharp and Dohme) intramuscularly at 0, 1, and 6 months. The results can be compared with those in another group of recruits of the same age who had been given 10 μg of the same manufacturer's plasma-derived vaccine at 0, 1, and 6 months in an earlier study.[3]

Seroconversion rates and geometric mean antibody titres (GMT) of anti-HBs (see table) were substantially higher than those reported by Jilg et al.[1] The final GMT was 2749 IU/l (95% confidence interval: 1676–4506) compared with 911 IU/l for 12 males reported by Jilg et al.[1] After the booster dose, all vaccinees had an anti-HBs titre above the protective level of 10 IU/l; 43 (81%) had titres above 1000 IU/l. The stronger immune response in our study than in Jilg's may be explained by the fact that our vaccinees were younger (17–19 vs 21–34). We observed only minor side-effects in 20% of participants; this is as reported by Jilg et al.[1]

The seroconversion rates were the same as those obtained in our earlier trial of a 10 μg dose of the plasma-derived vaccine.[3] In contrast to Jilg et al[1] GMT antibody levels in our recombinant group in the first 3 months were similar ($p>0 \cdot 05$) to those induced by the plasma-derived vaccine, although levels after the booster dose were significantly lower ($p<0 \cdot 001$) in the recombinant group (Mann-Whitney tests, separately at each time).

Our results accord with those of Jilg et al in confirming the safety and immunogenicity of the Merck Sharp and Dohme recombinant vaccine. The minor differences in immune response show the need for further trials in population groups under consideration for vaccination, before a dose and vaccination scheme are decided on. In assessing the efficacy of this vaccine, information on the quality of the anti-HBs induced should complement the anti-HBs levels achieved.[4]

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STUDY 891

SUMMARY - HEALTHY CHILDREN

To date, a total of 258 healthy infants and children, 3 months to 11 years of age who were negative for hepatitis B markers, have been vaccinated with hepatitis B recombinant vaccine. Clinical data for all 3 injections are available on 100 infants and children. Seven to 8 month serology data are available on 97 infants and children. Antibody and clinical responses to 5, 2.5 and 1.25 mcg doses of the vaccine administered at 0, 1 and 6 months were evaluated. The vaccine was very immunogenic and well tolerated in this population. Clinical complaints were minimal and transient. In general, children 3 months to 11 years show an earlier response and develop higher titers of antibody than do adults. Seroconversion (S/N $\geq$2.1) exceeded 94% after 2 doses regardless of dose level. Protective levels of antibody (mIU/ml $\geq$10) were induced in 100% of vaccine recipients, one month after the third injection, regardless of dose level administered. At 12 months, all children surveyed still had titers of mIU/ml $\geq$10.

Immunogenicity

Antibody to hepatitis B surface antigen was measured at 1, 2, 3, 6, 7/8 and 12 months post vaccination. Data from study 809 involving 80 children who received either 5, 2.5 or 1.25 mcg doses were statistically analyzed. No significant effect of log dose level on seroconversion rates was found using either a cutoff of S/N $\geq$2.1 or mIU/ml $\geq$10 (see Appendix I for statistical methods used). Seroconversion for all three dose levels and either cutoff was greater than 82% at 3 months, 91% at 6 months and 100% at 7/8 months (Table 1).

When each dose level was analyzed for the effect of age on seroconversion rates, younger children (under 4 years vs 5-12 years) who received the 2.5 mcg dose showed a significantly higher rate at 1 month for a cutoff of S/N $>$2.1 ($p = 0.028$) and at 3 months when the cutoff was mIU/ml $\geq$10 ($p = 0.022$) (Table 2). However, seroconversion was excellent for both age groups by 6 months.

Log titers increased significantly with log dose level at 6 ($p = 0.03$) and 7/8 months ($p < 0.01$) (Table 3). Geometric mean titers for all vaccinees at 7 months were 15965.5 mIU/ml, 6230.2 mIU/ml and 2181.1 mIU/ml for 5, 2.5 and 1.25 mcg doses, respectively. Geometric mean titers at 12 months were 3481.6 mIU/ml, 3051.5 mIU/ml and 819.2 mIU/ml for 5, 2.5 and 1.25 mcg doses, respectively. Figure 1 presents confidence limits on the mean predicted titer at each dose level for a one year old and a 9 year old.

Serologic data from children vaccinated with 5 mcg doses in study 865 were summarized but not included in the statistical analysis. Twenty-one of these children received three injections at 0 and 1 and 6 months, while ninety-six received two injections given at 0 and 1 month. Table 1 illustrates that seroconversion rates at 6 months were 98% and 85% for a cutoff of S/N $\geq$2.1 and mIU/ml $\geq$10, respectively. For those children who received a third injection at 6 months, seroconversion rates increased to 100% regardless of cutoff. A large boost in titer was seen among those children who received the third injection

(Table 3). Geometric mean titers at 8 months were 1894.81 mIU/ml and 84.50 mIU/ml for those in the three and two immunization groups, respectively.

Safety

Clinical complaints among children following 231 injections given in study 809 were available for analysis (Tables 4-6). The incidence of local (injection site) complaints, of systemic complaints, of either local or systemic complaints and of fever (oral temperature of 100°F or more) were analyzed. The incidence at each dose was defined as the number of subjects with the complaint at any time during the 5 day period following vaccination divided by the number reporting; while the total was the sum over the three injections divided by the number of injections with follow-up (Table 4). The frequency of systemic complaints is shown in Tables 5 and 6. All complaints were minimal and transient. The statistical methods used in this analysis are shown in Appendix 1.

None of the incidences of complaints were found to be a function of log dose level. Children who received 2.5 mcg of vaccine tended to report fewer complaints with each dose level. However, the incidences of local and systemic complaints were highest after the second injection in children who received 5 mcg of vaccine. Over all doses and dose levels, fever (oral temperature of 100°F or greater) occurred after 12.7% (24/189) of injections with follow-up. Injection site complaints (15/229, 2.2%) reported were soreness, tenderness, or ecchymosis, while systemic complaints most often were respiratory (18/229 injections, 3.5%) or fatigue (7/229 injections, 3.1%).

Clinical data from children following 282 injections of 5 mcg doses in study 865 were summarized but not included in the statistical analysis (Tables 4 and 7). Fever was reported after 10.3% (29/282) of injections with follow-up. The only injection site complaint was soreness (1.8%), while systemic complaints were mainly digestive (2.5%) or respiratory (1.4%).

The vaccine has been well tolerated in this population. No serious reactions have been reported.

In summary, the vaccine has been well tolerated by infants and children. Although seroconversion rates were excellent with all dosages of vaccine utilized, the highest antibody titers were obtained with the 5 mcg dose of vaccine.

FIGURE 1

Confidence Intervals on the Predicted Mean at 7/8 Months
By Age and Dose in Healthy Children
Who Received Yeast Recombinant Hepatitis B Vaccine
Prepared by the (b) (4) Method

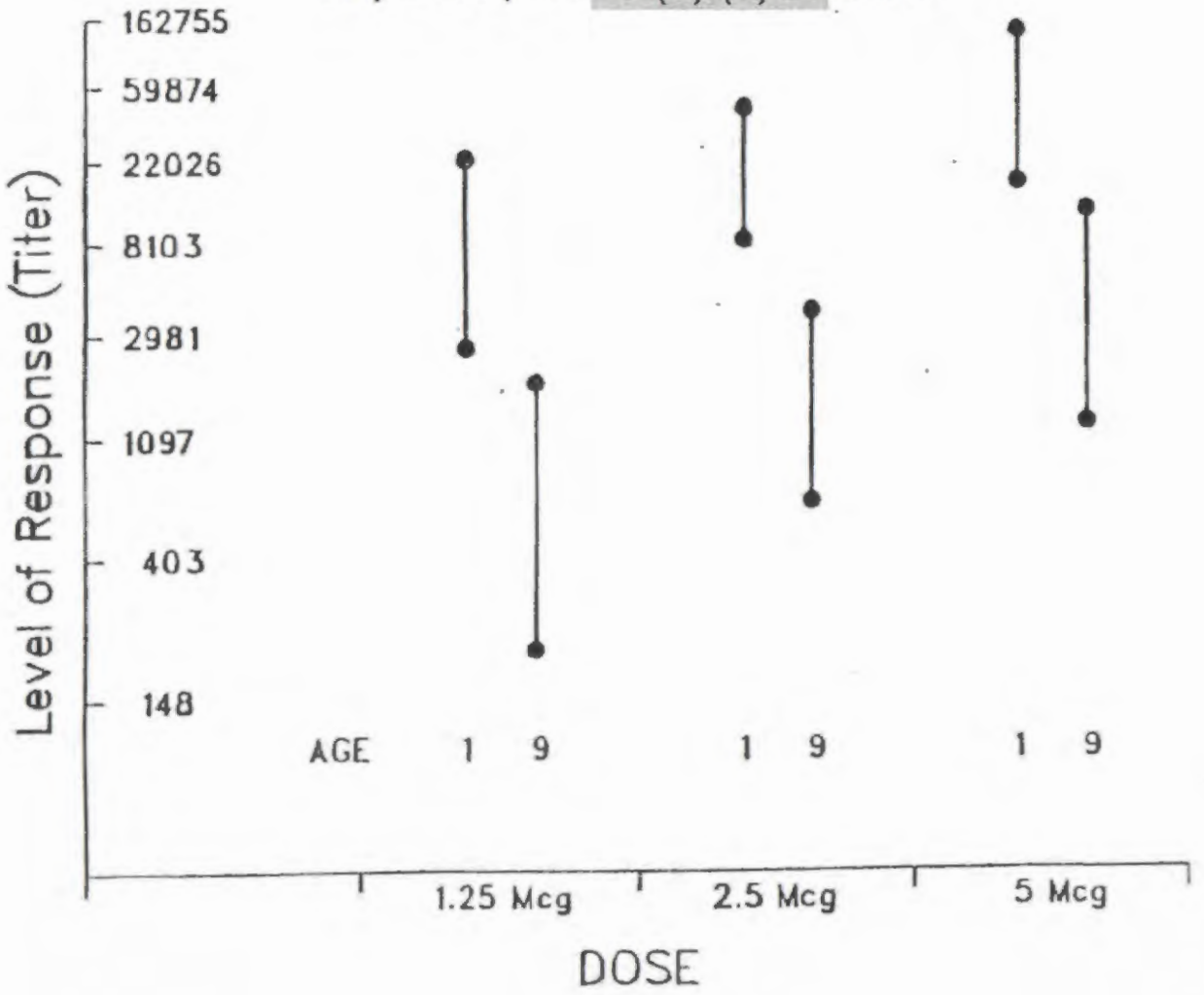

Table 1

Percent Seroconversion (Proportion) by Dose in Healthy Children Who Received Yeast Recombinant Hepatitis B Vaccine

Study No.	Dose	Month 1		Month 3		Month 6		Month 7/8		Month 12	
		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	S/N ≥2.1	mIU/ml ≥10
809	1.25	40.0 (10/25)	8.0 (2/25)	100.0 (7/7)	85.7 (6/7)	100.0 (21/21)	90.5 (19/21)	100.0 (17/17)	100.0 (17/17)	100.0 (9/9)	100.0 (9/9)
809	2.50	44.4 (12/27)	22.2 (6/27)	100.0 (17/17)	82.4 (14/17)	96.4 (27/28)	92.9 (26/28)	100.0 (21/21)	100.0 (21/21)	100.0 (19/19)	100.0 (19/19)
809	5.0	47.0 (9/19)	16.0 (3/19)	100.0 (10/10)	100.0 (10/10)	100.0 (19/19)	100.0 (26/28)	100.0 (14/14)	100.0 (14/14)	100.0 (13/13)	100.0 (13/13)
865	5.0	36.6 (52/142)	13.4 (19/142)	94.0 (110/117)	81.2 (95/117)	97.9 (94/96)	85.4 (82/96)	100.0 (21/21)* 95.8 (23/24)**	100.0 (21/21)* 87.5 (21/24)**	-	-

* Received a 3rd injection at 6 months.

** Did not receive a third injection at 6 months.

Table 2

Percent Seroconversion (Proportion) By Dose and Age Group in Healthy Children
Who Received Yeast Recombinant Hepatitis B Vaccine (Study 809)

Dose (MCG)	Age Group (Years)	Month 1		Month 3		Month 6		Month 7/8*	
		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
1.25	<=4	41.7 (5/12)	8.3 (1/12)	100.0 (3/3)	100.0 (3/3)	100.0 (8/8)	100.0 (8/8)	100.0 (7/7)	100.0 (7/7)
1.25	5 - 12	38.5 (5/13)	7.7 (1/13)	100.0 (4/4)	75.0 (3/4)	100.0 (13/13)	84.6 (11/13)	100.0 (10/10)	100.0 (10/10)
2.50	<=4	64.3 (9/14)	35.7 (5/14)	100.0 (9/9)	100.0 (9/9)	100.0 (15/15)	93.3 (14/15)	100.0 (12/12)	100.0 (12/12)
2.50	5 - 12	23.1 (3/13)	7.7 (1/13)	100.0 (8/8)	62.5 (5/8)	92.3 (12/13)	92.3 (12/13)	100.0 (9/9)	100.0 (9/9)
5.0	<=4	54.5 (6/11)	18.2 (2/11)	100.0 (6/6)	100.0 (6/6)	100.0 (11/11)	100.0 (11/11)	100.0 (8/8)	100.0 (8/8)
5.00	5 - 12	37.5 (3/8)	12.5 (1/8)	100.0 (4/4)	100.0 (4/4)	100.0 (8/8)	100.0 (8/8)	100.0 (6/6)	100.0 (6/6)

* Month 7/8 included 9 month data when 7 or 8 month was not available.

Table 3

Geometric Mean Titers by Dose in Healthy Children Who
Received Yeast Recombinant Hepatitis B Vaccine

Study #	Dose	Month 1				Month 3				Month 6				Month 7/8				Month 12			
		GMT (mIU/ml)				GMT (mIU/ml)				GMT (mIU/ml)				GMT (mIU/ml)				GMT (mIU/ml)			
				Responders				Responders				Responders				Responders				Responders	
		N	All Vacc.	S/N ≥2.1	mIU/ml ≥10	N	All Vacc.	S/N ≥2.1	mIU/ml ≥10	N	All Vacc.	S/N ≥2.1	mIU/ml ≥10	N	All Vacc.	S/N ≥2.1	mIU/ml ≥10	N	All Vacc.	S/N ≥2.1	mIU/ml ≥10
809	1.25	25	1.2	7.4	69.7	7	52.7	52.7	77.5	21	75.9	75.9	100.7	14	2181.1	2181.1	2181.1	9	819.2	819.2	819.2
809	2.50	27	1.9	11.4	28.9	17	86.9	86.9	144.7	28	125.2	156.5	175.7	21	6230.2	6230.2	6230.2	19	3051.5	3051.5	3051.5
809	5.0	19	2.0	11.7	63.9	10	189.3	189.3	189.3	19	308.4	308.4	308.4	14	15965.5	15965.5	15965.5	13	3481.6	3481.6	3481.6
865	5.0	142	0.9	8.8	26.1	117	44.7	63.5	81.2	96	59.4	74.7	98.6	21 24	1894.8* 84.5**	1894.8* 107.9**	1894.8* 144.9**				

* Received a third injection at 6 months.

** Did not receive a third injection at 6 months.

Table 4

Percent (Proportion) of Healthy Children (Ages 1-12) with Clinical Complaints During a 5-Day Period Following Vaccination With Yeast Recombinant Hepatitis B Vaccine

Study 809

Type of Complaint	First Injection	Second Injection	Third Injection	All Injections
	1.25 mcg of Vaccine			
Local (Injection Site)	0 (0/26)	0 (0/26)	4.0 (1/25)	1.3 (1/77)
Systemic	19.2 (5/26)	11.5 (3/26)	12.0 (3/25)	14.3 (11/77)
Any Local or Systemic	19.2 (5/26)	11.5 (3/26)	16.0 (4/25)	15.6 (12/77)
Fever ≥100° F (Oral)	20.0 (4/20)	11.1 (2/18)	7.1 (1/14)	13.5 (7/52)
	2.5 mcg of Vaccine			
Local (Injection Site)	6.3 (2/32)	3.2 (1/31)	0 (0/30)	3.2 (3/93)
Systemic	18.8 (6/32)	12.6 (4/31)	6.7 (2/30)	12.9 (12/93)
Any Local or Systemic	21.9 (7/32)	16.1 (5/31)	6.7 (2/30)	15.1 (14/93)
Fever ≥100° F (Oral)	13.3 (4/30)	11.5 (3/26)	11.5 (3/26)	12.2 (10/82)
	5 mcg of Vaccine			
Local (Injection Site)	0 (0/21)	5.6 (1/18)	0 (0/20)	1.7 (1/59)
Systemic	14.3 (3/21)	22.2 (4/18)	5.0 (1/20)	13.6 (8/59)
Any Local or Systemic	14.3 (3/21)	27.8 (5/18)	5.0 (1/20)	15.3 (9/59)
Fever ≥ 100°F (Oral)	19.1 (4/21)	6.3 (1/16)	11.1 (2/18)	12.7 (7/55)

Study 865

Type of Complaint	First Injection	Second Injection	Third Injection	All Injections
	5 mcg of Vaccine			
Local (Injection Site)	2.1 (3/141)	1.7 (2/116)	0 (0/25)	1.8 (5/282)
Systemic	5.7 (8/141)	4.3 (5/116)	4.0 (1/25)	5.0 (14/282)
Any Local or Systemic	7.8 (11/141)	6.0 (7/116)	4.0 (1/25)	6.7 (19/282)
Fever ≥ 100°F (Oral)	9.9 (14/141)	12.1 (14/116)	4.0 (1/25)	10.3 (29/282)

Table 5

Frequency of Systemic Complaints by Body System Occurring Within 5 Days Among Healthy Children Following 231 Injections of Yeast Recombinant Hepatitis B Vaccine

Study: 809
Number of Vaccine Recipients: 80

Body System/Complaint	Frequency as % (Number)
Whole Body/General	5 (12)
Fatigue/Weakness	3 (7)
Headache	0.8 (2)
Sweating	0.4 (1)
Bruise from venipuncture	0.4 (1)
Illness, NOS	0.4 (1)
Digestive	4 (10)
Diarrhea	2 (5)
Vomiting	1.3 (3)
Diminished Appetite	0.4 (1)
Loose Stool	0.4 (1)
Nausea	0.4 (1)
Teething	0.4 (1)
Respiratory	4 (9)
Upper Respiratory Infection, NOS	2.6 (6)
Pharyngitis	0.8 (2)
Rhinitis	0.8 (2)
Cough	0.4 (1)
Croup	0.4 (1)
Psychiatric/Behavioral	2 (5)
Irritability	1.7 (4)
Insomnia/Disturbed Sleep	0.4 (1)
Infectious Syndromes	2 (4)
Viral Infection	1.7 (4)
Integumentary	1 (3)
Papular rash	0.8 (2)
Rash, NOS	0.4 (1)
Urticaria/Hives	0.4 (1)
Organs of Special Sense	0.4 (1)
Otitis Media	0.4 (1)

Table 6

Percentage (Number) of Healthy Children with Specific Systemic Complaints During a 5 Day Period Following 231 Injections of Yeast Recombinant Hepatitis B Vaccine

Study: 809
Number of Vaccine Recipients: 80

Complaint Frequency 1 - 3%	
Fatigue/Weakness	3 (7)
Upper Respiratory Infection NOS	2.6 (6)
Diarrhea	2 (5)
Vomiting	1.3 (3)
Irritability	1.7 (4)
Viral Infection	1.7 (4)
Complaint Frequency 0.5 - 0.97%	
Headache	0.8 (2)
Pharyngitis	0.8 (2)
Rhinitis	0.8 (2)
Papular Rash	0.8 (2)
Complaint Frequency 0.1 - 0.49%	
Sweating	0.4 (1)
Bruise from venipuncture	0.4 (1)
Illness, NOS	0.4 (1)
Diminished Appetite	0.4 (1)
Loose Stool	0.4 (1)
Nausea	0.4 (1)
Teething	0.4 (1)
Cough	0.4 (1)
Croup	0.4 (1)
Insomnia/Disturbed Sleep	0.4 (1)
Rash, NOS	0.4 (1)
Urticaria/Hives	0.4 (1)
Otitis Media	0.4 (1)

Table 7

Frequency of Systemic Complaints by Body System Occurring Within 5 Days Among Healthy Children Following 282 Injections of Recombinant Hepatitis B Vaccine

Study: 865
Number of Vaccine Recipients: 141

Body System	# Complaints	Frequency as %
Digestive	7	2.5
Respiratory	4	1.4
Whole Body	3	1.1

APPENDIX 1

STATISTICAL METHODS

All tests of significance were two-sided at 0.05 significance level.

A. Clinical Complaints

1. The incidence of the various clinical complaints in dialysis patients on the three dose regimen, healthy teenagers and healthy children were evaluated as a function of log dose level using the Mantel-Haenszel Test[1] for trend.

2. All other differences in the incidences of the various clinical complaints in dialysis patients due to dose level or regimen and in health care personnel receiving vaccine from consistency lots were assessed by the Likelihood Ratio Chi-Square.

B. Seroconversion Rates

1. The effect of dose level on seroconversion rates in healthy adults, healthy teenagers and healthy children was analyzed over studies using the Mantel Haenszel Test[1] for trend.

2. Differences in seroconversion rates in healthy adults due to age or sex were evaluated over studies using the Mantel Haenszel Test[1] for heterogeneity.

3. Differences in seroconversion rates due to age in healthy children, dose level in dialysis patients, and vaccine lot in health care personnel were assessed by the Likelihood Ratio Chi-Square.

C. Level of Response (Titers)

The effect of age, sex, lot (consistency lots only in Study 880), or dose level (all other studies) in health care personnel and other healthy adults, of dose level in healthy teenagers, of dose level and age in healthy children, and of dose level and regimen in dialysis patients were analyzed by fitting these variables to a regression model. Subjects who were negative for antibody to hepatitis B surface antigen were assigned a titer of 0.3 mIU/ml in the analysis.

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HEALTHY CHILDREN

Study 809 - Philadelphia, PA - Dr. S. Plotkin and Dr. S. Starr

Healthy adults and children (1-11 years of age), who are seronegative for hepatitis B virus markers, are enrolled in Study 809. Healthy children receive either 1.25 mcg or 2.5 mcg injections of vaccine lot C-K723 or 2.5 mcg or 5 mcg injections of lot C-K444. All injections are administered at 0, 1, and 6 months.

Twenty-six children have received two 1.25 mcg injections of vaccine and 25 of these have received the third injection. At 7/8 months, 100% (14/14) of the subjects seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT for all vaccinees was 2181.1 mIU/ml.

Thirty-two children have received two 2.5 mcg injections of vaccine and 30 of these have received the third injection. At 7/8 months, 100% (21/21) of the vaccinees seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT for all vaccinees was 6230.2 mIU/ml.

In the 5 mcg dose regimen, 22 children have received two injections of vaccine and 21 of these have received the third injection. At 7/8 months, 100% (14/14) of the children seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT for all vaccinees was 15965.5 mIU/ml.

Anti-HBs titers were higher in the children who received 5 mcg injections than in the children who received 1.25 mcg or 2.5 mcg injections of vaccine.

No serious or alarming adverse experiences related to vaccine have been reported. The study continues in progress.

Study 865 - Hone Kong - Dr. E. K. Yeoh

Healthy infants and children, ages 3 months through 11 years, who are negative for hepatitis B serologic markers are enrolled in Study 865. The children are assigned to receive 5 mcg injections of vaccine lot C-K732 at 0 and 1 months or at 0, 1, and 6 months.

Ninety children, in the two injection regimen, have received one 5 mcg injection of vaccine and 70 of these have received the second injection. At 6 months, 98% (49/50) of the children seroconverted (S/N $\geq$2.1) for anti-HBs and 94% (47/50) developed protective levels of antibody (mIU/ml $\geq$10). The GMT for all vaccinees at that time was 81.6 mIU/ml and 102.5 for responders (mIU/ml $\geq$10). At 8 months, 87.5% (21/24) of the vaccinees were positive for anti-HBs (mIU/ml $\geq$10) with a GMT of 145.0 mIU/ml.

Eighty-eight children, in the three injection regimen, have received the first 5 mcg injection of vaccine. Seventy-two and 46 subjects have been administered the second and third injections, respectively. At 8 months, 100%

Study 865 - Hong Kong - Dr. E. K. Yeoh (Cont.)

(21/21) seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees as 1894.8 mIU/ml.

No serious or alarming adverse reactions attributable to vaccine have been reported. Vaccination and follow-up continue in progress.

Study 891 - China - Dr. Z. H. Hu

The study population consists of healthy adults and healthy children who are negative for hepatitis B serologic markers. Healthy adults receive either 10 mcg injections of yeast recombinant vaccine or 20 mcg injections of plasma-derived vaccine. Healthy children received either 5 mcg injections of yeast recombinant vaccine or 10 mcg injections of plasma-derived vaccine. All injections are administered at 0, 1, and 6 months. Yeast recombinant vaccine lot C-K564 and plasma-derived vaccine lot 0027L are being utilized.

Twenty-five children have received the first injection of yeast recombinant vaccine and 25 have received the first injection of plasma-derived vaccine. None have received second or third injections of vaccine. Serology data are not presently available. No serious or alarming adverse events attributable to vaccine have been reported. Vaccination and follow-up continues in progress.

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.

Study 809

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 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 CHILDREN:

1.25 mcg Lot # 985/C-K732 at 0, 1, and 6 months
2.5 mcg Lot # 985/C-K732 at 0, 1, and 6 months
2.5 mcg Lot # 972/C-K444 at 0, 1, and 6 months
5 mcg Lot # 972/C-K444 at 0, 1, and 6 months

1. Number Vaccinated:

Dose Level	Injection No. 1	2	3
1.25 mcg	26	26	25
2.5 mcg	32	32	30
5 mcg	22	22	21

Study 809

RESULTS: (Cont.)

2. Serologic Results:

Serologic data are available for 14, 22, and 14 participants at 7/8 months, who received 1.25 mcg, 2.5 mcg and 5 mcg injections of vaccine, respectively. One hundred percent of the subjects (all dose levels) seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10) at that time. Anti-HBs responses and GMTs for 7/8 month data are summarized in the following table.

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
1.25 mcg	100(14/14)	100 (14/14)	2181.1	2181.1	2181.1
2.5 mcg	100(21/21)	100 (21/21)	6230.2	6230.2	6230.2
5 mcg	100(14/14)	100 (14/14)	15965.5	15965.5	15965.5

Among participants with serology data at 12 months, 100% (9/9), 95% (18/19) and 100% (13/13) were positive for anti-HBs (mIU/ml ≥10) from dose level 1.25 mcg, 2.5 mcg and 5.0 mcg, respectively. The GMTs for all vaccinees from these dose levels were 819.2, 3051.5, and 3481.6 mIU/ml, respectively.

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 25, 30, and 18 participants, after each injection, in the 1.25 mcg, 2.5 mcg, and 5 mcg dose level, respectively. The overall frequencies of complaints follow.

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RESULTS (CONT.):

Type of Complaint	Dose Level	Frequency in % by Injection No. 1	2	3
Injection Site	1.25 mcg	0(0/26)	0(0/26)	4(1/25)
	2.5 mcg	6(2/32)	3(1/31)	0(0/30)
	5.0 mcg	0(0/21)	6(1/18)	0(0/20)
Systemic	1.25 mcg	19(5/26)	12(3/26)	12(3/25)
	2.5 mcg	19(6/32)	13(4/31)	7(2/30)
	5.0 mcg	14(3/21)	22(4/18)	5(1/20)

Refer to Tables 2 through 4 for listings of specific complaints by injection number and dose level. Maximum temperature data are provided in Tables 5 through 7.

There have been no serious or alarming reactions attributable to vaccine.

Table 1

Antibody Responses Among Healthy Children Following Vaccination with
1.25, 2.5, or 5 mcg Injections of Yeast Recombinant Hepatitis B Vaccine
Lot # 972/C-K444 and 985/C-K732 at 0, 1, and 6 Months

	1.25 mcg					2.5 mcg					5 mcg				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
				Responders					Responders					Responders	
Time (Mos.)	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	40 (10/25)	8 (2/25)	1.2	7.4	69.7	44 (12/27)	22 (6/27)	1.9	11.4	28.9	47 (9/19)	16 (3/19)	2.0	11.7	63.9
2	92 (11/12)	58 (7/12)	26.2	36.0	129.2	88 (7/8)	63 (5/8)	37.8	75.5	236.4	100 (6/6)	67 (4/6)	23.7	23.7	43.5
3	100 (7/7)	86 (6/7)	52.7	52.7	77.5	100 (11/11)	82 (14/11)	86.9	86.9	144.7	100 (10/10)	100 (10/10)	189.3	189.3	189.3
6	100 (21/21)	90 (19/21)	75.9	75.9	100.7	96 (27/28)	93 (26/28)	125.2	156.5	175.7	100 (19/19)	100 (19/19)	308.4	308.4	308.4
7/8	100 (14/14)	100 (14/14)	2181.1	2181.1	2181.1	100 (21/21)	100 (21/21)	6230.2	6230.2	6230.2	100 (14/14)	100 (14/14)	15965.5	15965.5	15965.5
12	100 (9/9)	100 (9/9)	819.2	819.2	819.2	100 (19/19)	95 (18/19)	3051.5	3051.5	4205.1	100 (13/13)	100 (13/13)	3481.6	3481.6	3481.6

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (26 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	1 (3.8%)	2 (7.7%)	1 (3.8%)	3 (11.5%)	3 (11.5%)	2 (7.7%)	5 (19.2%)
WHOLE BODY/GENERAL	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
FATIGUE/WEAKNESS	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
VIRAL INFECTION, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
INTEGUMENTARY STSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
PAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
RESPIRATORT	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
DIARRHEA	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)

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

STUDY : 0609
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

	TOTAL VACCINEES (26 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						
CLINICAL COMPLAINTS	0	1	2	3	4	5	NUMBER WITH COMPLAINTS
DIMINISHED APPETITE	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
ORGANS OF SPECIAL SENSE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
OTITIS MEDIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	2 (7.7%)
IRRITABILITY	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
INSOMNIA/DISTURBED SLEEP	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
PERSONS WITH COMPLAINTS	1 (3.8%)	2 (7.7%)	1 (3.8%)	3 (11.5%)	3 (11.5%)	2 (7.7%)	5 (19.2%)
PERSONS WITH NO COMPLAINTS	25 (96.2%)	24 (92.3%)	25 (96.2%)	23 (88.5%)	23 (88.5%)	24 (92.3%)	21 (80.8%)
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 : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (26 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	2 (7.7%)	2 (7.7%)	2 (7.7%)	1 (3.8%)	2 (7.7%)	2 (7.7%)	3 (11.5%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
SWEATING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
RESPIRATORY	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	1 (3.8%)
RHINITIS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	1 (3.8%)
PHARYNGITIS (SORE THROAT)	1 (3.8%)	1 (3.8%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)
DIGESTIVE SYSTEM	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)
DIARRHEA	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	1 (3.8%)	1 (3.8%)
PSYCHIATRIC/BEHAVIORAL	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)
IRRITABILITY	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.8%)

Table 2 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (26 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	2 (7.7%)	2 (7.7%)	2 (7.7%)	1 (3.8%)	2 (7.7%)	2 (7.7%)	3 (11.5%)
PERSONS WITH NO COMPLAINTS	24 (92.3%)	24 (92.3%)	24 (92.3%)	25 (96.2%)	24 (92.3%)	24 (92.3%)	23 (88.5%)
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 : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (25 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	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	0 (0.0%)	0 (0.0%)	1 (4.0%)	2 (8.0%)	3 (12.0%)	0 (0.0%)		3 (12.0%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)		2 (8.0%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (4.0%)
ILLNESS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	0 (0.0%)		1 (4.0%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)	2 (8.0%)	0 (0.0%)		2 (8.0%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)		1 (4.0%)
LOOSE STOOL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.0%)	1 (4.0%)	0 (0.0%)		1 (4.0%)
PERSONS WITH COMPLAINTS	1 (4.0%)	0 (0.0%)	1 (4.0%)	2 (8.0%)	3 (12.0%)	0 (0.0%)		4 (16.0%)
PERSONS WITH NO COMPLAINTS	24 (96.0%)	25 (100.0%)	24 (96.0%)	23 (92.0%)	22 (88.0%)	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 3

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 PATIENTS) - DOSE 1							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	2 (6.3%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (6.3%)
SORENESS	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
TENDERNESS	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
SYSTEMIC	1 (3.1%)	2 (6.3%)	1 (3.1%)	0 (0.0%)	2 (6.3%)	3 (9.4%)		6 (18.8%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)		1 (3.1%)
HEADACHE	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)		1 (3.1%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	2 (6.3%)	1 (3.1%)		3 (9.4%)
VIRAL INFECTION, NOS	0 (0.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)	2 (6.3%)	1 (3.1%)		3 (9.4%)
RESPIRATORY	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)		2 (6.3%)
UPPER RESPIRATORY INFECT., NOS	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
CROUP	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)		1 (3.1%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NAUSEA	0 (0.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.1%)
PERSONS WITH COMPLAINTS	3 (9.4%)	3 (9.4%)	1 (3.1%)	0 (0.0%)	2 (6.3%)	3 (9.4%)		7 (21.9%)
PERSONS WITH NO COMPLAINTS	29 (90.6%)	29 (90.6%)	31 (96.9%)	32 (100.0%)	30 (93.8%)	29 (90.6%)		25 (78.1%)
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 : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 PATIENTS) DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
SORENESS	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
SYSTEMIC	1 (3.2%)	2 (6.5%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	0 (0.0%)		4 (12.9%)
WHOLE BODY/GENERAL	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
FATIGUE/WEAKNESS	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
INTEGUMENTARY SYSTEM	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
URTICARIA/HIVES	0 (0.0%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.2%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)		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%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (6.5%)
DIARRHEA	0 (0.0%)	1 (3.2%)	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (6.5%)
PERSONS WITH COMPLAINTS	2 (6.5%)	3 (9.7%)	1 (3.2%)	0 (0.0%)	1 (3.2%)	0 (0.0%)		5 (16.1%)

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

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
PERSONS WITH NO COMPLAINTS	29 (90.5%)	28 (90.3%)	30 (96.8%)	31 (100.0%)	30 (96.8%)	31 (100.0%)		26 (83.9%)
PERSONS WITH NO DATA	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)		1 (3.1%)

Table 3 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (30 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	1 (3.3%)	0 (0.0%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
WHOLE BODY/GENERAL	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
HEADACHE	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%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
VOMITING	0 (0.0%)	0 (0.0%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		1 (3.3%)
PERSONS WITH COMPLAINTS	1 (3.3%)	0 (0.0%)	1 (3.3%)	1 (3.3%)	0 (0.0%)	0 (0.0%)		2 (6.7%)
PERSONS WITH NO COMPLAINTS	29 (96.7%)	30 (100.0%)	29 (96.7%)	29 (96.7%)	30 (100.0%)	30 (100.0%)		28 (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 4
PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	1 (4.8%)	1 (4.8%)	2 (9.5%)	3 (14.3%)	3 (14.3%)	0 (0.0%)	3 (14.3%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)	2 (9.5%)	0 (0.0%)	2 (9.5%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	1 (4.8%)
HEADACHE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	1 (4.8%)
INTEGUMENTART SYSTEM	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	1 (4.8%)
PAPULAR RASH	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	1 (4.8%)
RASH, NOS	1 (4.8%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
RHINITIS	0 (0.0%)	0 (0.0%)	1 (4.8%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
PERSONS WITH COMPLAINTS	1 (4.8%)	1 (4.8%)	2 (9.5%)	3 (14.3%)	3 (14.3%)	0 (0.0%)	3 (14.3%)
PERSONS WITH NO COMPLAINTS	20 (95.2%)	20 (95.2%)	19 (90.5%)	18 (85.7%)	18 (85.7%)	21 (100.0%)	18 (85.7%)
PERSONS WITH NO DATA	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)	1 (4.5%)

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

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
ECCHYMOSIS	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
SYSTEMIC	2 (11.1%)	2 (11.1%)	1 (5.6%)	2 (11.1%)	0 (0.0%)	1 (5.6%)	4 (22.2%)
WHOLE BODY/GENERAL	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	3 (16.7%)
FATIGUE/WEAKNESS	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	2 (11.1%)
BRUISE FROM VENIPUNCTURE	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (5.6%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	2 (11.1%)
TEETHING	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	1 (5.6%)

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

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (22 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
PSYCHIATRIC/BEHAVIORAL	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (11.1%)
IRRITABILITY	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (11.1%)
PERSONS WITH COMPLAINTS	2 (11.1%)	3 (16.7%)	1 (5.6%)	2 (11.1%)	0 (0.0%)	1 (5.6%)		5 (27.8%)
PERSONS WITH NO COMPLAINTS	16 (88.9%)	15 (83.3%)	17 (94.4%)	16 (88.9%)	18 (100.0%)	17 (94.4%)		13 (72.2%)
PERSONS WITH NO DATA	4 (18.2%)	4 (18.2%)	4 (18.2%)	4 (18.2%)	4 (18.2%)	4 (18.2%)		4 (18.2%)

Table 4 (cont)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

CLINICAL COMPLAINTS	TOTAL VACCINEES (21 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
SYSTEMIC	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		1 (5.0%)
RESPIRATORY	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		1 (5.0%)
UPPER RESPIRATORY INFECT., NOS	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		1 (5.0%)
PERSONS WITH NO COMPLAINTS	19 (95.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)		19 (95.0%)
PERSONS WITH NO DATA	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)	1 (4.8%)		1 (4.8%)

Table 5

PATIENT COUNT MAXIMUM TEMPERATURES

RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (26 PATIENTS) - DOSE 1 DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH MAX TEMP
NORMAL	1 (5.3%)	1 (5.3%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)		1 (5.0%)
< 99	10 (52.6%)	13 (68.4%)	13 (65.0%)	12 (60.0%)	14 (70.0%)	13 (65.0%)		8 (40.0%)
99 - 99.9	6 (31.6%)	4 (21.1%)	3 (15.0%)	5 (25.0%)	4 (20.0%)	4 (20.0%)		7 (35.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (5.0%)		1 (5.0%)
101 - 101.9	2 (10.5%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
102 - 102.9	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
103 - 103.9	0 (0.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
TEMPERATURE TAKEN	19 (73.1%)	19 (73.1%)	20 (76.9%)	20 (76.9%)	20 (76.9%)	20 (76.9%)		20 (76.9%)
TEMPERATURE NOT TAKEN	7 (26.9%)	7 (26.9%)	6 (23.1%)	6 (23.1%)	6 (23.1%)	6 (23.1%)		6 (23.1%)

Table 5 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (26 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (5.6%)	1 (5.6%)	1 (5.9%)	1 (5.6%)	1 (5.9%)	1 (6.3%)			1 (5.6%)
< 99	9 (50.0%)	10 (55.6%)	9 (52.9%)	7 (38.9%)	9 (52.9%)	9 (56.3%)			6 (33.3%)
99 - 99.9	8 (44.4%)	7 (38.9%)	6 (35.3%)	9 (50.0%)	6 (35.3%)	6 (37.5%)			9 (50.0%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	1 (5.9%)	0 (0.0%)			1 (5.6%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)			1 (5.6%)
TEMPERATURE TAKEN	18 (69.2%)	18 (69.2%)	17 (65.4%)	18 (69.2%)	17 (65.4%)	16 (61.5%)			18 (69.2%)
TEMPERATURE NOT TAKEN	8 (30.8%)	8 (30.8%)	9 (34.6%)	8 (30.8%)	9 (34.6%)	10 (38.5%)			8 (30.8%)

Table 5 (cont)
PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK732
DOSE : 1.25 MCG
PATIENT CLASS: HEALTHY CHILDREN

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	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)
< 99	10 (71.4%)	10 (71.4%)	8 (57.1%)	9 (64.3%)	10 (71.4%)	11 (78.6%)			6 (42.9%)
99 - 99.9	4 (28.6%)	4 (28.6%)	4 (28.6%)	5 (35.7%)	4 (28.6%)	3 (21.4%)			7 (50.0%)
102 - 102.9	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (7.1%)
TEMPERATURE TAKEN	14 (56.0%)	14 (56.0%)	14 (56.0%)	14 (56.0%)	14 (56.0%)	14 (56.0%)			14 (56.0%)
TEMPERATURE NOT TAKEN	11 (44.0%)	11 (44.0%)	11 (44.0%)	11 (44.0%)	11 (44.0%)	11 (44.0%)			11 (44.0%)

Table 6

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (32 PATIENTS) - DOSE 1								
	DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	3 (10.0%)	3 (10.3%)	3 (10.0%)	3 (10.0%)	3 (10.3%)	3 (10.0%)			3 (10.0%)
< 99	14 (46.7%)	20 (69.0%)	16 (53.3%)	20 (66.7%)	17 (58.6%)	18 (60.0%)			10 (33.3%)
99 - 99.9	11 (36.7%)	5 (17.2%)	8 (26.7%)	5 (16.7%)	7 (24.1%)	7 (23.3%)			13 (43.3%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (3.3%)	2 (6.7%)	1 (3.4%)	2 (6.7%)			1 (3.3%)
101 - 101.9	2 (6.7%)	1 (3.4%)	2 (6.7%)	0 (0.0%)	1 (3.4%)	0 (0.0%)			3 (10.0%)
TEMPERATURE TAKEN	30 (93.8%)	29 (90.6%)	30 (93.8%)	30 (93.8%)	29 (90.6%)	30 (93.8%)			30 (93.8%)
TEMPERATURE NOT TAKEN	2 (6.3%)	3 (9.4%)	2 (6.3%)	2 (6.3%)	3 (9.4%)	2 (6.3%)			2 (6.3%)

Table 6 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (32 PATIENTS) - DOSE 2								
	DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	5 (20.0%)	5 (20.8%)	5 (20.8%)	5 (20.0%)	5 (20.8%)	5 (20.8%)			5 (19.2%)
< 99	10 (40.0%)	10 (41.7%)	13 (54.2%)	14 (56.0%)	14 (58.3%)	13 (54.2%)			8 (30.8%)
99 - 99.9	7 (28.0%)	8 (33.3%)	6 (25.0%)	6 (24.0%)	4 (16.7%)	5 (20.8%)			10 (38.5%)
100 - 100.9	3 (12.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	1 (4.2%)	1 (4.2%)			3 (11.5%)
TEMPERATURE TAKEN	25 (78.1%)	24 (75.0%)	24 (75.0%)	25 (78.1%)	24 (75.0%)	24 (75.0%)			26 (81.3%)
TEMPERATURE NOT TAKEN	7 (21.9%)	8 (25.0%)	8 (25.0%)	7 (21.9%)	8 (25.0%)	8 (25.0%)			6 (18.8%)

Table 6 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
DOSE : 2.5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (30 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	5 (19.2%)	5 (19.2%)	6 (23.1%)	5 (19.2%)	5 (19.2%)	5 (19.2%)			5 (19.2%)
< 99	9 (34.6%)	14 (53.8%)	13 (50.0%)	13 (50.0%)	16 (61.5%)	16 (61.5%)			4 (15.4%)
99 - 99.9	11 (42.3%)	7 (26.9%)	6 (23.1%)	7 (26.9%)	4 (15.4%)	5 (19.2%)			14 (53.8%)
100 - 100.9	1 (3.8%)	0 (0.0%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	0 (0.0%)			3 (11.5%)
TEMPERATURE TAKEN	26 (86.7%)	26 (86.7%)	26 (86.7%)	26 (86.7%)	26 (86.7%)	26 (86.7%)			26 (86.7%)
TEMPERATURE NOT TAKEN	4 (13.3%)	4 (13.3%)	4 (13.3%)	4 (13.3%)	4 (13.3%)	4 (13.3%)			4 (13.3%)

Table 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (22 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (4.8%)	1 (5.0%)	1 (4.8%)	1 (5.0%)	1 (5.0%)	1 (5.0%)			1 (4.8%)
< 99	9 (42.9%)	11 (55.0%)	11 (52.4%)	11 (55.0%)	12 (60.0%)	10 (50.0%)			5 (23.8%)
99 - 99.9	8 (38.1%)	7 (35.0%)	7 (33.3%)	8 (40.0%)	6 (30.0%)	8 (40.0%)			11 (52.4%)
100 - 100.9	3 (14.3%)	1 (5.0%)	2 (9.5%)	0 (0.0%)	1 (5.0%)	1 (5.0%)			4 (19.0%)
TEMPERATURE TAKEN	21 (95.5%)	20 (90.9%)	21 (95.5%)	20 (90.9%)	20 (90.9%)	20 (90.9%)			21 (95.5%)
TEMPERATURE NOT TAKEN	1 (4.5%)	2 (9.1%)	1 (4.5%)	2 (9.1%)	2 (9.1%)	2 (9.1%)			1 (4.5%)

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (22 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	3 (18.8%)	3 (18.8%)	3 (20.0%)	3 (18.8%)	3 (18.8%)	3 (21.4%)			3 (18.8%)
< 99	7 (43.8%)	8 (50.0%)	8 (53.3%)	9 (56.3%)	9 (56.3%)	8 (57.1%)			5 (31.3%)
99 - 99.9	5 (31.3%)	4 (25.0%)	3 (20.0%)	3 (18.8%)	3 (18.8%)	3 (21.4%)			7 (43.8%)
100 - 100.9	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.3%)	1 (6.3%)	0 (0.0%)			0 (0.0%)
101 - 101.9	1 (6.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (6.3%)
TEMPERATURE TAKEN	16 (72.7%)	16 (72.7%)	15 (68.2%)	16 (72.7%)	16 (72.7%)	14 (63.6%)			16 (72.7%)
TEMPERATURE NOT TAKEN	6 (27.3%)	6 (27.3%)	7 (31.8%)	6 (27.3%)	6 (27.3%)	8 (36.4%)			6 (27.3%)

Table 7 (cont)

PATIENT COUNT MAXIMUM TEMPERATURES

RECOMBINANT HEPATITIS B VACCINE

STUDY : 0809
TREATMENT :
LOT NUMBER : CK444
DOSE : 5 MCG
PATIENT CLASS: HEALTHY CHILDREN

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (21 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	4 (22.2%)	4 (22.2%)	4 (22.2%)	4 (22.2%)	4 (22.2%)	4 (22.2%)			4 (22.2%)
< 99	4 (22.2%)	9 (50.0%)	11 (61.1%)	10 (55.6%)	11 (61.1%)	11 (61.1%)			2 (11.1%)
99 - 99.9	8 (44.4%)	4 (22.2%)	3 (16.7%)	4 (22.2%)	3 (16.7%)	3 (16.7%)			10 (55.6%)
100 - 100.9	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.6%)
101 - 101.9	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.6%)
TEMPERATURE TAKEN	18 (85.7%)	18 (85.7%)	18 (85.7%)	18 (85.7%)	18 (85.7%)	18 (85.7%)			18 (85.7%)
TEMPERATURE NOT TAKEN	3 (14.3%)	3 (14.3%)	3 (14.3%)	3 (14.3%)	3 (14.3%)	3 (14.3%)			3 (14.3%)

PROGRAM:	Yeast Recombinant Hepatitis B Vaccine, Study 865
PURPOSE:	To evaluate antibody and clinical responses to two or three 5 mcg doses of vaccine among healthy infants and children, ages 3 months through 11 years, who are seronegative for hepatitis B markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot # 985/C-K732 (5 mcg/ml)
PRIMARY INVESTIGATOR:	Prof. E. K. Yeoh, M.D. Consultant Physician Medical A Unit Queen Elizabeth Hospital Wylie Road Kowloon, Hong Kong
SECONDARY INVESTIGATOR:	W. K. Chang, M.P., B.S., F.R.C. Path. Consultant Microbiologist Queen Mary Hospital Pokfulam Road Hong Kong Ching Lung Lai, M.B., M.R.C.P., F.R.C.P. Consultant Physician Queen Mary Hospital Pokfulam Road Hong Kong
STUDY LOCATION:	Queen Elizabeth Hospital Wylie Road Kowloon, Hong Kong Queen Mary Hospital Pokfulam Road Hong Kong
DATE INITIATED:	2/1/85
DATE COMPLETED:	In progress
STUDY POPULATION:	The study population will consist of 100-200 infants and children, ages 3 months through 11 years, who are negative for hepatitis B serologic markers and have not previously received any hepatitis B vaccine.

Study 865

PROCEDURE:

Participants are randomly assigned to one of 2 groups with 50-100 children or infants in each group. Group one receives intramuscular injections of vaccine at 0 and 1 month (5 mcg doses). Participants in group 2 receive their injections at 0, 1 and 6 months. The parent or guardian is asked to record the child's temperature for 5 days after each injection and note any local or systemic complaints.

Blood samples are obtained prior to vaccination and at 1, 3, 6, 8, 12 and 24 months post initial injection. All samples are assayed for HBsAg, anti-HBs, anti-HBc and ALT by Dr. Yeoh. Some samples may be tested for yeast antibody at MSDRL. Samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested to determine anti-a and anti-d activity.

RESULTS:

HEALTHY INFANTS AND CHILDREN:

5 mcg Lot #985/C-K732 at 0 and 1 month
5 mcg Lot #985/C-K732 at 0, 1, and 6 months

1. Number Vaccinated:

Group #	Dose Level	Injection No. 1	2	3
1	5 mcg	90	70	-
2	5 mcg	88	72	46

2. Serologic Results:

Serologic data at 6 months are available for 24 participants in the two injection regimen. At that time 98% (49/50) of the children seroconverted (S/N $\geq$2.1) for anti-HBs and 94% (47/50) developed protective levels of antibody (mIU/ml $\geq$10). Among the 21 participants for whom 8 month serologic data are available in the three injection regimen, 100% (21/21) seroconverted and developed protective levels of antibody (mIU/ml $\geq$10).

A large boost in titer was seen among those children who received the third injection. Geometric mean titers at 8 months were 1894.8

Study 865

RESULTS (CONT.)

mIU/ml and 84.50 mIU/ml for those in the three and two injection groups, respectively. Table 1 lists seroconversion rates and GMTs for one to three months of follow-up.

3. Clinical Complaints:

Clinical follow-up data are available for 142, 117 and 25 participants following injections one, two and three, respectively.

Type of Complaint	Frequency in % by Injection		
Injection Site	2 (3/141)	2 (2/116)	0 (0/25)
Systemic	6 (8/141)	4 (5/116)	4 (1/25)

There have been no serious or alarming adverse experiences attributable to the vaccine.

Table 1

Antibody Responses Among Healthy Children and Infants Following Vaccination with
5 mcg Injections of Yeast Recombinant Hepatitis B Vaccine
Lot #985/C-K732 at 0, 1, and 6 Months or 0 and 1 Month in Study 865

	Group 1 0 and 1 Month					Group 2 0, 1 and 6 Months				
Time (Months)	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10	S/N ≥ 2.1	mIU/ml ≥ 10	All Vaccinees	S/N ≥ 2.1	mIU/ml ≥ 10
1	33(23/70)	11(8/70)	0.8	8.6	21.9	40(29/72)	15(11/72)	1.1	9.1	29.7
3	97(57/59)	83(49/59)	52.9	63.5	93.7	91(53/58)	79(46/58)	37.7	63.4	88.6
6	98(49/50)	94(47/50	81.6	91.5	102.5	98(45/46)	76(35/46)	42.1	58.9	93.7
8	96(23/24)	88(21/24)	84.5	107.9	144.9	100(21/21)	100(21/21)	1894.8	1894.8	1894.8

23921/3
1/18/86

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 891
PURPOSE:	To compare the antibody and clinical responses to recombinant hepatitis B vaccine and plasma-derived hepatitis B vaccine among healthy adults and children who are negative for hepatitis B virus serologic markers.
VACCINES:	1. Yeast Recombinant Hepatitis B Vaccine Lot 979/C-K564 (10 mcg HBsAg/ml) 2. Plasma-Derived Hepatitis B Vaccine Lot 0027L (20 mcg HBsAg/ml)
PRIMARY INVESTIGATOR:	Dr. Hu Zong-Han Department of Biological Products Inspection Bureau of Pharmaceutical and Biological Inspection Ministry of Health Temple of Heaven, West Gate Beijing, People's Republic of China
SECONDARY INVESTIGATOR:	Dr. Shi Guiyong Director of Epidemic Department Chinese Medical University Shen Yang, People's Republic of China
STUDY LOCATION:	Shen Yang Municipal Anti-Epidemic Station Shen Yang, People's Republic of China
DATE STUDY INITIATED:	December, 1985
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of 200 healthy adults and 200 healthy children of either sex (exluding pregnant women), who are negative for HBsAg, anti-HBc and HBs, have a normal ALT level and have not previously received any hepatitis B vaccine.

Study 891

STUDY PROCEDURE: Participants are grouped by age and randomly assigned to receive the yeast recombinant or plasma-derived hepatitis B vaccine as follows:

Group	Population	Vaccine	Dose	Number	Regimen
1	Adults (≥30 years)	Recombinant	10 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
2	Adults (18–29 years)		10 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
3	Children (5–10 years)		5 mcg	100	0.5 ml intramuscular injection of vaccine at 0, 1, and 6 months
4	Adults (≥30 years)	Plasma	20 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
5	Adults (18–29 years)		20 mcg	50	1.0 ml intramuscular injection of vaccine at 0, 1, and 6 months
6	Children (5–10 years)		10 mcg	100	0.5 ml intramuscular injection of vaccine at 0, 1, and 6 months

Study participants or the participant's parent or guardian record their temperature or that of their child, 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 to three weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 3, 6, 7, 8, 9, 12, and 24 months. All serum samples are assayed for HBsAg, anti-HBc, anti-HBs, and ALT.

Study 891

RESULTS: (Contd) To date 100 adults and children have received one injection of yeast recombinant or plasma-derived hepatitis B vaccine. No serious or alarming reactions attributable to vaccination have been reported. Clinical follow-up data and serologic results are not yet available. The study continues in progress.

DIALYSIS/PRE-DIALYSIS

SUMMARY - DIALYSIS AND PREDIALYSIS PATIENTS

To date, 288 patients with chronic renal insufficiency, including 210 patients who are receiving dialysis treatments (dialysis patients) and 78 patients who are not yet receiving such treatments (predialysis patients), have received one or more injections of the yeast recombinant vaccine.

Predialysis patients receive an injection of the yeast recombinant hepatitis B vaccine (10, 20, or 40 mcg dose) at 0, 1, and 6 months. Dialysis patients receive an injection of the vaccine (20, 40, or 100 mcg dose) either at 0, 1, and 6 months or according to a more intensified regimen (20 or 40 mcg dose) at 0, 1, 2, 3, 4 and 5 months. In four of the studies, patients received the vaccine as an intramuscular injection in the deltoid. However, in one study (Study 838), vaccine was administered in the buttock.

Post-vaccination clinical data are available on 135 dialysis and 49 predialysis patients following the third injection of vaccine, and for 33 dialysis patients following a sixth injection. Serologic data following the last injection of vaccine are available for 50 predialysis patients and 84 dialysis patients who received three injections of vaccine and 32 dialysis patients on the six injection regimen.

IMMUNOGENICITY

Predialysis Patients

Deltoid Injection: At 7-8 months 15% (10 mcg dose), 68% (20 mcg dose) and 67% (40 mcg dose) of predialysis patients who received three injections of vaccine in the deltoid had an anti-HBs titer of S/N $\geq$2.1. Protective levels of antibody (S/N or mIU/ml $\geq$10) were induced in 15% (10 mcg dose), 58% (20 mcg dose), and 61% (40 mcg dose) of vaccine recipients. Among patients with a minimum titer of S/N $\geq$2.1, and for whom titers are currently available in units of mIU/ml, the geometric mean titers were 67.7 mIU/ml (10 mcg dose), 213.7 mIU/ml (20 mcg dose), and 120.9 mIU/ml (40 mcg dose) at this time. For responders with titers of at least 10 mIU/ml, the geometric mean titers were 67.7 mIU/ml (10 mcg dose), 120.9 mIU/ml (20 mg dose) and 186.4 mIU/ml (40 mcg dose). By 12 months titers had declined with 0% (10 mcg dose), 50% (20 mcg dose), and 40% (40 mcg dose) still retaining titers of S/N or mIU/ml $\geq$10 (Table 1).

Buttock Injection: One month after the first injection of vaccine, 13% of predialysis patients receiving a 10 mcg dose in the buttock have detectable antibody (S/N $\geq$2.1) with a geometric mean titer among responders of 4.6 mIU/ml. None had achieved a titer of mIU/ml $\geq$10 (Table 1).

Dialysis Patients

Deltoid Injection: At 7/8 months, among dialysis patients who had completed the standard three injection regimen in the deltoid, 59% (20 mcg dose) and 94%

(40 mcg dose) had an anti-HBs titer of S/N ≥2.1, while 48% (20 mcg dose) and 88% (40 mcg dose) achieved protective levels of antibody (mIU/ml ≥10). The geometric mean titers at 7-8 months for patients with anti-HBs ≥2.1 S/N was 69.1 mIU/ml (20 mcg dose) and 331.8 mIU/ml (40 mcg dose), while for responders with a titer of mIU/ml ≥10 the GMTs were 118.6 mIU/ml (20 mcg dose) and 445.5 mIU/ml (40 mcg dose) (Table 2). Forty mcg doses of vaccine produced significantly higher seroconversion rates (S/N ≥2.1 and mIU/ml ≥10) and levels of response (GMT of all vaccinees) at 3, 6, and 7-8 months (See Appendix 1 for statistical methods). By 12 months antibody levels had declined with 41% (20 mcg dose) and 71% (40 mcg dose) still retaining titers of mIU/ml ≥10. Geometric mean titers of responders with protective levels of antibody decreased to 79.9 mIU/ml (20 mcg dose) and 165.6 mIU/ml (40 mcg dose).

At 3 months (2 months after the second injection) 68% of dialysis patients receiving 100 mcg doses of vaccine in the deltoid seroconverted (S/N ≥2.1), with 25% developing protective levels of antibody (mIU/ml ≥10). The GMT of responders with antibody levels of S/N ≥2.1 was 8.4 mIU/ml at this time, while among responders with titers of mIU/ml ≥10 the GMT was 33.3 mIU/ml (Table 2). This study is still in progress and serologic results are not yet available after the third dose of vaccine.

Buttock Injection: At 7-8 months 64% of dialysis patients who received 40 mcg doses of vaccine in the buttock at 0, 1, and 6 months had an anti-HBs titer of S/N ≥2.1, while 58% achieved a protective titer of mIU/ml ≥10. By 10 months, 65% still retained titers of S/N ≥2.1, although the proportion with titers of mIU/ml ≥10 had declined slightly to 54%. At 7/8 months the geometric mean titers of responders with titers of S/N ≥2.1 was 90.2 mIU/ml, while responders with titers of mIU/ml ≥10 had a GMT of 115.5 mIU/ml. The GMT of responders with protective levels of antibody remained fairly constant through 10 months (Table 3).

Among dialysis patients administered vaccine in the buttock at 0, 1, 2, 3, 4, and 5 months, 56% (20 mcg dose) and 69% (40 mcg dose) seroconverted (S/N ≥2.1) at 6 months, with 44% (20 mcg dose) and 69% (40 mcg dose) achieving a protective titer of mIU/ml ≥10 (Table 3). There were no significant differences found in these seroconversion rates by dose level at either cutoff. At 10 months, 50% (20 mcg dose) and 67% (40 mcg dose) retained an anti-HBs titer of S/N ≥2.1, while 44% (20 mcg dose) and 50% still retained titers of mIU/ml ≥10. Responders with S/N ≥2.1 had a geometric mean titer of 87.3 mIU/ml (20 mcg dose) and 189.8 mIU/ml (40 mcg dose) at 6 months. Responders with mIU/ml ≥10 had GMTs of 190 mIU/ml for both the 20 and 40 mcg doses at this time. Through six months, levels of response (all vaccinees) were not shown to increase significantly with log dose level. By 10 months the geometric mean titers among patients with protective levels of antibody declined to 55 mIU/ml (20 mcg) and 27.7 mIU/ml (40 mcg).

When seroconversion rates and titers among dialysis patients who received three 40 mcg doses of vaccine in the buttock are compared to those who received six 40 mcg doses of vaccine in the buttock, the two regimens were not shown to be significantly different one month after the last injection of vaccine. (The statistical analysis included two subjects with 9 month data instead of 7/8 month data in addition to those subjects summarized above at 7/8 months).

SAFETY

The vaccine has been very well tolerated in predialysis and dialysis patients. No serious reactions attributable to vaccination have been reported. Most importantly none has occurred to date among individuals who have received at least two 100 mcg doses or as many as six 40 mcg doses of vaccine.

Predialysis Patients

Among predialysis patients, mild transient injection site reactions and systemic complaints were reported following injection of vaccine at frequencies of 6% and 8%, respectively (Table 4). The frequency of complaints after the first injection was higher than after the second or third injections. The most frequent injection site reaction was soreness (6%) (Table 7). The most frequent specific systemic complaints were nausea (3%), symptoms of upper respiratory infection (2%), chills (1%), and headache (1%) (Table 8). A temperature $\geq$100°F oral was reported following 8% of all injections (Table 4).

Dialysis Patients

The incidences of local (injection site) complaints, of systemic complaints, of either local or systemic complaints, and of fever (oral temperature of 100°F or more) were analyzed statistically to evaluate the safety of the vaccine in dialysis patients (See Appendix 1 for statistical methods). The incidence at each injection was defined as the number of subjects with the complaint at any time during the five-day period following vaccination divided by the number reporting, while the total was the sum of complaints following the three or six injections divided by the number of injections with follow-up.

Mild transient injection site reactions and systemic complaints were reported in dialysis patients following injection of vaccine at frequencies of 3% and 7%, respectively (Tables 5, 6).

Among those dialysis patients who received three injections of 20, 40, or 100 mcg administered in the deltoid or the buttock (Studies 816, 825, 838), local complaints increased significantly with log dose level at the second injection while systemic complaints decreased with dose level at the first injection. The most frequent injection site reaction was soreness (3%) (Tables 9, 11), and the most common systemic complaint was fatigue (2%) (Tables 10, 11). A temperature of $\geq$100°F (oral) was reported following 4% of all injections (Table 5). The rate of complaints appeared to be highest after the first injection and lowest after the second injection.

Among dialysis patients who received six injections of 20 or 40 mcg of vaccine administered in the buttock, complaints were not shown to be a function of log dose level . Very few complaints were reported at either dose level. No trend was found in incidence of complaints over the six injections for either dose level. A single individual reported an injection site reaction (pruritis) (Table 12), while systemic complaints occurring at

frequencies ≥1% included fatigue/weakness (5%), nausea (2%), headache (1%) and arthralgia (1%) (Table 13). A temperature of ≥100°F (oral) was reported following 4% of all injections (Table 8).

The three and six injection regimens in dialysis patients who received 20 or 40 mcg doses of vaccine in the deltoid or buttock were compared at each of the first three injections to determine if monthly injections caused greater or fewer complaints than those spaced further apart. The only significant difference found was in the incidence of systemic complaints after the second injection in dialysis patients who received 40 mcg doses of vaccine. Ten percent (2/20) of dialysis patients on the six injection regimen had a systemic complaint versus 0% (0/83) on the three injection regimen.

Although significant differences in complaint frequencies were found over dose levels, they were not of clinical consequence. The incidence of any clinical complaint was low.

SUMMARY

Predialysis and dialysis patients did not respond to the vaccine as well as healthy adults. The response rate and level of anti-HBs attained after three injections of vaccine does increase with dose level, and it would appear that responses are better if vaccine is administered in the deltoid rather than the buttock. Preliminary data suggest that 100 mcg doses of vaccine may induce antibody earlier than lower doses. Patients vaccinated under an intensified six injection regimen did not respond better than those receiving three injections of vaccine.

Table 1

Antibody Responses Among Initially Seronegative Predialysis Patients Who Received
Yeast Recombinant Hepatitis B Vaccine (Three Injection Regimen)

Studies: 789, 811

	DELTOID INJECTION															BUTTOCK INJECTION				
	3 x 10 mcg					3 x 20 mcg					3 x 40 mcg					3 x 10 mcg				
	% Seroconversion		GMT (mIU/ml)			% Seroconversion		GMT (mIU/ml) **			% Seroconversion		GMT (mIU/ml) **			% Seroconversion		GMT (mIU/ml)		
				Responders			S/N or		Responders			S/N or		Responders						Responders	
Time (Mos.)	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10 *	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10 *	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	0 (0/14)	0 (0/14)	0.3	---	---	0 (0/28)	0 (0/28)	0.3 (14)	--	--	4 (1/28)	0 (0/28)	0.3 (13)	--	--	13 (1/8)	0 (0/8)	0.7	4.6	---
3	0 (0/14)	0 (0/14)	0.3	---	---	22 (6/27)	7 (2/27)	0.5 (14)	90.0	90.0	23 (6/26)	12 (3/26)	0.3 (12)	--	--					
6	0 (0/13)	0 (0/13)	0.3	---		38 (8/21)	29 (6/21)	1.0 (14)	23.6	23.6	42 (8/19)	26 (5/19)	1.7 (12)	19.4	19.4					
7/8	15 (2/13)	15 (2/13)	0.7	67.7	67.7	68 (13/19)	58 (11/19)	13.8 (12)	213.7	213.7	67 (12/18)	61 (11/18)	23.6 (11)	120.9	186.4					
12	8 (1/12)	0 (0/12)	0.4	6.0	---	71 (10/14)	50 (7/14)	8.5 (10)	78.5	78.5	40 (4/10)	40 (4/10)	3.3 (10)	117.3	117.3					

* Serologic results obtained in Study 789 reported in S/N only.
** GMTs summarized obtained in Study 811 only. (N)

31251/1
1/22/86

Table 2

Antibody Responses Among Initially Seronegative Dialysis Patients
Who Received Yeast Recombinant Hepatitis B Vaccine In the Deltoid (Three Injection Regimen)

Studies: 816, 825

Time (Mos.)	3 x 20 mcg					3 x 40 mcg					3 x 100 mcg				
	% Seroconversion		GMT (mIU/ml)			% Seroconversion		GMT (mIU/ml)			% Seroconversion		GMT (S/N)		
				Responders					Responders					Responders	
	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	8 (2/26)	4 (1/26)	0.4	5.4	18.5	15 (4/26)	8 (2/26)	0.6	8.1	17.9	13 (5/38)	0 (0/38)	1.3	3.0	---
3	21 (5/24)	4 (1/24)	0.6	6.5	76.1	52 (13/25)	28 (7/25)	2.3	15.0	32.9	68 (19/28)	25 (7/28)	4.4	8.4	33.3
6	33 (8/24)	13 (3/24)	1.0	6.4	21.7	81 (13/16)	63 (10/16)	10.8	21.5	35.2					
7/8	59 (17/29)	48 (14/29)	7.8	69.1	118.6	94 (16/17)	88 (15/17)	219.7	331.8	445.5					
12	52 (15/29)	41 (12/29)	5.1	49.2	79.9	81 (17/21)	71 (15/21)	41.6	107.9	165.6					

66900

Table 3

Antibody Responses Among Initially Seronegative Dialysis Patients Who Received
Yeast Recombinant Hepatitis B Vaccine In The Buttock

Study 838

Time (Mos.)	3 x 40 mcg					6 x 40 mcg					6 x 20 mcg				
	% Seroconversion		GMT (mIU/ml)**			% Seroconversion		GMT (mIU/ml)**			% Seroconversion		GMT (mIU/ml)**		
				Responders					Responders					Responders	
	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	0 (0/48)	0 (0/48)	0.3	---	---	0 (0/20)	0 (0/20)	0.3	---	---	0 (0/20)	0 (0/20)	0.3	---	---
3	35 (16/46)	22 (10/46)	1.3	16.5	31.0	35 (7/20)	20 (4/20)	1.2	17.4	33.5	32 (6/19)	26 (5/19)	1.2	23.6	31.4
6	34 (12/35)	29 (10/35)	1.4	26.1	33.8	69 (11/16)	69 (11/16)	32.2	189.8	189.8	56 (9/16)	44 (7/16)	9.7	87.3	190.0
7/8	64 (23/36)	58 (21/36)	12.3	90.2	115.5										
10	65 (24/37)	54 (20/37)	12.8	73.8	117.6	67 (10/15)	60 (9/15)	6.7	24.5	27.7	50 (9/18)	44 (8/18)	4.7	45.0	55.0

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Table 4

Percent of Predialysis Patients With Clinical Complaints*
During a Five-Day Period Following Vaccination With
Yeast Recombinant Hepatitis B Vaccine (Three Injection Regimen)

Studies: 789, 811

10 mcg Dose - Deltoid Injection

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	0 (0/14)	0 (0/14)	0 (0/12)	0 (0/40)
Systemic	0 (0/14)	0 (0/14)	8 (1/12)	3 (1/40)
Any Local or Systemic Complaint	0 (0/14)	0 (0/14)	8 (1/12)	3 (1/40)
Temperature ≥100°F Oral	7 (0/14)	0 (0/13)	0 (0/11)	3 (1/38)

20 mcg Dose - Deltoid Injection

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	18 (5/28)	11 (3/28)	5 (1/20)	12 (9/76)
Systemic	18 (5/28)	14 (4/28)	10 (2/20)	15 (11/76)
Any Local or Systemic Complaint	29 (8/28)	21 (6/28)	15 (3/20)	22 (17/76)
Temperature ≥100°F Oral	7 (2/27)	12 (3/26)	10 (2/20)	10 (7/73)

40 mcg Dose - Deltoid Injection

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	7 (2/27)	4 (1/26)	0 (0/17)	4 (3/70)
Systemic	4 (1/27)	8 (2/26)	6 (1/17)	6 (4/70)
Any Local or Systemic Complaint	11 (3/27)	8 (2/26)	6 (1/17)	9 (6/70)
Temperature ≥100°F Oral	7 (2/27)	8 (2/26)	18 (3/17)	10 (7/70)

40 mcg Dose - Buttock Injection

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	0 (0/8)	Data	Data	0 (0/8)
Systemic	0 (0/8)	not	not	0 (0/8)
Any Local or Systemic Complaint	0 (0/8)	available	available	0 (0/8)
Temperature ≥100°F Oral	0 (0/8)			0 (0/8)

*A complaint is recorded here if it occurred during any fraction of the five-day period following vaccination.

31091/2
1/10/86

Table 5

Percent of Dialysis Patients with Clinical Complaints*
During a Five-Day Period Following Vaccination With
Yeast Recombinant Hepatitis B Vaccine In The Deltoid
(Three Injection Regimen)

Studies: 816, 825

20 mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	8 (3/38)	0 (0/34)	0 (0/33)	3 (3/105)
Systemic	24 (9/38)	3 (1/34)	12 (4/33)	13 (14/105)
Any Local or Systemic Complaint	29 (11/38)	3 (1/34)	12 (4/33)	15 (16/105)
Temperature ≥100°F Oral	5 (2/37)	0 (0/34)	9 (3/32)	5 (5/103)

40 mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	11 (4/36)	3 (1/34)	0 (0/24)	5 (5/94)
Systemic	22 (8/36)	0 (0/34)	8 (2/24)	11 (10/94)
Any Local or Systemic Complaint	25 (9/36)	3 (1/34)	8 (2/24)	13 (12/94)
Temperature ≥100°F Oral	11 (4/36)	3 (1/33)	0 (0/24)	5 (5/94)

100 mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	9 (4/44)	8 (3/39)	Data	8 (7/83)
Systemic	7 (3/44)	0 (0/39)	Not	4 (3/83)
Any Local or Systemic Complaint	16 (7/44)	8 (3/39)	Available	12 (10/83)
Temperature ≥100°F Oral	7 (3/43)	3 (1/39)		5 (4/82)

* A complaint is recorded here if it occurred during any fraction of the five-day period following vaccination.

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1/2/86

Table 6

Percent of Dialysis Patients with Clinical Complaints*
During a Five-Day Period Following Vaccination
with Yeast Recombinant Hepatitis B Vaccine In The Buttock

Study 838

3 x 40 mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	All
Injection Site	0 (0/51)	0 (0/49)	0 (0/38)	0 (0/138)
Systemic	8 (4/51)	0 (0/49)	3 (1/38)	4 (5/138)
Any Local or Systemic Complaint	8 (4/51)	0 (0/49)	3 (1/38)	4 (5/138)
Temperature ≥100°F Oral	4 (2/51)	0 (0/48)	3 (1/38)	2 (3/137)

6 x 40 mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	ALL
Injection Site	0 (0/20)	0 (0/20)	0 (0/20)	0 (0/19)	0 (0/19)	0 (0/16)	0 (0/114)
Systemic	15 (3/20)	10 (2/20)	15 (3/20)	16 (3/19)	0 (0/19)	0 (0/16)	10 (11/114)
Any Local or Systemic Complaint	15 (3/20)	10 (2/20)	15 (3/20)	16 (3/19)	0 (0/19)	0 (0/16)	10 (11/114)
Temperature ≥ 100°F Oral**	10 (2/20)	5 (1/19)	5 (1/19)	0 (0/18)	6 (1/18)	7 (1/15)	6 (6/109)

6 x 20 Mcg Dose

Type of Complaint	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	ALL
Injection Site	0 (0/20)	0 (0/20)	5 (1/20)	0 (0/20)	0 (0/20)	0 (0/17)	0.9 (1/117)
Systemic	5 (1/20)	10 (2/20)	5 (1/20)	5 (1/20)	0 (0/20)	0 (0/17)	4 (5/117)
Any Local or Systemic Complaint	5 (1/20)	10 (2/20)	10 (2/20)	5 (1/20)	0 (0/20)	0 (0/17)	5 (6/117)
Temperature ≥100°F Oral	6 (1/18)	0 (0/19)	0 (0/20)	5 (1/20)	0 (0/20)	0 (0/16)	2 (2/113)

*A complaint is recorded here if it occurred during any fraction of the five-day period following vaccination.
**Fever was reported in one vaccine recipient (temperature not recorded)

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Table 7

Frequency of Local and Systemic Complaints
Among Predialysis Patients During a
Five-Day Period Following 186 Deltoid Injections of
Yeast Recombinant Hepatitis B Vaccine
(Three Injection Regimen)

Studies: 789, 811

Number of Vaccine Recipients: 69

Body System/ Complaint	% Frequency (Number)
Local/Injection Site	6 (11)
Soreness	6 (11)
Stiffness/Tightness	2 (3)
Ecchymosis	0.5 (1)
Pain	0.5 (1)
Swelling	0.5 (1)
Whole Body/General	3 (5)
Chills	1 (2)
Headache	1 (2)
Fatigue/Weakness	0.5 (1)
Sensation of Warmth General	0.5 (1)
Illness, Nos	0.5 (1)
Digestive	3 (5)
Nausea	3 (5)
Vomiting	0.5 (1)
Abdominal Tenderness	0.5 (1)
Respiratory	2 (4)
Upper Respiratory Infection, Nos.	2 (3)
Pharyngitis	0.5 (1)
Musculoskeletal	1 (2)
Arthralgia, Other	0.5 (1)
Shoulder Pain	0.5 (1)
Knee Pain	0.5 (1)
Psychiatric/Behavioral	1 (2)
Depression	1 (2)
Nervous System	0.5 (1)
Somnolence	0.5 (1)

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Table 8

Percent (Number) of Predialysis Patients With
Specific Systemic Complaints During a Five-Day Period Following
186 Deltoid Injections of Yeast Recombinant Hepatitis B Vaccine
(Three Injection Regimen)

Studies: 789, 811

Number of Vaccine Recipients: 69

Complaint Frequency 1-3%		
Nausea	3	(5)
Upper Respiratory Infection, Nos	2	(3)
Chills	1	(2)
Depression	1	(2)
Headache	1	(2)

Complaint Frequency <1%		
Abdominal Tenderness	0.5	(1)
Illness, Nos	0.5	(1)
Knee Pain	0.5	(1)
Pharyngitis (Sore Throat)	0.5	(1)
Shoulder Pain	0.5	(1)
Somnolence	0.5	(1)
Fatigue/Weakness	0.5	(1)
Arthralgia	0.5	(1)
Sensation of Warmth, General	0.5	(1)
Vomiting	0.5	(1)

Table 9

Frequency of Local and Systemic Complaints
Among Dialysis Patients During a Five-Day Period Following
341 Injections (Deltoid or Buttock) of Yeast Recombinant Hepatitis B Vaccine
(Three Injection Regimen)

Studies: 816, 838

Number of Vaccine Recipients: 127

Body System/ Complaint	% Frequency (Number)
Local/Injection Site	3 (10)
Soreness	2 (7)
Ecchymosis	0.5 (2)
Pain	0.5 (2)
Stiffness/Tightness	0.5 (2)
Whole Body/General	5 (17)
Fatigue/Weakness	2 (6)
Headache	1 (5)
Chills	1 (4)
Sensation of warmth, General	0.5 (2)
Lightheaded	0.5 (2)
Illness, Nos	0.2 (1)
Malaise	0.2 (1)
Digestive	1 (5)
Nausea	0.8 (3)
Vomiting	0.5 (2)
Increased Appetite	0.2 (1)
Diarrhea	0.2 (1)
Respiratory	0.8 (3)
Pharyngitis	0.2 (1)
Upper Respiratory Infection, Nos	0.2 (1)
Bronchitis, Nos	0.2 (1)
Musculoskeletal	1 (4)
Arthralgia, Other	0.2 (1)
Arthralgia, Mono-articular	0.2 (1)
Arthritis	0.2 (1)
Arm Pain	0.2 (1)
Hand Cramps	0.2 (1)
Muscle Cramps	0.2 (1)
Nervous System	0.8 (3)
Dizziness	0.5 (2)
Tremor	0.2 (1)
Infections Syndromes	0.2 (1)
Influenza, Nos	0.2 (1)
Psychiatric/Behavioral	0.2 (1)
Insomnia/Disturbed	0.2 (T)
Cardiovascular	0.5 (2)
Hypertension	0.2 (1)
Other	0.2 (1)

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Table 10

Percent (Number) of Dialysis Patients With
Specific Systemic Complaints During a Five-Day Period Following
341 Injections (Deltoid or Buttock) of Yeast Recombinant Hepatitis B Vaccine
(Three Injection Regimen)

Studies: 816, 838

Number of Vaccine Recipients: 127

Complaint Frequency 1-2%		
Fatigue/Weakness	2	(6)
Headache	1	(5)
Chills	1	(4)

Complaint Frequency <1% (Number)	
Nausea	0.8 (3)
Lightheaded	0.5 (2)
Sensation of Warmth, General	0.5 (2)
Dizziness	0.5 (2)
Vomiting	0.5 (2)
Appetite Increased	0.2 (1)
Arm Pain	0.2 (1)
Arthralgia, Other	0.2 (1)
Arthralgia, Monoarticular	0.2 (1)
Arthritis, Other	0.2 (1)
Bronchitis	0.2 (1)
Diarrhea	0.2 (1)
Hand Cramps	0.2 (1)
Hypertension	0.2 (1)
Illness, Nos	0.2 (1)
Influenza, Nos	0.2 (1)
Insomnia/Disturbed Sleep	0.2 (1)
Malaise	0.2 (1)
Muscle Cramps	0.2 (1)
Pharyngitis (Sore Throat)	0.2 (1)
Tremor	0.2 (1)
Upper Respiratory Infection, Nos	0.2 (1)
Other	0.2 (1)

Table 11

Frequency of Local and Systemic Complaints
Among Dialysis Patients During a Five-Day Period
Following 83 Deltoid Injections of Yeast Recombinant Hepatitis B Vaccine
Containing 100 mcg HBsAg (Three Injection Regimen)

Study 825

Number of Vaccine Recipients: 44

Body System/Complaint	% Frequency (Number)
Local/Injection Site	8 (7)
Soreness	7 (6)
Erythema	1 (1)
Inflammation	1 (1)
Pruritis	1 (1)
Stiffness/Tightness	1 (2)
Whole Body/General	2 (2)
Fatigue/Weakness	1 (1)
Other	1 (1)
Respiratory	1 (1)
Pharyngitis	1 (1)
Cough	1 (1)
Musculoskeletal	1 (1)
Arthralgia, Other	1 (1)

Table 12

Frequency of Local and Systemic Complaints Among Dialysis Patients During a Five-Day Period Following 231 Buttock Injections of Yeast Recombinant Hepatitis B Vaccine (Six Injection Regimen)

Study 838

Number of Vaccine Recipients: 40

Body System/ Complaint	% Frequency (Number)
Local/Injection Site	0.4 (1)
Pruritis	0.4 (1)
Whole Body/General	6 (15)
Fatigue/Weakness	5 (11)
Headache	1 (3)
Illness, Nos	0.4 (1)
Lightheaded	0.4 (1)
Chills	0.4 (1)
Digestive	3 (8)
Nausea	2 (4)
Diarrhea	0.8 (2)
Abdominal Pains/ Cramps	0.4 (1)
Diminished Appetite	0.4 (1)
Respiratory	0.4 (1)
Cough	0.4 (1)
Musculoskeletal	1 (3)
Arthralgia, Other	1 (3)
Psychiatric/Behavioral	0.4 (1)
Depression	0.4 (1)
Cardiovascular	0.8 (2)
Hypotension	0.4 (1)
Other	0.4 (1)

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APPENDIX 1

STATISTICAL METHODS

All tests of significance were two-sided at 0.05 significance level.

A. Clinical Complaints

1. The incidence of the various clinical complaints in dialysis patients on the three dose regimen, healthy teenagers and healthy children were evaluated as a function of log dose level using the Mantel-Haenszel Test[1] for trend.

2. All other differences in the incidences of the various clinical complaints in dialysis patients due to dose level or regimen and in health care personnel receiving vaccine from consistency lots were assessed by the Likelihood Ratio Chi-Square.

B. Seroconversion Rates

1. The effect of dose level on seroconversion rates in healthy adults, healthy teenagers and healthy children was analyzed over studies using the Mantel Haenszel Test[1] for trend.

2. Differences in seroconversion rates in healthy adults due to age or sex were evaluated over studies using the Mantel Haenszel Test[1] for heterogeneity.

3. Differences in seroconversion rates due to age in healthy children, dose level in dialysis patients, and vaccine lot in health care personnel were assessed by the Likelihood Ratio Chi-Square.

C. Level of Response (Titers)

The effect of age, sex, lot (consistency lots only in Study 880), or dose level (all other studies) in health care personnel and other healthy adults, of dose level in healthy teenagers, of dose level and age in healthy children, and of dose level and regimen in dialysis patients were analyzed by fitting these variables to a regression model. Subjects who were negative for antibody to hepatitis B surface antigen were assigned a titer of 0.3 mIU/ml in the analysis.

REFERENCE

1. Tarone RE, Ware J: On Distribution-Free Tests for Equality of Survival Distributions. Biometrika 64: 156-160, 1977.

Dialysis and Predialysis Patients

Study 789 - Durham, NC - Dr. G. Hamilton

The study population consists of adults with chronic renal insufficiency (pre-dialysis) who are negative for hepatitis B serologic markers. Participants receive either 20 mcg or 40 mcg injections of yeast recombinant vaccine lot C-K446 or 40 mcg injections of plasma-derived vaccine lot 2449H or 1885K. All injections are administered at 0, 1, and 6 months.

Fifteen participants have received two 40 mcg injections of yeast recombinant vaccine and seven of these have received the third injection. At 7/8 months, 71% (5/7) of these vaccinees seroconverted for anti-HBs (S/N $\geq$2.1). Fifty-seven percent (4/7) developed protective levels of anti-HBs (S/N $\geq$10). The GMT for all vaccinees at that time was 12.7 S/N and 60.2 for responders (S/N $\geq$10).

Fourteen subjects have received two 20 mcg injections of yeast recombinant vaccine and seven of these have received the third injection. Eighty-six percent of the vaccinees seroconverted for anti-HBs (S/N $\geq$2.1) at 7/8 months. Fifty-seven percent (4/7) developed protective levels of anti-HBs (S/N $\geq$10). The GMT for all vaccinees at that time was 25.3 S/N and 130.0 for responders (S/N $\geq$10).

Sixteen predialysis patients have received two 40 mcg injections of plasma derived vaccine. Six of these have been administered the third injection. At 7/8 months, 67% (4/6) of the subjects seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (S/N $\geq$10). The GMT for all vaccinees at that time was 27.7 S/N and 168.6 for responders (S/N $\geq$10).

No serious or alarming adverse experiences attributable to either vaccine have been reported. The study continues in progress.

Study 811 - Switzerland - Dr. P. Grob

Predialysis patients and health care personnel are enrolled in Study 811. Predialysis patients are assigned to one of five groups and receive yeast recombinant vaccine lot C-K446 or plasma-derived vaccine (Heptavax) lot 1510J. Group 1, 2, and 3 participants receive 10 mcg, 20 mcg, and 40 mcg injections of yeast recombinant vaccine, respectively. Group 4 and 5 participants receive 20 mcg and 40 mcg injections of plasma-derived vaccine, respectively. The vaccine is administered at 0, 1, and 6 months for all groups.

Fourteen predialysis patients (group 1) have received two 10 mcg injections of yeast recombinant vaccine and 13 of these have received the third injection. At 7/8 months, 15% (2/13) of the subjects seroconverted (S/N $\geq$2.1) and developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT for all

Study 811 - Switzerland - Dr. P. Grob (Cont.)

vaccinees was 7.0 mIU/ml and 67.7 for responders (mIU/ml ≥10). No patient tested, seroconverted before 7/8 months.

Fourteen predialysis patients (group 2) have received two 20 mcg injections of yeast recombinant vaccine and 13 of these have received the third injection. At 7/8 months, 58% (7/12) of the subjects seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 13.8 mIU/ml and 213.7 for all responders (mIU/ml ≥10).

In group 3, thirteen predialysis patients have received two 40 mcg injections of yeast recombinant vaccine. Twelve of these have been administered the third injection. Sixty-four percent (7/11) seroconverted (S/N ≥2.1) for anti-HBs at 7/8 months. Fifty-four percent (6/11) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees at that time was 13.6 mIU/ml and 186.4 for responders (mIU/ml ≥10).

Eleven predialysis patients (group 4) have received two 20 mcg injections of plasma-derived vaccine and 10 of these have received the third injection. At 7/8 months, 25% (2/8) of the subjects seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 1.3 mIU/ml and 101.2 for responders (mIU/ml ≥10).

In group 5, 11 predialysis patients received two 40 mcg injections of plasma-derived vaccine and 10 of these have received the third injection. Fifty percent (4/8) of the patients seroconverted for anti-HBs (S/N ≥2.1) at 7/8 months. Thirty-eight percent (3/8) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees at 7/8 months was 8.7 mIU/ml and 791.5 for responders (mIU/ml ≥10).

There have been no serious or alarming reactions attributable to vaccine. The study continues in progress. Refer to the summary on health care personnel/healthy adults for data regarding other subjects vaccinated in this study.

Study 816 - Philadelphia, PA - Dr. S. Plotkin and Dr. S. Starr

The study population consists of health care personnel and adult hemodialysis patients (including hemodialysis patients who were previous non-responders to plasma-derived vaccine). Health care personnel received 10 mcg injections of yeast recombinant vaccine lot C-K446. Dialaysis patients received either 20 mcg injections (group 1) or 40 mcg injections (group 2) of yeast recombinant vaccine lot C-K446. All vaccine is administered at 0, 1, and 6 months.

Thirty-nine hemodialysis patients (group 1) have received one 20 mcg injection of vaccine. Thirty-four of these have received the second injection and 32 the third injection. At 7/8 months, 57% (16/28) of the patients seroconverted

Study 816 - Philadelphia, PA - Dr. S. Plotkin and Dr. S. Starr (Cont.)

for anti-HBs (S/N ≥2.1). Forty-six percent (13/28) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees at 7/8 months was 7.5 mIU/ml and 132.4 for responders (mIU/ml ≥10).

In group 2, 36 dialysis patients have received one 40 mcg injection of vaccine and 34 of these have received the second injection. The third injection has been administered to 24 patients. Eighty percent (16/20) of these patients seroconverted for anti-HBs (S/N ≥2.1) at 7/8 months. Seventy-five percent (15/20) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees was 81.8 mIU/ml and 418.4 for responders (mIU/ml ≥10).

No serious or alarming reactions attributable to vaccine have been reported. The study continues in progress. Refer to the summary on health care personnel/healthy adults for data regarding other subject vaccinated in this study.

Study 825 - Bethesda, MD - Dr. H. Alter

The study population consists of adult hemodialysis patients who are negative for hepatitis B serologic markers. Dialysis patients who were nonresponders to previously administered plasma-derived vaccine may also be included in the study population. Participants receive a 100 mcg injection of vaccine lot C-L915 at 0, 1, and 6 months.

Forty-four hemodialysis patients have received one 100 mcg injection of vaccine and forty-one of these have received the second injection. No subject has yet received the third injection of vaccine. Serology data are available through 3 months of follow-up. Sixty-eight percent (19/28) of the patients seroconverted for anti-HBs (S/N ≥2.1) at 3 months. Twenty-five percent (7/28) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT for all vaccinees at 3 months was 4.4 S/N and 33.3 for responders (S/N ≥10).

No serious or alarming reactions attributable to vaccine have been reported. The study continues in progress.

Study 838 - West Germany - Dr. F. Deinhardt

The population of STudy 838 consists of adult hemodialysis patients, predialysis patients and health care personnel. Yeast recombinant hepatitis B vaccine lot C-K733 is being utilized. Dialysis patients may receive 40 mcg injections at 0, 1, and 6 months, or 20 or 40 mcg injections of vaccine at 0, 1, 2, 3, 4, and 6 months. Predialysis patients receive either 10 mcg or 40 mcg injections of vaccine at 0, 1, and 6 months. All injections were administered in the buttock.

Fifty-one dialysis patients have been enrolled in the three 40 mcg injection regimen. All 51 patients have received two 40 mcg injections and 48 of these have received the third injection. At 7/8 months, 64% (23/36) of the patients seroconverted for anti-HBs (S/N ≥2.1). Fifty-eight percent (21/36) developed

Study 838 - West Germany - Dr. F. Deinhardt (Cont.)

protective levels of anti-HBs (mIU/ml ≥10). The GMT at that time for all vaccinees was 12.3 mIU/ml and 115.5 for responders (mIU/ml ≥10).

Twenty dialysis patients have been enrolled in the six 40 mcg injection regimen. All 20 subjects have received the first three injections and 19 of these have received the fourth and fifth injections. Seventeen patients have been administered all six 40 mcg injections of vaccine. At 10 months. 67% (10/15) of the patients seroconverted for anti-HBs (S/N ≥2.1). Sixty percent (9/15) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT at 10 months for all vaccinees was 6.7 mIU/ml and 27.7 for responders (mIU/ml ≥10).

Twenty dialysis patients in the six 20 mcg injection regimen have all received five injections of vaccine. Seventeen of these have received the sixth injection. Fifty percent (9/18) of the patients seroconverted for anti-HBs (S/N ≥2.1) at 10 months. Forty-four percent (8/18) developed protective levels of anti-HBs (mIU/ml ≥10) at that time. The GMT for all vaccinees was 4.7 mIU/ml and 55.0 for responders (mIU/ml ≥10).

Eight predialysis patients have been enrolled in the three 40 mcg injection regimen. All eight patients have received the first two injections of vaccine. None has yet received the third injection. Serology data are available through one month of follow-up. Thirteen percent (1/8) of the subjects seroconverted for anti-HBs (S/N ≥2.1). The GMT for all vaccinees was 0.7 mIU/ml and 4.6 mIU/ml for responders (S/N ≥2.1). None of the participants developed protective levels of anti-HBs (mIU/ml ≥10) at one month.

No serious or alarming adverse experiences attributable to vaccine have been reported. The study continues in progress. Refer to the summary of health care personnel/healthy adults for data regarding other subject vaccinated in this study.

STUDY 789

PROGRAM:	Yeast Recombinant Hepatitis B Vaccine, Study 789
PURPOSE:	To compare antibody and clinical responses to plasma and yeast recombinant vaccines at 2 dose levels among uremic patients not yet undergoing dialysis who are negative for HBV markers.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #974/C-K446 (20 mcg HBsAg/ml) HEPTAVAX Plasma-Derived Hepatitis B Vaccine Lot 2449H (20 mcg HBsAg/ml) Lot 1885K (20 mcg HBsAg/ml)
PRINCIPAL INVESTIGATOR:	John Hamilton, M.D. VA Medical Center Durham, NC 27705
SECONDARY INVESTIGATOR:	Joan Drucker, M.D. Division of Infectious Diseases Duke University Medical Center Durham, NC 27710 Robert Gutman, M.D. Division of Nephrology Duke University Medical Center Durham, NC 27710
STUDY LOCATION:	Duke University Medical Center Durham, NC 27710 Veteran's Administration Medical Center 508 Fulton Street Durham, NC 27705
DATE INITIATED:	May 23, 1984
DATE COMPLETED:	In progress.
STUDY PROCEDURE:	The study population consists of 45 adults of either sex, aged 16-60 years, who have chronic renal insufficiency not severe enough to require dialysis (creatinine levels of 2.0 mgm/dl or greater), who are negative for HBsAg, anti-HBc and anti-HBs, and have a normal ALT level.

Study 789

STUDY PROCEDURE (CONT.):

To assure that patients in the treatment groups are similar, assignment to vaccine and dosage is stratified by sex, age and creatinine level. Participants are randomly assigned to one of the following groups.

Group	Vaccine	Number	Dose	Regimen
1	Lot 974	14	20 mcg	1 - 1.0 ml intramuscular injection on day 0, 1 mo. and 6 mos.
2	Lot 974	15	40 mcg	2 - 1.0 ml intramuscular injections on day 0, 1 mo. and 6 mos.
3	HEPTAVAX Lot 2449H or Lot 1885K	16	40 mcg	2 - 1.0 ml intramuscular injections on day 0, 1 mo. and 6 mos.

Vaccinees are asked to record their temperature daily for 5 days after each injection and also to record any local or systemic complaints they may have during this period.

A blood specimen (10-15 ml) is obtained from each participant approximately 2 weeks before the first vaccination. Post-vaccination blood samples are obtained at 1, 3, 6, 7, 9 and 12 months. The samples are assayed for HBsAg, anti-HBc, anti-HBs, ALT, and creatinine. Samples with anti-HBs titers $\geq$25 mIU/ml may be tested for the proportions of anti-a and anti-d activity. Samples may be tested for yeast antibody at MSDRL.

RESULTS:

Pre-Dialysis Patients:

20 mcg Lot #974/C-K446 at 0, 1, and 6 months
40 mcg Lot #974/C-K446 at 0, 1, and 6 months
40 mcg HEPTAVAX Lot #2449H at 0, 1, and 6 months
40 mcg HEPTAVAX Lot #1885K at 0, 1, and 6 months

Study 789

RESULTS (CONT.): 1. Number Vaccinated:

Dose Level	---Injection Number--- 1	2	3
40 mcg Recombinant	15	15	7
20 mcg Recombinant	14	14	7
40 mcg Plasma	16	16	6

2. Serologic Results:

Serologic data at 7/8 months are available for 7, 7, and 6 recipients of 40 mcg recombinant, 20 mcg recombinant, and 40 mcg doses of plasma-derived vaccine, respectively. The following anti-HBs responses were observed at that time. Table 1 shows seroconversion rates and GMTs for up to one year of follow-up.

Dose Level	% with Anti-HBs S/N ≥2.1	S/N ≥10	GMT (S/N) Vaccinees	S/N ≥2.1	S/N ≥10
40 mcg Recombinant	71 (5/7)	57 (4/7)	12.7	35.4	60.2
20 mcg Recombinant	86 (6/7)	57 (4/7)	25.3	43.4	130.0
40 mcg Plasma	67 (4/6)	67 (4/6)	27.7	168.6	168.6

3. Clinical Complaints

Clinical follow-up data are available for 15, 15, and 7 participants following the first, second, and third injections of 40 mcg recombinant vaccine; 14, 14, and 7 participants who received 20 mcg recombinant vaccine; and for 16, 16, and 6 who received 40 mcg of plasma vaccine.

Study 789

RESULTS (CONT.): Clinical complaints and maximum temperatures reported following each injection are provided in Tables 2-7.

Type of Complaint	Dose Level	Frequency in % by Injection No. 1	2	3
Injection Site	40 mcg Recombinant	13 (2/15)	7 (1/15)	0 (0/7)
	20 mcg Recombinant	36 (5/14)	14 (2/14)	14 (1/7)
	40 mcg Plasma	6 (1/16)	6 (1/16)	17 (1/6)
Systemic	40 mcg Recombinant	7 (1/15)	13 (2/15)	14 (1/7)
	20 mcg Recombinant	29 (4/14)	29 (4/14)	29 (2/7)
	40 mcg Plasma	6 (1/16)	13 (2/16)	17 (1/6)

ALT Elevations

Vaccine recipients included one person in the 20 mcg recombinant group who had a pre-vaccination ALT level 2-3 times the upper limit of normal. His ALT level remained elevated through 9 months of follow-up but had dropped to normal at his one year bleeding. He remained negative for HBsAg and has shown no signs of infection. There was also one person in the 40 mcg plasma group and one in the 40 mcg recombinant group with normal pre-vaccination ALT levels who had transient elevated ALT levels approximately 1.5 - 2 times the upper limit of normal 2 months after the first dose of vaccine. All subsequent ALTs were normal. These subjects have not shown any clinical or serologic signs (HBsAg or anti-HBc) of hepatitis B.

Adverse Reactions Reported to OoBRR

Case (b)(6) a 30-year old male, died on (b)(6) from hemorrhage of esophageal varices and subsequent complications. He had received two 40 mcg immunizations of plasma-derived vaccine Lot 2449H, on (b)(6) and on (b)(6) The patient had a history of polycystic kidney and liver disease, as well as previous episodes of variceal bleeding. The death is not believed to be vaccine related.

Case (b)(6) a 58-year old male, had a history of hypertension and chronic renal failure (predialysis).

Table 1

Antibody Responses Among Pre-Dialysis Patients Following Vaccination with 40 or 20 mcg Doses of Recombinant Hepatitis B Vaccine Lot #974/C-K446 or 40 mcg Doses of Plasma Vaccine Lot 2449H or Lot 1885K at 0, 1, and 6 Months in Study 789

	40 mcg Recombinant					20 mcg Recombinant					40 mcg Plasma				
	% with Anti-HBs		GMT (S/N)			% with Anti-HBs		GMT (S/N)			% with Anti-HBs		GMT (S/N)		
				Responders					Responders					Responders	
Time (Mos.)	S/N≥2.1	S/N ≥ 10	All Vaccinees	S/N≥2.1	S/N ≥ 10	S/N≥2.1	S/N ≥ 10	All Vaccinees	S/N≥2.1	S/N ≥ 10	S/N≥2.1	S/N ≥ 10	All Vaccinees	S/N≥2.1	S/N ≥ 10
1	7 (1/15)	0 (0/15)	1.0	5.7	---	0 (0/14)	0 (0/14)	0.8	---	---	13 (2/16)	0 (0/16)	1.1	4.1	---
3	43 (6/14)	21 (3/14)	3.4	12.4	29.3	38 (5/13)	8 (1/13)	2.3	7.8	26.7	67 (10/15)	40 (6/15)	5.9	14.1	30.2
6	43 (3/7)	0 (0/7)	1.7	4.1	---	57 (4/7)	29 (2/7)	3.0	7.4	21.4	60 (3/5)	60 (3/5)	6.9	37.8	37.8
7	71 (5/7)	57 (4/7)	12.7	35.4	60.2	86 (6/7)	57 (4/7)	25.3	43.3	130.0	67 (4/6)	67 (4/6)	27.7	168.6	168.6
9	100 (1/1)	100 (1/1)	12.6	12.6	12.6	100 (3/3)	33 (1/3)	14.9	14.9	141.2	100 (2/2)	100 (2/2)	73.8	73.8	73.8
12						100 (4/4)	25 (1/4)	6.0	6.0	33.3					

00720

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (14 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	5 (35.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (35.7%)
SORENESS	5 (35.7%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		5 (35.7%)
SWELLING	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
STIFFNESS/TIGHTNESS	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
SYSTEMIC	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	2 (14.3%)	1 (7.1%)		4 (28.6%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)		1 (7.1%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)		1 (7.1%)
MUSCULOSKELETAL	1 (7.1%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		2 (14.3%)
ARTHRALGIA (OTHER)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
SHOULDER PAIN	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
KNEE PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		1 (7.1%)
NERVOUS SYSTEM	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (14 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SOMNOLENCE	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
PERSONS WITH COMPLAINTS	6 (42.9%)	2 (14.3%)	1 (7.1%)	1 (7.1%)	2 (14.3%)	1 (7.1%)	7 (50.0%)
PERSONS WITH NO COMPLAINTS	8 (57.1%)	12 (85.7%)	13 (92.9%)	13 (92.9%)	12 (85.7%)	13 (92.9%)	7 (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%)

00722

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (14 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (14.3%)
SORENESS	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (14.3%)
STIFFNESS/TIGHTNESS	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
SYSTEMIC	1 (7.1%)	2 (14.3%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		4 (28.6%)
WHOLE BODY/GENERAL	1 (7.1%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		3 (21.4%)
CHILLS	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		1 (7.1%)
ILLNESS, NOS	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
RESPIRATORY	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (14.3%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (7.1%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (14.3%)
PERSONS WITH COMPLAINTS	3 (21.4%)	2 (14.3%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)		5 (35.7%)

00723

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (14 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO COMPLAINTS	11 (78.6%)	12 (85.7%)	13 (92.9%)	13 (92.9%)	13 (92.9%)	13 (92.9%)	9 (64.3%)
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%)

00724

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (7 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (14.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (14.3%)
SORENESS	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (14.3%)
STIFFNESS/TIGHTNESS	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (14.3%)
ECCHYMOSIS	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (14.3%)
SYSTEMIC	2 (28.6%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	2 (28.6%)	1 (14.3%)		2 (28.6%)
WHOLE BODY/GENERAL	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)		1 (14.3%)
CHILLS	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)		1 (14.3%)
DIGESTIVE SYSTEM	1 (14.3%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	2 (28.6%)	1 (14.3%)		2 (28.6%)
NAUSEA	1 (14.3%)	1 (14.3%)	1 (14.3%)	2 (28.6%)	2 (28.6%)	1 (14.3%)		2 (28.6%)
VOMITING	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)		1 (14.3%)
PERSONS WITH COMPLAINTS	3 (42.9%)	2 (28.6%)	1 (14.3%)	2 (28.6%)	2 (28.6%)	1 (14.3%)		3 (42.9%)
PERSONS WITH NO COMPLAINTS	4 (57.1%)	5 (71.4%)	6 (85.7%)	5 (71.4%)	5 (71.4%)	6 (85.7%)		4 (57.1%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (7 PATIENTS) - DOSE 3							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%)

00726

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE
LOT 8CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (14 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	2 (14.3%)	2 (14.3%)	2 (14.3%)	2 (14.3%)	2 (14.3%)	2 (14.3%)			2 (14.3%)
< 99	9 (64.3%)	10 (71.4%)	11 (78.6%)	10 (71.4%)	9 (64.3%)	11 (78.6%)			6 (42.9%)
99 - 99.9	2 (14.3%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	3 (21.4%)	1 (7.1%)			4 (28.6%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)			1 (7.1%)
102 - 102.9	1 (7.1%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (7.1%)
TEMPERATURE TAKEN	14 (100.0%)	14 (100.0%)	14 (100.0%)	14 (100.0%)	14 (100.0%)	14 (100.0%)			14 (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
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (14 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (7.7%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	1 (7.1%)			1 (7.1%)
< 99	11 (84.6%)	9 (64.3%)	9 (64.3%)	11 (78.6%)	12 (85.7%)	12 (85.7%)			6 (42.9%)
99 - 99.9	0 (0.0%)	2 (14.3%)	3 (21.4%)	1 (7.1%)	1 (7.1%)	0 (0.0%)			4 (28.6%)
100 - 100.9	0 (0.0%)	2 (14.3%)	1 (7.1%)	1 (7.1%)	0 (0.0%)	0 (0.0%)			1 (7.1%)
102 - 102.9	1 (7.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)			2 (14.3%)
TEMPERATURE TAKEN	13 (92.9%)	14 (100.0%)	14 (100.0%)	14 (100.0%)	14 (100.0%)	14 (100.0%)			14 (100.0%)
TEMPERATURE NOT TAKEN	1 (7.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

00728

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 20 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (7 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (14.3%)	2 (28.6%)	2 (28.6%)	2 (28.6%)	2 (28.6%)	2 (28.6%)			1 (14.3%)
< 99	3 (42.9%)	4 (57.1%)	4 (57.1%)	3 (42.9%)	2 (28.6%)	4 (57.1%)			2 (28.6%)
99 - 99.9	3 (42.9%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	1 (14.3%)	1 (14.3%)			2 (28.6%)
100 - 100.9	0 (0.0%)	1 (14.3%)	1 (14.3%)	0 (0.0%)	1 (14.3%)	0 (0.0%)			0 (0.0%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)			1 (14.3%)
104 - 104.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)			1 (14.3%)
TEMPERATURE TAKEN	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)			7 (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%)

00729

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT 8CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (15 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	0 (0.0%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (13.3%)
SORENESS	0 (0.0%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (13.3%)
SYSTEMIC	0 (0.0%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
NAUSEA	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
DEPRESSION	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
PERSONS WITH COMPLAINTS	0 (0.0%)	3 (20.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)		3 (20.0%)
PERSONS WITH NO COMPLAINTS	15 (100.0%)	12 (80.0%)	14 (93.3%)	14 (93.3%)	15 (100.0%)	15 (100.0%)		12 (80.0%)
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
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (15 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
SORENESS	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
SYSTEMIC	0 (0.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)		2 (13.3%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
UPPER RESPIRATORY INFECT., NOS	0 (0.0%)	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)		1 (6.7%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)		1 (6.7%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
DEPRESSION	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.7%)
PERSONS WITH COMPLAINTS	1 (6.7%)	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)		2 (13.3%)
PERSONS WITH NO COMPLAINTS	14 (93.3%)	14 (93.3%)	14 (93.3%)	15 (100.0%)	15 (100.0%)	14 (93.3%)		13 (86.7%)
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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (7 PATIENTS) - DOSE 3							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
ABDOMINAL TENDERNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)		1 (14.3%)
PERSONS WITH NO COMPLAINTS	6 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	6 (85.7%)		6 (85.7%)
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%)

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Table 5

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE
LOT 8CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (15 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (7.1%)	1 (7.1%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (7.1%)			1 (6.7%)
< 99	10 (71.4%)	11 (78.6%)	12 (80.0%)	12 (80.0%)	12 (80.0%)	11 (78.6%)			8 (53.3%)
99 - 99.9	2 (14.3%)	1 (7.1%)	0 (0.0%)	2 (13.3%)	2 (13.3%)	1 (7.1%)			4 (26.7%)
101 - 101.9	1 (7.1%)	1 (7.1%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	1 (7.1%)			2 (13.3%)
TEMPERATURE TAKEN	14 (93.3%)	14 (93.3%)	15 (100.0%)	15 (100.0%)	15 (100.0%)	14 (93.3%)			15 (100.0%)
TEMPERATURE NOT TAKEN	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.7%)			0 (0.0%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (15 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (7.1%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)			1 (6.7%)
< 99	10 (71.4%)	11 (73.3%)	10 (66.7%)	13 (86.7%)	14 (93.3%)	14 (93.3%)			8 (53.3%)
99 - 99.9	3 (21.4%)	2 (13.3%)	2 (13.3%)	1 (6.7%)	0 (0.0%)	0 (0.0%)			4 (26.7%)
100 - 100.9	0 (0.0%)	0 (0.0%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (6.7%)
101 - 101.9	0 (0.0%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (6.7%)
TEMPERATURE TAKEN	14 (93.3%)	15 (100.0%)	15 (100.0%)	15 (100.0%)	15 (100.0%)	15 (100.0%)			15 (100.0%)
TEMPERATURE NOT TAKEN	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE
LOT #CK446

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (7 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	1 (16.7%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	1 (14.3%)			1 (14.3%)
< 99	3 (50.0%)	5 (71.4%)	5 (71.4%)	6 (85.7%)	4 (57.1%)	4 (57.1%)			2 (28.6%)
99 - 99.9	2 (33.3%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (14.3%)			1 (14.3%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (28.6%)	0 (0.0%)			1 (14.3%)
101 - 101.9	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (14.3%)			2 (28.6%)
TEMPERATURE TAKEN	6 (85.7%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)	7 (100.0%)			7 (100.0%)
TEMPERATURE NOT TAKEN	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)

00735

Table 6

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (16 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
SORENESS	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
SYSTEMIC	1 (6.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
WHOLE BODY/GENERAL	1 (6.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
SENSATION OF WARMTH, GENERAL	1 (6.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
PERSONS WITH COMPLAINTS	2 (12.5%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (12.5%)
PERSONS WITH NO COMPLAINTS	14 (87.5%)	15 (93.8%)	16 (100.0%)	16 (100.0%)	16 (100.0%)	16 (100.0%)		14 (87.5%)
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%)

00736

Table 6 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (16 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
PAIN	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
SYSTEMIC	0 (0.0%)	1 (6.3%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)		2 (12.5%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
ARTHRALGIA (OTHER)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)		1 (6.3%)
PERSONS WITH COMPLAINTS	1 (6.3%)	1 (6.3%)	0 (0.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)		2 (12.5%)
PERSONS WITH NO COMPLAINTS	15 (93.8%)	15 (93.8%)	16 (100.0%)	15 (93.8%)	16 (100.0%)	16 (100.0%)		14 (87.5%)
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%)

00737

Table 6 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

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%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
DIGESTIVE SYSTEM	1 (16.7%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
NAUSEA	1 (16.7%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
VOMITING	0 (0.0%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
LOOSE STOOL	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)
PERSONS WITH COMPLAINTS	2 (33.3%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	2 (33.3%)
PERSONS WITH NO COMPLAINTS	4 (66.7%)	5 (83.3%)	5 (83.3%)	5 (83.3%)	6 (100.0%)	6 (100.0%)	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 7

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (16 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)	1 (6.7%)			1 (6.7%)
< 99	12 (80.0%)	12 (80.0%)	13 (86.7%)	11 (73.3%)	11 (73.3%)	12 (80.0%)			10 (66.7%)
99 - 99.9	1 (6.7%)	2 (13.3%)	1 (6.7%)	3 (20.0%)	3 (20.0%)	2 (13.3%)			3 (20.0%)
104 - 104.9	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (6.7%)
TEMPERATURE TAKEN	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)			15 (93.8%)
TEMPERATURE NOT TAKEN	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)			1 (6.3%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (16 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
NORMAL	2 (13.3%)	2 (13.3%)	2 (13.3%)	2 (13.3%)	2 (13.3%)	2 (13.3%)			2 (12.5%)
< 99	11 (73.3%)	12 (80.0%)	13 (86.7%)	13 (86.7%)	12 (80.0%)	12 (80.0%)			11 (68.8%)
99 - 99.9	2 (13.3%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.7%)			3 (18.8%)
TEMPERATURE TAKEN	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)	15 (93.8%)			16 (100.0%)
TEMPERATURE NOT TAKEN	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)	1 (6.3%)			0 (0.0%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
PLASMA-DERIVED HEPATITIS B VACCINE
LOT #2449H

STUDY : 0789
TREATMENT :
DOSE : 40 MCG
PATIENT CLASS: PRE-DIALYSIS PATIENTS

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	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)	1 (16.7%)		1 (16.7%)
< 99	4 (66.7%)	4 (66.7%)	4 (66.7%)	4 (66.7%)	5 (83.3%)	5 (83.3%)		4 (66.7%)
99 - 99.9	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
100 - 100.9	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
102 - 102.9	0 (0.0%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (16.7%)
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%)

STUDY 811

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)

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Study 811

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STUDY LOCATION:	University Hospital Haldeliweg 4 CH - 8044 Zurich Switzerland
DATE INITIATED:	April 10, 1984
DATE COMPLETED:	In progress

Study 811

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.

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 a 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.

Study 811

PROCEDURE (Cont.): 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.

RESULTS:

PREDIALYSIS PATIENTS:

10 mcg Lot #974/C-K446 at 0, 1, and 6 months
20 mcg Lot #974/C-K446 at 0, 1, and 6 months
40 mcg Lot #974/C-K446 at 0, 1, and 6 months
20 mcg Lot #1510J at 0, 1, and 6 months
40 mcg Lot #1510J at 0, 1, and 6 months

1. Number Vaccinated:

Vaccine	Dose Level	Injection # 1	2	3
Recomb.	10 mcg	14	14	13
	20 mcg	14	14	13
	40 mcg	13	13	12
H-B-Vax	20 mcg	11	11	10
	40 mcg	11	11	10

2. Serologic Results:

Seven/eight month serology data are available for 13, 12, and 11 participants who received 10, 20 and 40 mcg injections of vaccine, respectively. Serology data for 7/8 months of follow-up are available for 8 subjects in each of the plasma-derived vaccine dose regimens.

Study #811

RESULTS: (Cont.)

Anti-HBs responses and GMTs for recipients of yeast recombinant and plasma-derived vaccine are summarized below:

Vaccine	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
Recomb.	10 mcg	15 (2/13)	15 (2/13)	0.7	67.7	67.7
	20 mcg	58 (7/12)	58 (7/12)	13.8	213.7	213.7
	40 mcg	64 (7/11)	54 (6/11)	13.6	120.9	186.4
H-B-Vax	20 mcg	25 (2/8)	25 (2/8)	1.3	101.2	101.2
	40 mcg	50 (4/8)	38 (3/8)	8.7	251.0	791.5

Refer to Tables 1 and 2 for anti-HBs responses and GMTs through 12 months of follow-up

3. Clinical Complaints:

Clinical follow-up data are available for at least 12 participants, after each injection, who were enrolled in the 10 mcg dose regimen, 13 participants who received 20 mcg injections, and at least 10 subjects who received 40 mcg injections of yeast recombinant vaccine.

At least 5 participants in each of the plasma-derived vaccine dose groups have clinical follow-up data after each injection.

The overall frequencies of complaints among vaccinees who received yeast recombinant or plasma-derived vaccine are presented below:

Study 811

RESULTS: (Cont.)

Type of Complaint	Vaccine	Dose Level	Frequency in % by Injection # 1	2	3
Injection Site	Recomb.	10 mcg	0(0/14)	0(0/14)	0(0/12)
		20 mcg	0(0/14)	7(1/14)	0(0/13)
		40 mcg	0(0/12)	0(0/11)	0(0/10)
	H-B-Vax	20 mcg	10(1/10)	0(0/8)	0(0/5)
		40 mcg	0(0/10)	0(0/10)	0(0/5)
Systemic	Recomb.	10 mcg	0(0/14)	0(0/14)	8(1/12)
		20 mcg	7(1/14)	0(0/14)	0(0/13)
		40 mcg	0(0/12)	0(0/11)	0(0/10)
	H-B-Vax	20 mcg	14(1/10)	0(0/8)	0(0/5)
		40 mcg	0(0/10)	0(0/10)	0(0/5)

No serious or alarming adverse experiences attributable to vaccine have been reported.

HBV MARKERS (Anti-HBc)

One subject in the 10 mcg yeast recombinant vaccine group was positive for anti-HBc at 1 and 3 months after the first injection of vaccine. The sera of this participant retested negative for anti-HBc. All samples were negative for HBsAg and ALT levels were normal.

Two subjects in the 20 mcg yeast recombinant vaccine group were positive for anti-HBc at 8 months post the first injection of vaccine. The patients were negative for HBsAg and ALT levels were normal. In both cases, the 12 month follow-up serum samples were negative for anti-HBc.

A predialysis patient in the 40 mcg yeast recombinant vaccine group was positive for anti-HBc IgG and negative for anti-HBc IgM at 6, 8, and 12 months post the initial vaccine injection. Serum samples were negative HBsAg and ALT levels were normal.

Study 811

RESULTS: (Cont.)

A subject in the 20 mcg plasma-derived vaccine group was positive for anti-HBc at 1 month after the first injection. The participant was negative for anti-HBc at 3 months. Serum samples were negative for HBsAg and ALT levels were within normal limits.

One participant in the 40 mcg plasma-derived vaccine group tested positive for anti-HBc at 1 month. The 3 and 6 month serum samples were negative for anti-HBc. The subject was negative HBsAg and ALT levels were normal.

There have been no reports of clinical hepatitis in any of the above vaccine recipients.

Reactions Reported to the OoBRR

A 28 year-old male (Case (b) (6) with underlying renal disease and recently initiated hemodialysis, died approximately one month after administration of the first injections of vaccine. The investigator reported death was due to vasculitis.

Table 1

Antibody Responses Among Predialysis Patients Following Vaccination with 10, 20, and 40 mcg Injections of Yeast Recombinant Hepatitis B Vaccine Lot # 974/C-K446 at 0, 1, and 6 Months in Study #811

	10 mcg					20 mcg					40 mcg				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
				Responders					Responders					Responders	
Time (Mos.)	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	0 (0/14)	0 (0/14)	0.3	---	---	0 (0/14)	0 (0/14)	0.3	---	---	0 (0/13)	0 (0/13)	0.3	---	---
3	0 (0/14)	0 (0/14)	0.3	---	---	7 (1/14)	7 (1/14)	0.5	90.0	90.0	0 (0/12)	0 (0/12)	0.3	---	---
6	0 (0/13)	0 (0/13)	0.3		---	28 (4/14)	28 (4/14)	1.0	23.6	23.6	42 (5/12)	42 (5/12)	1.7	19.4	19.4
7/8	15 (2/13)	15 (2/13)	0.7	67.7	67.7	58 (7/12)	58 (7/12)	13.8	213.7	213.7	64 (7/11)	54 (6/11)	23.6	120.9	186.4
12	8 (1/12)	0 (0/12)	0.4	6.0	---	60 (6/10)	60 (6/10)	8.5	78.5	78.5	40 (4/10)	40 (4/10)	3.3	117.3	117.3

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Table 2

Antibody Responses Among Predialysis Patients Following Vaccination with
20 and 40 mcg Injections of Plasma Derived Hepatitis B Vaccine
Lot # 1510J at 0, 1, and 6 Months in Study 811

Time (Months)	20 mcg					40 mcg				
	% 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	0(0/11)	0(0/11)	0.3	---	---	0(0/11)	0(0/11)	0.3	---	---
3	10(1/10)	10(1/10)	0.5	29.0	29.0	10(1/10)	0(0/10)	0.4	6.0	---
6	22(2/9)	11(1/9)	0.6	8.1	13.0	50(5/10)	40(4/10)	3.7	45.2	78.5
7/8	25(2/8)	25(2/8)	1.3	101.2	101.2	50(4/8)	38(3/8)	8.7	251.0	191.5
12	0(0/3)	0(0/3)	0.3	---	---	50(3/6)	50(3/6)	13.7	93.0	220.1

* One responder who received the third injection of vaccine at 3 months was excluded from the summary.

25151-9
1/13/86

00750

STUDY 816

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.

Study 816

RESULTS:

DIALYSIS PATIENTS

20 mcg Lot 974/C-K446 at 0, 1, and 6 months *
40 mcg Lot 974/C-K446 at 0, 1, and 6 months *

1. Number Vaccinated:

Dose (mcg)	Injection No. 1	2	3
20	39	34	33
40	36	34	25

One dialysis patient who was initially anti-HBc positive received vaccine. The patient has remained anti-HBc positive through 12 months. The subject has not developed HBsAg or elevated ALT levels. At one month, the patient became anti-HBs positive.

Four dialysis patients (40 mcg dose) received 1.0 ml vaccine in the deltoid and 1.0 ml in the buttock.

* Two patients received a third 20 or 40 mcg dose of Lot 986/C-K733.

2. Serologic Results:

Serologic data at 7/8 months are available for 29 dialysis patients who received a 20 mcg dose and 21 dialysis patients who received a 40 mcg dose of vaccine.

Study 816

RESULTS: (Contd)

At 7/8 and 12 months, anti-HBs responses are as follows:

Time (Months)	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
7/8	20	59(17/29)	48(14/29)	7.8	69.1	118.6
	* 40	94(16/17)	88(15/17)	219.7	331.8	445.5
12	20	52(15/19)	41(12/29)	5.1	49.2	79.9
	* 40	81(17/21)	71(15/21)	41.6	107.9	165.6

* Serologic results included in the above summary do not include 4 dialysis patients (40 mcg dose) who received 1.0 ml vaccine in the deltoid and 1.0 ml in the buttock.

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

3. Clinical Results:

Clinical follow-up data are available for 74, 68, and 56 dialysis patients following the first, second and third injections of vaccine, respectively. 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	20	8(3/38)	0(0/34)	0(0/33)
	40	11(4/36)	3(1/34)	0(0/25)
Systemic	20	24(9/38)	3(1/34)	12(4/33)
	40	22(8/36)	0(0/34)	8(2/25)

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

Study 816

RESULTS: (Contd)

Events reported to OoBRR

Seven deaths have occurred among dialysis patients who received recombinant hepatitis B vaccine Lot 974/C-K446. The investigator does not consider any of the deaths to be related to vaccination.

1. Case no. (b) (6) a 57 year-old female, died approximately six months after receiving athird 40 mcg dose of vaccine. The cause of death was cardiac arrest.

2. Case no. (b) (6) a 57 year-old male, died approximately one month after receiving a third 20 mcg dose of vaccine. The cause of death was attributed to a myocardial infarction and end-stage renal disease.

3. Case no. (b) (6) a 49 year-old male, died approximately four months after receiving a second 40 mcg dose of vaccine. Death was due to respiratory arrest, aspiration asphyxia, end-stage renal and coronary artery disease.

4. Case no. (b) (6) a 79 year-old male, died approximately four months after receiving a second 40 mcg dose of vaccine. Death was caused by cardiac arrest, atherosclerosis, end-stage renal disease and multiple myeloma.

5. Case no. (b) (6) a 71 year-old female, died approximately one month after receiving one 20 mcg dose of vaccine. Death was due to cardio-pulmonary arrest, uremia, chronic renal failure and abdominal aortic aneurysm without rupture.

6. Case no. (b) (6) a 49 year-old male, died approximately four months after receiving a second 40 mcg dose of vaccine. The death was due to cardiac arrest, pulmonary edema, and end-stage kidney disease.

7. Case no. (b) (6) a 37 year-old female, died approximately two months after receiving a second 40 mcg dose of vaccine. The death was caused by sepsis, end-stage renal disease, acute respiratory distress syndrome, infected dialysis graft, and diabetes mellitus.

Table 1

Antibody Responses Among Dialysis Patients Following Vaccination with
20 or 40 mcg Doses of Yeast Recombinant Hepatitis B Vaccine
Lot 974/C-K446 * at 0, 1, and 6 Months in Study 816

Time (Months)	Dialysis Patients									
	20 mcg					40 mcg **				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
	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
1	8(2/26)	4(1/26)	0.4	5.4	18.5	15(4/26)	8(2/26)	0.6	8.1	17.9
3	21(5/24)	4(1/24)	0.6	6.5	76.1	52(13/25)	28(7/25)	2.3	15.0	32.9
6	33(8/24)	13(3/24)	1.0	6.4	21.7	81(13/16)	63(10/16)	10.8	21.5	35.2
7/8	59(17/29)	48(14/29)	7.8	69.1	118.6	94(16/17)	88(15/17)	219.7	331.8	445.5
12	52(15/29)	41(12/29)	5.1	49.2	79.9	81(17/21)	71(15/21)	41.6	107.9	165.6

* Two dialysis patients received a third 20 or 40 mcg dose of Lot 986/C-K733.

** Four dialysis patients (40 mcg dose) received 1.0 ml vaccine in the deltoid and 1.0 ml in the buttock. At 7/8 months, 25% (1/4) seroconverted (S/N ≥2.1) and developed protective levels of anti-HBs (mIU/ml ≥10). These four subjects are not included in the above summary.

2538I-11
1/22/86

00756

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (39 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	3 (7.9%)
PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
SORENESS	1 (2.6%)	1 (2.6%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (7.9%)
STIFFNESS/TIGHTNESS	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
SYSTEMIC	4 (10.5%)	3 (7.9%)	4 (10.5%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	9 (23.7%)
WHOLE BODY/GENERAL	1 (2.6%)	3 (7.9%)	3 (7.9%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	6 (15.8%)
CHILLS	0 (0.0%)	2 (5.3%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	3 (7.9%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	2 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.3%)
HEADACHE	1 (2.6%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.3%)
DIGESTIVE SYSTEM	1 (2.6%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	1 (2.6%)	1 (2.6%)	2 (5.3%)
DIARRHEA	1 (2.6%)	0 (0.0%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (2.6%)	1 (2.6%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (39 PATIENTS) - DOSE 1 — DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (2.6%)		1 (2.6%)
NERVOUS SYSTEM	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
VERTIGO/DIZZINESS	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
PSYCHIATRIC/BEHAVIORAL	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
INSOMNIA/DISTURBED SLEEP	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
PERSONS WITH COMPLAINTS	4 (10.5%)	4 (10.5%)	5 (13.2%)	2 (5.3%)	1 (2.6%)	1 (2.6%)		11 (28.9%)
PERSONS WITH NO COMPLAINTS	34 (89.5%)	34 (89.5%)	33 (86.8%)	36 (94.7%)	37 (97.4%)	37 (97.4%)		27 (71.1%)
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 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (34 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	1 (2.9%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	1 (2.9%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	1 (2.9%)
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	1 (2.9%)
PERSONS WITH NO COMPLAINTS	34 (100.0%)	34 (100.0%)	34 (100.0%)	34 (100.0%)	33 (97.1%)	34 (100.0%)	33 (97.1%)
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%)

00759

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)	1 (3.1%)	3 (9.4%)	4 (12.5%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
SENSATION OF WARMTH, GENERAL	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
INFECTIOUS SYNDROMES	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
INFLUENZA, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
RESPIRATORY	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	2 (6.3%)	2 (6.3%)
UPPER RESPIRATORY INFECT., NOS	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
BRONCHITIS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
NERVOUS SYSTEM	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
TREMOR	0 (0.0%)	0 (0.0%)	1 (3.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
PERSONS WITH COMPLAINTS	1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)	1 (3.1%)	3 (9.4%)	4 (12.5%)
PERSONS WITH NO COMPLAINTS	31 (96.9%)	30 (93.8%)	29 (90.6%)	29 (90.6%)	31 (96.9%)	29 (90.6%)	28 (87.5%)

00760

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (32 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%)

00761

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (1 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	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)		1 (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%)

00762

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (39 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	11 (29.7%)	11 (29.7%)	11 (29.7%)	11 (29.7%)	11 (31.4%)	11 (34.4%)		11 (29.7%)
< 99	14 (37.8%)	18 (48.6%)	19 (51.4%)	18 (48.6%)	16 (45.7%)	16 (50.0%)		8 (21.6%)
99 - 99.9	12 (32.4%)	7 (18.9%)	7 (18.9%)	7 (18.9%)	7 (20.0%)	4 (12.5%)		16 (43.2%)
100 - 100.9	0 (0.0%)	1 (2.7%)	0 (0.0%)	1 (2.7%)	1 (2.9%)	1 (3.1%)		2 (5.4%)
TEMPERATURE TAKEN	37 (94.9%)	37 (94.9%)	37 (94.9%)	37 (94.9%)	35 (89.7%)	32 (82.1%)		37 (94.9%)
TEMPERATURE NOT TAKEN	2 (5.1%)	2 (5.1%)	2 (5.1%)	2 (5.1%)	4 (10.3%)	7 (17.9%)		2 (5.1%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (34 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	15 (46.9%)	15 (45.5%)	15 (44.1%)	15 (45.5%)	15 (45.5%)	15 (46.9%)		15 (44.1%)
< 99	11 (34.4%)	15 (45.5%)	16 (47.1%)	16 (48.5%)	13 (39.4%)	16 (50.0%)		10 (29.4%)
99 - 99.9	6 (18.8%)	3 (9.1%)	3 (8.8%)	2 (6.1%)	5 (15.2%)	1 (3.1%)		9 (26.5%)
TEMPERATURE TAKEN	32 (94.1%)	33 (97.1%)	34 (100.0%)	33 (97.1%)	33 (97.1%)	32 (94.1%)		34 (100.0%)
TEMPERATURE NOT TAKEN	2 (5.9%)	1 (2.9%)	0 (0.0%)	1 (2.9%)	1 (2.9%)	2 (5.9%)		0 (0.0%)

00764

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0016
TREATMENT :
LOT NUMBER : CK446
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (32 PATIENTS) - DOSE 3 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
NORMAL	15 (50.0%)	15 (48.4%)	15 (50.0%)	15 (50.0%)	14 (45.2%)	14 (46.7%)		14 (45.2%)
< 99	11 (36.7%)	14 (45.2%)	11 (36.7%)	12 (40.0%)	13 (41.9%)	13 (43.3%)		7 (22.6%)
99 - 99.9	3 (10.0%)	2 (6.5%)	3 (10.0%)	2 (6.7%)	3 (9.7%)	2 (6.7%)		7 (22.6%)
100 - 100.9	1 (3.3%)	0 (0.0%)	1 (3.3%)	0 (0.0%)	1 (3.2%)	0 (0.0%)		1 (3.2%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)	0 (0.0%)	1 (3.3%)		2 (6.5%)
TEMPERATURE TAKEN	30 (93.8%)	31 (96.9%)	30 (93.8%)	30 (93.8%)	31 (96.9%)	30 (93.8%)		31 (96.9%)
TEMPERATURE NOT TAKEN	2 (6.3%)	1 (3.1%)	2 (6.3%)	2 (6.3%)	1 (3.1%)	2 (6.3%)		1 (3.1%)

00765

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (1 PATIENTS) - DOSE 3							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)		1 (100.0%)
TEMPERATURE TAKEN	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)		1 (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%)

00766

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (36 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	3 (8.3%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		4 (11.1%)
SORENESS	2 (5.6%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		3 (8.3%)
STIFFNESS/TIGHTNESS	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
ECCHYMOSIS	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
SYSTEMIC	2 (5.6%)	3 (8.3%)	5 (13.9%)	2 (5.6%)	4 (11.1%)	2 (5.6%)		8 (22.2%)
WHOLE BODY/GENERAL	2 (5.6%)	2 (5.6%)	3 (8.3%)	2 (5.6%)	3 (8.3%)	1 (2.8%)		6 (16.7%)
SENSATION OF WARMTH, GENERAL	1 (2.8%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
FATIGUE/WEAKNESS	1 (2.8%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	2 (5.6%)	0 (0.0%)		3 (8.3%)
MALAISE	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
HEADACHE	1 (2.8%)	2 (5.6%)	1 (2.8%)	1 (2.8%)	1 (2.8%)	0 (0.0%)		2 (5.6%)
LIGHTHEADED	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.8%)
ILLNESS, NOS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)		1 (2.8%)

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (36 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
RESPIRATORY	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	1 (2.8%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)	2 (5.6%)
MUSCLE CRAMPS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	1 (2.8%)
ARM PAIN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	1 (2.8%)	1 (2.8%)	2 (5.6%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	1 (2.8%)
VOMITING	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	1 (2.8%)
APPETITE INCREASED	0 (0.0%)	0 (0.0%)	1 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.8%)
PERSONS WITH COMPLAINTS	5 (13.9%)	4 (11.1%)	6 (16.7%)	2 (5.6%)	4 (11.1%)	2 (5.6%)	9 (25.0%)
PERSONS WITH NO COMPLAINTS	31 (86.1%)	32 (88.9%)	30 (83.3%)	34 (94.4%)	32 (88.9%)	34 (94.4%)	27 (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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (34 PATIENTS) - DOSE 2							
	DAYS POST VACCINATION							NUMBER WITH COMPLAINTS
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)		1 (2.9%)
ECCHYMOSIS	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)		1 (2.9%)
PERSONS WITH COMPLAINTS	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)	1 (2.9%)		1 (2.9%)
PERSONS WITH NO COMPLAINTS	33 (97.1%)	33 (97.1%)	33 (97.1%)	33 (97.1%)	33 (97.1%)	33 (97.1%)		33 (97.1%)
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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (24 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	1 (4.2%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.3%)
WHOLE BODY/GENERAL	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)
HEADACHE	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)
HAND CRAMPS	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.2%)
PERSONS WITH COMPLAINTS	1 (4.2%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.3%)
PERSONS WITH NO COMPLAINTS	23 (95.8%)	24 (100.0%)	23 (95.8%)	24 (100.0%)	24 (100.0%)	24 (100.0%)	22 (91.7%)
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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (1 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	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)	1 (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%)

00771

Table 5

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (36 PATIENTS) - DOSE 1							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	11 (33.3%)	11 (32.4%)	11 (31.4%)	11 (30.6%)	11 (31.4%)	11 (31.4%)		11 (30.6%)
< 99	17 (51.5%)	17 (50.0%)	17 (48.6%)	18 (50.0%)	21 (60.0%)	18 (51.4%)		12 (33.3%)
99 - 99.9	4 (12.1%)	4 (11.8%)	5 (14.3%)	6 (16.7%)	1 (2.9%)	5 (14.3%)		9 (25.0%)
100 - 100.9	1 (3.0%)	2 (5.9%)	2 (5.7%)	1 (2.8%)	2 (5.7%)	0 (0.0%)		3 (8.3%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)		1 (2.8%)
TEMPERATURE TAKEN	33 (91.7%)	34 (94.4%)	35 (97.2%)	36 (100.0%)	35 (97.2%)	35 (97.2%)		36 (100.0%)
TEMPERATURE NOT TAKEN	3 (8.3%)	2 (5.6%)	1 (2.8%)	0 (0.0%)	1 (2.8%)	1 (2.8%)		0 (0.0%)

00772

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (34 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	13 (43.3%)	13 (40.6%)	13 (40.6%)	13 (39.4%)	13 (43.3%)	13 (40.6%)		13 (39.4%)
< 99	10 (33.3%)	14 (43.8%)	15 (46.9%)	16 (48.5%)	16 (53.3%)	16 (50.0%)		11 (33.3%)
99 - 99.9	6 (20.0%)	4 (12.5%)	4 (12.5%)	4 (12.1%)	1 (3.3%)	3 (9.4%)		8 (24.2%)
100 - 100.9	1 (3.3%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (3.0%)
TEMPERATURE TAKEN	30 (88.2%)	32 (94.1%)	32 (94.1%)	33 (97.1%)	30 (88.2%)	32 (94.1%)		33 (97.1%)
TEMPERATURE NOT TAKEN	4 (11.8%)	2 (5.9%)	2 (5.9%)	1 (2.9%)	4 (11.8%)	2 (5.9%)		1 (2.9%)

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK446
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

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	14 (58.3%)	14 (60.9%)	14 (60.9%)	14 (60.9%)	14 (60.9%)	14 (58.3%)			14 (58.3%)
< 99	8 (33.3%)	8 (34.8%)	7 (30.4%)	6 (26.1%)	7 (30.4%)	9 (37.5%)			5 (20.8%)
99 - 99.9	2 (8.3%)	1 (4.3%)	2 (8.7%)	3 (13.0%)	2 (8.7%)	1 (4.2%)			5 (20.8%)
TEMPERATURE TAKEN	24 (100.0%)	23 (95.8%)	23 (95.8%)	23 (95.8%)	23 (95.8%)	24 (100.0%)			24 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	1 (4.2%)	1 (4.2%)	1 (4.2%)	1 (4.2%)	0 (0.0%)			0 (0.0%)

00774

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0816
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

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

00775

STUDY 825

PROGRAM:	Yeast Recombinant Hepatitis B Vaccine, Study 825
PURPOSE:	To evaluate antibody and clinical responses to a high dose (100 mcg) level of yeast recombinant hepatitis B vaccine among adult hemodialysis patients.
VACCINE:	Yeast Recombinant Hepatitis B Vaccine Lot #1005/C-L915 (100 mcg/ml)
PRIMARY INVESTIGATOR:	Harvey J. Alter, M.D. Chief, Immunology Section Clinical Center Blood Bank National Institutes of Health Bethesda, Maryland 20205
SECONDARY INVESTIGATOR:	Beverly Elder, R.N. Clinical Center Blood Bank National Institutes of Health Bethesda, Maryland 20205 Barry Strauch, M.D. Fairfax Dialysis Unit 8316 Arlington Blvd. Fairfax, Virginia 23022 James Shih, Ph.D. Clinical Center Blood Bank National Institutes of Health Bethesda, Maryland 20205
STUDY LOCATION:	Fairfax Dialysis Unit 8316 Arlington Boulevard Fairfax, Virginia 23022 Bio-Medical Applications of Annapolis 203 Ridgely Avenue Annapolis, Maryland 21401 Bio-Medical Applications of Washington 4905 Del Ray Avenue Bethesda, Maryland 10105

Study 825

DATE INITIATED: April 10, 1985

DATE COMPLETED: In progress

STUDY POPULATION: The study population consists of 75 - 100 adult hemodialysis patients of either sex (excluding pregnant women) who are negative for HBsAg, anti-HBs, anti-HBc and who have a normal ALT. Patients who have been shown to be nonresponders to three or more doses of plasma derived vaccine may be eligible for participation in the study. Dialysis patients must not be receiving any immunosuppressive therapy or be allergic to yeast.

PROCEDURE: Participants receive intramuscular injections of vaccine (100 mcg) on Day 0, 1 and 6 months. Study subjects are asked to record their temperature for five days after each injection and note any local or systemic complaints.

Blood specimens are obtained prior to vaccination, monthly for three months and at 6, 9, 12 and 24 months post initial injection. All specimens are assayed for anti-HBs, anti-HBc, HBsAg and ALT by Dr. Alter. Samples with an anti-HBs titer $\geq$ 25 mIU/ml may be tested to determine anti-a and anti-d activity. Samples may be tested for yeast antibody at MSDRL.

RESULTS: DIALYSIS PATIENTS:

100 mcg #Lot #1005/C-L915 at 0, 1 and 6 months.

1. Number Vaccinated:

Injection Number		
1	2	3
44	41	0

Study 825

RESULTS: (Cont.)

2. Serologic Results:

Serologic data are available for 28 study participants at 3 months. At that time, 68% (19/28) seroconverted (S/N ≥2.1) while 25% (7/28) developed protective levels of antibody. The GMT for all vaccinees was 4.4. Table 1 shows seroconversion rates and GMT's through 3 months of follow-up.

3. Clinical Complaints:

Clinical follow-up data is available for 44 and 39 participants following injections one and two, respectively. Specific complaints and maximum temperatures reported during the 5 days following these injections are provided in Tables 2 and 3.

Type of Complaint	Dose Level	Frequency in % by Injection No. 1	2	3
Injection Site	100 mcg	9(4/44)	8(3/39)	
Systemic	100 mcg	7(3/44)	0(0/39)	

There have been no serious or alarming adverse reactions attributable to vaccine.

ALT Elevations

Three subjects have had elevations of ALT ranging from 3-5 times the upper limit of normal. One of these elevations occurred one month after receiving the first dose of vaccine, was transient, and returned to normal within a month. The other two elevations occurred one to two months after receiving the first dose of vaccine. Both have remained elevated through three months of follow-up. No reason for these elevations have been discovered. The subjects have not shown any clinical or serologic signs (HBsAg or anti-HBc) of hepatitis B.

Study 825

RESULTS: (Cont.)

HBV Markers (anti-HBc)

Two subjects whose prevaccination sera were negative for anti-HBc had one or more positive serum samples post-vaccination. In the first case the positive anti-HBc occurred at 3 months and was transient. A 4-month sample was negative for anti-HBc. The subject has remained negative for anti-HBc through 6 months and has shown no other serologic or clinical signs of illness.

In the second case the positive anti-HBc occurred at 3 months. Samples taken at 4 and 6 months continued to be anti-HBc positive. The patient has been anti-HBs positive since 3 months. He has remained HBsAg negative and there has been no report of clinical illness. He continues to be closely monitored.

Reactions Reported to DoBRR

Case (b) (6) a 31 year old male hemodialysis patient with ESRD, diabetes mellitus and hypertension, died (b) (6) days after administration of his first injection of vaccine (100 mcg Lot 1005/C-L915) on (b) (6) No adverse effects due to vaccination were noted. The cause of death was reported as cardiac arrthymia secondary to end stage renal disease. The death was not related to vaccine.

Case (b) (6) a 73-year-old female, died on (b) (6) from cerebral vascular accident secondary to diabetes mellitus associated vascular disease. She had received two doses of 100 mc lot 1005/C-L915 on (b) (6). On (b) (6) the patient came for scheduled dialysis. While on dialysis, she complained of weakness on her left side. She was hospitalized until her death on (b) (6) The death is not considered to be vaccine related.

Table 1

ANTIBODY RESPONSES FOLLOWING VACCINATION WITH RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
POPULATION : DIALYSIS PATIENTS
DOSE : 100 MCG
LOT : CL915
REGIMEN : 0, 1, AND 6 MONTHS
INITIAL SEROLOGY: NEGATIVE

TIME (MONTHS)	% WITH ANTI-HBS				GMT (S/N)		
						RESPONDERS	
	S/N >= 2.1		S/N >= 10		ALL VACCINEES	S/N >= 2.1	S/N >= 10
1 MONTH	13%	(5/38)	0%	(0/38)	1.3	3.0	
2 MONTHS	37%	(14/38)	18%	(7/38)	2.5	10.2	26.9
3 MONTHS	68%	(19/28)	25%	(7/28)	4.4	8.4	33.3

Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
TREATMENT :
LOT NUMBER : CL915
DOSE : 100 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (44 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
REACTION, LOCAL (INJECT. SITE)	1 (2.3%)	2 (4.5%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (4.5%)		4 (9.1%)
SORENESS	1 (2.3%)	2 (4.5%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	2 (4.5%)		4 (9.1%)
STIFFNESS/TIGHTNESS	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
SYSTEMIC	1 (2.3%)	2 (4.5%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		3 (6.8%)
WHOLE BODY/GENERAL	1 (2.3%)	2 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (4.5%)
FATIGUE/WEAKNESS	1 (2.3%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
OTHER	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
PHARYNGITIS (SORE THROAT)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.3%)		1 (2.3%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)
ARTHRALGIA (OTHER)	0 (0.0%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.3%)

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
TREATMENT :
LOT NUMBER : CL915
DOSE : 100 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (44 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH COMPLAINTS	2 (4.5%)	4 (9.1%)	2 (4.5%)	1 (2.3%)	1 (2.3%)	3 (6.8%)	7 (15.9%)
PERSONS WITH NO COMPLAINTS	42 (95.5%)	40 (90.9%)	42 (95.5%)	43 (97.7%)	43 (97.7%)	41 (93.2%)	37 (84.1%)
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%)

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Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
TREATMENT :
LOT NUMBER : CL915
DOSE : 100 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (41 PATIENTS) - DOSE 2						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
REACTION, LOCAL (INJECT. SITE)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	3 (7.7%)
INFLAMMATION	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (2.6%)
SORENESS	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	2 (5.1%)
ERYTHEMA (REDNESS)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (2.6%)
PRURITIS (ITCHING)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (2.6%)	1 (2.6%)
PERSONS WITH COMPLAINTS	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	3 (7.7%)
PERSONS WITH NO COMPLAINTS	38 (97.4%)	38 (97.4%)	38 (97.4%)	38 (97.4%)	38 (97.4%)	38 (97.4%)	36 (92.3%)
PERSONS WITH NO DATA	1 (2.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)

Table 3

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
TREATMENT :
LOT NUMBER : CL915
DOSE : 100 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (44 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
NORMAL	1 (2.4%)	1 (2.7%)	1 (2.4%)	1 (2.6%)	1 (2.4%)	1 (2.8%)			1 (2.3%)
< 99	34 (81.0%)	31 (83.8%)	39 (92.9%)	31 (81.6%)	37 (90.2%)	29 (80.6%)			27 (62.8%)
99 - 99.9	7 (16.7%)	5 (13.5%)	2 (4.8%)	4 (10.5%)	3 (7.3%)	5 (13.9%)			12 (27.9%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.3%)	0 (0.0%)	1 (2.8%)			3 (7.0%)
TEMPERATURE TAKEN	42 (95.5%)	37 (84.1%)	42 (95.5%)	38 (86.4%)	41 (93.2%)	36 (81.8%)			43 (97.7%)
TEMPERATURE NOT TAKEN	2 (4.5%)	7 (15.9%)	2 (4.5%)	6 (13.6%)	3 (6.8%)	8 (18.2%)			1 (2.3%)

Table 3 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0825
TREATMENT :
LOT NUMBER : CL915
DOSE : 100 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (41 PATIENTS) - DOSE 2							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
NORMAL	0 (0.0%)	1 (2.9%)	1 (2.9%)	1 (3.0%)	1 (2.9%)	1 (2.9%)		0 (0.0%)
< 99	23 (74.2%)	29 (85.3%)	30 (85.7%)	30 (90.9%)	29 (82.9%)	33 (94.3%)		25 (64.1%)
99 - 99.9	7 (22.6%)	4 (11.8%)	4 (11.4%)	2 (6.1%)	5 (14.3%)	1 (2.9%)		13 (33.3%)
100 - 100.9	1 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
TEMPERATURE TAKEN	31 (75.6%)	34 (82.9%)	35 (85.4%)	33 (80.5%)	35 (85.4%)	35 (85.4%)		39 (95.1%)
TEMPERATURE NOT TAKEN	10 (24.4%)	7 (17.1%)	6 (14.6%)	8 (19.5%)	6 (14.6%)	6 (14.6%)		2 (4.9%)

00785

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)

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Study 838

SECONDARY INVESTIGATORS: (Cont.)

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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	10 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:

DIALYSIS PATIENTS:

40 mcg Lot #986/C-K733 at 0, 1, and 6 months
40 mcg Lot #986/C-K733 at 0, 1, 2, 3, 4, and 6 months
20 mcg Lot #986/C-K733 at 0, 1, 2, 3, 4, and 6 months

1. Number Vaccinated:

Regimen	Injection No. 1	2	3	4	5	6
3 x 40 mcg	51	51	48			
6 x 40 mcg	20	20	20	19	19	17
6 x 20 mcg	20	20	20	20	20	17

Note: All vaccine was administered into the buttock.

2. Serologic Results:

Serologic data are available for 36 participants at 7/8 months who received three 40 mcg injections of vaccine at 0, 1, and 6 months. Seroconversion (S/N $\geq$2.1) for anti-HBs at that time was 64% (23/36). Fifty-eight percent (21/36) of the patients developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT at 7/8 months for all vaccinees was 12.3 mIU/ml and 115.5 for responders (mIU/ml $\geq$10).

Serology data are available for 15 patients at 10 months who received six 40 mcg injections of vaccine at 0, 1, 2, 3, 4, and 6 months. Seroconversion (S/N $\geq$2.1) for anti-HBs at that time was 67% (10/15). Sixty percent (9/15) developed protective levels of anti-HBs (mIU/ml $\geq$10). The GMT at ten months for all vaccinees was 6.7 mIU/ml and 27.7 for responders(mIU/ml $\geq$10).

Eighteen subjects who received six 20 mcg injections of vaccine at 0, 1, 2, 3, 4, and 6 months, have serology data available for the ten month follow-up interval. Fifty percent (9/18) of the patients seroconverted for anti-HBs (S/N $\geq$2.1)

Study 838

RESULTS (CONT.): at that time. Forty-four percent (8/18) developed protective levels of anti-HBs (mIU/ml ≥10). The GMT at ten months for all vaccinees was 4.7 mIU/ml and 55.0 for responders(mIU/ml ≥10).

Refer to Table 1 for anti-HBs responses and GMTs, by dose regimen, for other time intervals.

3. Clinical Complaints:

Clinical follow-up data are available for at least 38, 16, and 17 participants after each injection in the 3 x 40 mcg, 6 x 40 mcg, and 6 x 20 mcg dose regimens, respectively. The overall frequencies of complaints are presented below.

Type of Complaint	Regimen	Frequency in % by Injection					
		1	2	3	4	5	6
Injection Site	3 x 40 mcg	0(0/51)	0(0/49)	0(0/38)			
	6 x 40 mcg	0(0/20)	0(0/20)	0(0/20)	0(0/19)	0(0/19)	0(0/16)
	6 x 20 mcg	0(0/20)	0(0/20)	5(1/20)	0(0/20)	0(0/20)	0(0/17)
Systemic	3 x 40 mcg	8(4/51)	0(0/49)	3(1/38)			
	6 x 40 mcg	15(3/20)	10(2/20)	15(3/20)	16(3/19)	0(0/19)	0(0/16)
	6 x 20 mcg	5(1/20)	10(2/20)	5(1/20)	5(1/20)	0(0/20)	0(0/17)

Refer to Tables 2 through 4 for listings of specific clinical complaints by dose regimen and injection number. Maximum temperature data are provided in Tables 5 through 7.

HBV Markers (Anti-HBc)

One patient enrolled in the 3 x 40 mcg group was anti-HBc positive and had an ALT level approximately 1.5 times the upper limit of normal prior to vaccination. He has remained anti-HBc positive post-vaccination. Post-vaccination ALT levels have not been ascertained. All pre- and post-vaccination samples were negative for HBsAg. There has been no report of illness in this subject. The patient has not developed protective levels of anti-HBs (mIU/ml ≥10).

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RESULTS (CONT.):

A patient in the 3 x 40 mcg group was anti-HBc positive prior to vaccination. In all subsequent post-vaccination samples, she was negative for anti-HBc. The subject developed protective levels of anti-HBs (mIU/ml ≥10) at two months after the second injection.

A male dialysis patient in the 6 x 20 mcg group became positive for anti-HBc one month after the sixth injection of vaccine. He was HBsAg negative. The subject had developed protective levels of anti-HBs (mIU/ml ≥10) at the time of his fourth injection with a titer of 29 mIU/ml. One month after the sixth injection his anti-HBs titer was 438 mIU/ml. There has been no report of illness in this patient.

Reactions Reported to the OoBRR

A 70-year old male with a history of coronary artery disease and end stage renal disease died of a myocardial infarction (b) (6) days after receiving the fifth injection of vaccine (6 x 40 mcg group). His death was not considered to be vaccine related.

A 46-year old male dialysis patient with a history of diabetes mellitus and diabetic nephropathy, died two months after administration of his third injection of vaccine (3 x 40 mcg group). Death was due to cardiac arrest secondary to hyperkalemia and was not considered vaccine related.

PUBLICATIONS:

Mueller R, Bommer J, Braas H, Deinhardt A, Jilg W, Kuttler G, et al. Erste erfahrungen mit rekombinanter hepatitis B-vaccine bei patienten unter chronischer haemodialyse-behandlung. Gastroenterol 1985; 23: 297.

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RESULTS (CONT.): PREDIALYSIS PATIENTS:

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

1. Number Vaccinated:

Injection No.		
1	2	3
8	8	0

2. Serologic Results:

One month serology data are available for all eight vaccinees. Anti-HBs responses at that time are summarized below:

% with Anti-HBs		GMT (mIU/ml)		
			Responders	
S/N ≥2.1	mIU/ml ≥10	All Vaccinees	S/N ≥2.1	mIU/ml ≥10
13(1/8)	0(0/8)	0.7	4.6	---

3. Clinical Complaints:

Clinical follow-up data are available for eight participants after the first injection. There were no clinical complaints or temperature elevations. No serious or alarming adverse experiences attributable to vaccine have been reported.

Table 1

Antibody Responses Among Dialysis Patients Following Vaccination with
Yeast Recombinant Hepatitis B Vaccine Lot # 986/C-K733 in Study #838

	40 mcg at 0, 1, and 6 Months					40 mcg at 0, 1, 2, 3, 4, and 6 Months*					20 mcg at 0, 1, 2, 3, 4, and 6 Months*				
	% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)			% with Anti-HBs		GMT (mIU/ml)		
				Responders					Responders					Responders	
Time (Mos.)	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10	S/N≥2.1	mIU/ml ≥ 10	All Vaccinees	S/N≥2.1	mIU/ml ≥ 10
1	0 (0/48)	0 (0/48)	0.3	---	---	0 (0/20)	0 (0/20)	0.3	---	---	0 (0/20)	0 (0/20)	0.3	---	---
2	30 (14/46)	13 (6/46)	0.9	---	---	21 (4/19)	5 (1/19)	0.6	10.0	50.0	15 (3/20)	10 (2/20)	0.5	16.5	25.0
3	35 (16/46)	22 (10/46)	1.3	16.5	31.0	35 (7/20)	20 (4/20)	1.2	17.4	33.5	32 (6/19)	26 (5/19)	1.2	23.6	31.4
6	34 (12/35)	29 (10/35)	1.4	26.1	33.8	69 (11/16)	69 (11/16)	32.2	189.8	189.8	56 (9/16)	44 (7/16)	9.7	87.3	190.0
7/8	64 (23/36)	58 (21/36)	12.3	90.2	115.5	---	--	----	-----	-----	—	--	---	----	-----
10	65 (24/37)	54 (20/37)	12.8	73.8	117.6	67 (10/15)	60 (9/15)	6.7	24.5	27.7	50 (9/18)	44 (8/18)	4.7	45.0	55.0

*Dose scheduled at 6 months was actually administered at 5 months in most cases.

NOTE: All injections were into the buttock.

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1/3/86

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Table 2

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (51 PATIENTS) - DOSE 1 — DAYS POST VACCINATION 0	1	2	3	4	5	NUMBER WITH COMPLAINTS
SYSTEMIC	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)	0 (0.0%)	4 (7.8%)
WHOLE BODY/GENERAL	1 (2.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.9%)
CHILLS	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
LIGHTHEADED	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
CARDIOVASCULAR	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
OTHER	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)
NERVOUS SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.0%)	0 (0.0%)	1 (2.0%)
VERTIGO/DIZZINESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.0%)	0 (0.0%)	1 (2.0%)
PERSONS WITH COMPLAINTS	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)	1 (2.0%)	0 (0.0%)	4 (7.8%)
PERSONS WITH NO COMPLAINTS	50 (98.0%)	50 (98.0%)	(98.0%)	50 (98.0%)	50 (98.0%)	51 (100.0%)	47 (92.2%)
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%)

* Three injection regimen

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (51 PATIENTS) - DOSE 2							
	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	49 (100.0%)	49 (100.0%)	49 (100.0%)	49 (100.0%)	49 (100.0%)	49 (100.0%)		49 (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%)

00795

Table 2 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (48 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1		3	4	5		
SYSTEMIC	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
CARDIOVASCULAR	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
HYPERTENSION	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
DIGESTIVE SYSTEM	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
NAUSEA	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
PERSONS WITH COMPLAINTS	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (2.6%)
PERSONS WITH NO COMPLAINTS	37 (97.4%)	38 (100.0%)	38 (100.0%)	38 (100.0%)	38 (100.0%)	38 (100.0%)		37 (97.4%)
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 CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	2 (10.0%)	2 (10.0%)	2 (10.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)
WHOLE BODY/GENERAL	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)
FATIGUE/WEAKNESS	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)
CARDIOVASCULAR	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
OTHER	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
MUSCULOSKELETAL	0 (0.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
ARTHRALGIA (OTHER)	0 (0.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	2 (10.0%)	2 (10.0%)	2 (10.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)
PERSONS WITH NO COMPLAINTS	18 (90.0%)	18 (90.0%)	18 (90.0%)	19 (95.0%)	18 (90.0%)	19 (95.0%)		17 (85.0%)
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%)

* Six injection regimen

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
SYSTEMIC	0 (0.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)		2 (10.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)		2 (10.0%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	1 (5.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)		2 (10.0%)
HEADACHE	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)		2 (10.0%)
PERSONS WITH NO COMPLAINTS	20 (100.0%)	19 (95.0%)	19 (95.0%)	18 (90.0%)	20 (100.0%)	20 (100.0%)		18 (90.0%)
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%)

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Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 3 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
SYSTEMIC	1 (5.0%)	1 (5.0%)	2 (10.0%)	3 (15.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		3 (15.0%)
FEVER (TEMP. NOT REPORTED)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
HEADACHE	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
ILLNESS, NOS	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
MUSCULOSKELETAL	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)		1 (5.0%)
ARTHRALGIA (OTHER)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)		1 (5.0%)
DIGESTIVE SYSTEM	1 (5.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		3 (15.0%)
ABDOMINAL PAINS/CRAMPS	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
NAUSEA	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		2 (10.0%)
PERSONS WITH COMPLAINTS	1 (5.0%)	1 (5.0%)	2 (10.0%)	3 (15.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)

Table 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 3						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
PERSONS WITH NO COMPLAINTS	19 (95.0%)	19 (95.0%)	18 (90.0%)	17 (85.0%)	18 (90.0%)	19 (95.0%)	17 (85.0%)
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 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (19 PATIENTS) - DOSE 4							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	1 (5.3%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	2 (10.5%)		3 (15.8%)
WHOLE BODY/GENERAL	1 (5.3%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	2 (10.5%)		3 (15.8%)
CHILLS	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)		1 (5.3%)
FATIGUE/WEAKNESS	1 (5.3%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	1 (5.3%)		2 (10.5%)
RESPIRATORY	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)		1 (5.3%)
COUGH	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)		1 (5.3%)
PERSONS WITH COMPLAINTS	1 (5.3%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	2 (10.5%)		3 (15.8%)
PERSONS WITH NO COMPLAINTS	18 (94.7%)	19 (100.0%)	18 (94.7%)	18 (94.7%)	18 (94.7%)	17 (89.5%)		16 (84.2%)
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 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (19 PATIENTS) - DOSE 5						
	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	19 (100.0%)	19 (100.0%)	19 (100.0%)	19 (100.0%)	19 (100.0%)	19 (100.0%)	19 (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 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (17 PATIENTS) - DOSE 6						
	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	16 (100.0%)	16 (100.0%)	16 (100.0%)	16 (100.0%)	16 (100.0%)	16 (100.0%)	16 (100.0%)
PERSONS WITH NO DATA	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)

Table 4

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 1						
	DAYS POST VACCINATION						NUMBER WITH COMPLAINTS
	0	1	2	3	4	5	
SYSTEMIC	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)
PERSONS WITH NO COMPLAINTS	20 (100.0%)	19 (95.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	19 (95.0%)	19 (95.0%)
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%)

* Six injection regimen

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 2							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)		2 (10.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
HEADACHE	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
LIGHTHEADED	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
DIGESTIVE SYSTEM	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)		2 (10.0%)
DIARRHEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)		1 (5.0%)
NAUSEA	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)		2 (10.0%)
PERSONS WITH NO COMPLAINTS	20 (100.0%)	19 (95.0%)	20 (100.0%)	20 (100.0%)	19 (95.0%)	20 (100.0%)		18 (90.0%)
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
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 3							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
REACTION, LOCAL (INJECT. SITE)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PRURITIS (ITCHING)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
SYSTEMIC	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (5.0%)		1 (5.0%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
FATIGUE/WEAKNESS	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
CARDIOVASCULAR	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
HYPOTENSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)		1 (5.0%)
NAUSEA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	1 (5.0%)		2 (10.0%)
PERSONS WITH NO COMPLAINTS	19 (95.0%)	20 (100.0%)	20 (100.0%)	19 (95.0%)	20 (100.0%)	19 (95.0%)		18 (90.0%)
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
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 4 — DAYS POST VACCINATION 0	1	2	3	4	5		NUMBER WITH COMPLAINTS
SYSTEMIC	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
FATIGUE/WEAKNESS	0 (0.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
MUSCULOSKELETAL	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
ARTHRALGIA (OTHER)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
DIGESTIVE SYSTEM	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
DIMINISHED APPETITE	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PSYCHIATRIC/BEHAVIORAL	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
DEPRESSION	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PERSONS WITH COMPLAINTS	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
PERSONS WITH NO COMPLAINTS	19 (95.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)	20 (100.0%)	20 (100.0%)		19 (95.0%)
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%)

00807

Table 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (20 PATIENTS) - DOSE 5							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	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	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)		20 (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 4 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

CLINICAL COMPLAINTS	TOTAL VACCINEES (17 PATIENTS) - DOSE 6							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	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 5

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (51 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	47 (92.2%)	46 (90.2%)	48 (94.1%)	48 (94.1%)	46 (92.0%)	43 (95.6%)			39 (76.5%)
99 - 99.9	3 (5.9%)	3 (5.9%)	3 (5.9%)	1 (2.0%)	4 (8.0%)	2 (4.4%)			10 (19.6%)
100 - 100.9	1 (2.0%)	2 (3.9%)	0 (0.0%)	2 (3.9%)	0 (0.0%)	0 (0.0%)			2 (3.9%)
TEMPERATURE TAKEN	51 (100.0%)	51 (100.0%)	51 (100.0%)	51 (100.0%)	50 (98.0%)	45 (88.2%)			51 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	6 (11.8%)			0 (0.0%)

* Three injection regimen

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (51 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	46 (95.8%)	46 (95.8%)	45 (93.8%)	42 (87.5%)	48 (100.0%)	45 (100.0%)			40 (83.3%)
99 - 99.9	2 (4.2%)	2 (4.2%)	3 (6.3%)	6 (12.5%)	0 (0.0%)	0 (0.0%)			8 (16.7%)
TEMPERATURE TAKEN	48 (94.1%)	48 (94.1%)	48 (94.1%)	48 (94.1%)	48 (94.1%)	45 (88.2%)			48 (94.1%)
TEMPERATURE NOT TAKEN	3 (5.9%)	3 (5.9%)	3 (5.9%)	3 (5.9%)	3 (5.9%)	6 (11.8%)			3 (5.9%)

00811

Table 5 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (48 PATIENTS) - DOSE 3								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	35 (92.1%)	36 (94.7%)	38 (100.0%)	38 (100.0%)	38 (100.0%)	38 (100.0%)			33 (86.8%)
99 - 99.9	2 (5.3%)	2 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			4 (10.5%)
101 - 101.9	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (2.6%)
TEMPERATURE TAKEN	38 (79.2%)	38 (79.2%)	38 (79.2%)	38 (79.2%)	38 (79.2%)	38 (79.2%)			38 (79.2%)
TEMPERATURE NOT TAKEN	10 (20.8%)	10 (20.8%)	10 (20.8%)	10 (20.8%)	10 (20.8%)	10 (20.8%)			10 (20.8%)

Table 6

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	17 (85.0%)	18 (90.0%)	18 (90.0%)	17 (85.0%)	17 (85.0%)	18 (90.0%)			13 (65.0%)
99 - 99.9	3 (15.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	3 (15.0%)	1 (5.0%)			5 (25.0%)
100 - 100.9	0 (0.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	1 (5.0%)			2 (10.0%)
TEMPERATURE TAKEN	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)			20 (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%)

* Six injection regimen

Table 6 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 2 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	17 (89.5%)	15 (78.9%)	16 (88.9%)	14 (82.4%)	16 (88.9%)	17 (100.0%)			13 (68.4%)
99 - 99.9	2 (10.5%)	3 (15.8%)	1 (5.6%)	3 (17.6%)	2 (11.1%)	0 (0.0%)			5 (26.3%)
100 - 100.9	0 (0.0%)	1 (5.3%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.3%)
TEMPERATURE TAKEN	19 (95.0%)	19 (95.0%)	18 (90.0%)	17 (85.0%)	18 (90.0%)	17 (85.0%)			19 (95.0%)
TEMPERATURE NOT TAKEN	1 (5.0%)	1 (5.0%)	2 (10.0%)	3 (15.0%)	2 (10.0%)	3 (15.0%)			1 (5.0%)

00814

Table 6 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 3 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
< 99	17 (89.5%)	16 (84.2%)	18 (94.7%)	18 (94.7%)	17 (94.4%)	17 (94.4%)			16 (84.2%)
99 - 99.9	2 (10.5%)	3 (15.8%)	1 (5.3%)	1 (5.3%)	1 (5.6%)	0 (0.0%)			2 (10.5%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)			1 (5.3%)
TEMPERATURE TAKEN	19 (95.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)	18 (90.0%)	18 (90.0%)			19 (95.0%)
TEMPERATURE NOT TAKEN	1 (5.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	2 (10.0%)			1 (5.0%)

Table 6 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (19 PATIENTS) - DOSE 4 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	18 (100.0%)	16 (88.9%)	18 (100.0%)	15 (83.3%)	16 (88.9%)	17 (94.4%)			15 (83.3%)
99 - 99.9	0 (0.0%)	2 (11.1%)	0 (0.0%)	3 (16.7%)	2 (11.1%)	1 (5.6%)			3 (16.7%)
TEMPERATURE TAKEN	18 (94.7%)	18 (94.7%)	18 (94.7%)	18 (94.7%)	18 (94.7%)	18 (94.7%)			18 (94.7%)
TEMPERATURE NOT TAKEN	1 (5.3%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	1 (5.3%)			1 (5.3%)

Table 6 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (19 PATIENTS) - DOSE 5								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	16 (94.1%)	16 (88.9%)	17 (100.0%)	17 (100.0%)	17 (100.0%)	17 (100.0%)			16 (88.9%)
99 - 99.9	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.6%)
100 - 100.9	1 (5.9%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.6%)
TEMPERATURE TAKEN	17 (89.5%)	18 (94.7%)	17 (89.5%)	17 (89.5%)	17 (89.5%)	17 (89.5%)			18 (94.7%)
TEMPERATURE NOT TAKEN	2 (10.5%)	1 (5.3%)	2 (10.5%)	2 (10.5%)	2 (10.5%)	2 (10.5%)			1 (5.3%)

Table 6 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 40 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (17 PATIENTS) - DOSE 6								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	13 (86.7%)	14 (93.3%)	15 (100.0%)	14 (93.3%)	14 (93.3%)	14 (100.0%)			13 (86.7%)
99 - 99.9	1 (6.7%)	0 (0.0%)	0 (0.0%)	1 (6.7%)	1 (6.7%)	0 (0.0%)			1 (6.7%)
100 - 100.9	1 (6.7%)	1 (6.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (6.7%)
TEMPERATURE TAKEN	15 (88.2%)	15 (88.2%)	15 (88.2%)	15 (88.2%)	15 (88.2%)	14 (82.4%)			15 (88.2%)
TEMPERATURE NOT TAKEN	2 (11.8%)	2 (11.8%)	2 (11.8%)	2 (11.8%)	2 (11.8%)	3 (17.6%)			2 (11.8%)

Table 7

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG *
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	15 (83.3%)	16 (88.9%)	16 (88.9%)	17 (94.4%)	17 (94.4%)	16 (88.9%)			14 (77.8%)
99 - 99.9	3 (16.7%)	2 (11.1%)	2 (11.1%)	1 (5.6%)	1 (5.6%)	1 (5.6%)			3 (16.7%)
100 - 100.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)			1 (5.6%)
TEMPERATURE TAKEN	18 (90.0%)	18 (90.0%)	18 (90.0%)	18 (90.0%)	18 (90.0%)	18 (90.0%)			18 (90.0%)
TEMPERATURE NOT TAKEN	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)	2 (10.0%)			2 (10.0%)

* Six injection regimen

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	18 (94.7%)	19 (100.0%)	19 (100.0%)	18 (100.0%)	19 (100.0%)	19 (100.0%)			18 (94.7%)
99 - 99.9	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.3%)
TEMPERATURE TAKEN	19 (95.0%)	19 (95.0%)	19 (95.0%)	18 (90.0%)	19 (95.0%)	19 (95.0%)			19 (95.0%)
TEMPERATURE NOT TAKEN	1 (5.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)	1 (5.0%)			1 (5.0%)

Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 3 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
< 99	18 (90.0%)	19 (95.0%)	17 (85.0%)	19 (95.0%)	19 (95.0%)	19 (95.0%)		15 (75.0%)
99 - 99.9	2 (10.0%)	1 (5.0%)	3 (15.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)		5 (25.0%)
TEMPERATURE TAKEN	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)		20 (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 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 4 — DAYS POST VACCINATION							NUMBER WITH MAX TEMP
	0	1	2	3	4	5		
< 99	19 (95.0%)	19 (95.0%)	19 (95.0%)	18 (90.0%)	20 (100.0%)	20 (100.0%)		16 (80.0%)
99 - 99.9	1 (5.0%)	0 (0.0%)	1 (5.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)		3 (15.0%)
100 - 100.9	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (5.0%)
TEMPERATURE TAKEN	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)		20 (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 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (20 PATIENTS) - DOSE 5 — DAYS POST VACCINATION 0	1	2	3	4	5			NUMBER WITH MAX TEMP
< 99	20 (100.0%)	20 (100.0%)	19 (95.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)			19 (95.0%)
99 - 99.9	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			1 (5.0%)
TEMPERATURE TAKEN	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)			20 (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%)

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Table 7 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0838
TREATMENT :
LOT NUMBER : CK733
DOSE : 20 MCG
PATIENT CLASS: DIALYSIS PATIENTS

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (17 PATIENTS) - DOSE 6							NUMBER WITH MAX TEMP
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
< 99	15 (93.8%)	15 (93.8%)	16 (100.0%)	16 (100.0%)	16 (100.0%)	15 (93.8%)		13 (81.3%)
99 - 99.9	1 (6.3%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (6.3%)		3 (18.8%)
TEMPERATURE TAKEN	16 (94.1%)	16 (94.1%)	16 (94.1%)	16 (94.1%)	16 (94.1%)	16 (94.1%)		16 (94.1%)
TEMPERATURE NOT TAKEN	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)	1 (5.9%)		1 (5.9%)

Erste Erfahrungen mit rekombinanter Hepatitis B-Vaccine bei Patienten unter chronischer Haemodialyse-Behandlung.

R. Müller[1], J. Bommer[2], H. Braas[3], F. Deinhardt[4], A. Feuerhake[1], W. Jilg[4], G. Küttler[3], B. Weinel[3], Abteilung für Gastroenterologie und Hepatologie, Medizinische Hochschule Hannover[1]; Sektion Nephrologie, Medizinische Klinik Universität Heidelberg[2]; Medizinische Klinik II, Städt. Krankenanstalten Ludwigshafen[3]; Max von Pettenkofer Institut der Ludwig-Maximilian-Universität München[4].

Die Immunogenität natürlicher, aus Humanplasma gewonnener Hepatitis B-Vaccine hat sich bei endogen oder exogen immunsupprimierten Patienten beträchtlich schwächer erwiesen als bei gesunden Personen. Es erschien daher interessant zu prüfen, ob nach Impfung mit einer gentechnologisch gewonnenen HB-Vaccine bei chronischen Haemodialyse-Patienten höhere Seronkonversionsraten für anti-HB, erzielt werden können als mit natürlichem HB-Impfstoff. 51 HBV empfängliche Patienten unter chronischer Haemodialyse-Behandlung erhielten 3 Impfungen mit je 40 ug Hb,Ag Protein, das in einem DNS-rekombiniertem Stamm der Hefe Saccharomyces cerovisiae hergestellt wurde (Hepatitis B-Vaccine [recombinant] MSD, Westpoint USA; Lot 934/C-J625). Die zweite und dritte Impfung erfolgten einen bzw. 6 Monate nach der ersten Impfung. Einen Monat nach der 2. Impfung hatten 20 von 48 (42%) der Patienten anti-HB, gebildet. Der mittlere Antikörper-Gehalt betrug 24,7 IU/ml. Bei 21 Patienten ist das Impfprogramm abgeschlossen, 13 von ihnen wiesen im 7. Monat nach Impfbeginn eine Serokonversion nach anti-HB, auf. Der mittlere anti-HB,-Gehalt war auf 151 IU/ml angestiegen. Danach lassen sich bei Dialyse-Patienten mit rekombinat hergestellter HB-Vaccine ähnliche Serokonversionsraten erzielen wie mit HB-Impfstoff, der aus Humanplasma gewonnen wurde.

Muller R, Bommer J, Brass H, Deinhardt A, Jilg W, Kuttler G, et al. Erste erfahrungen mit rekombinanter hepatitis B-vaccine bei patienten unter chronischer haemodialyse-behandlung. Gastroenterol 1985; 23:297.

NOTE: There is no missing material. There was an error in numbering.

Janurary 1986

REPORT NO. 3

in Support for a License Application for

RECOMBIVAX

(Yeast Recombinant Hepatitis B Vaccine, MSD)

CLINICAL DATA*

VOLUME 3 OF 3

Merck Sharp & Dohme Research Laboratories

MENTALLY RETARDED

SUMMARY - MENTALLY RETARDED INDIVIDUALS

Two studies (Study 815 and 889) are being conducted to evaluate antibody and clinical responses to yeast recombinant hepatitis B vaccine among institutionalized mentally retarded individuals who are negative for hepatitis B virus serologic markers. Mentally retarded individuals receive three 10 or 20 mcg doses of yeast recombinant vaccine (Study 815 and 889) or three 20 mcg doses of plasma-derived vaccine (Study 815) at 0, 1, and 6 months.

A total of 200 mentally retarded individuals have completed a three injection regimen of vaccination. No serious or alarming adverse reactions attributable to vaccine have been reported.

Serologic data after one injection of vaccine are available for 201 individuals. At one month 19-20% of vaccine recipients who received either one 10 or 20 mcg dose had detectable antibody (S/N $\geq$2.1). Titers of at least 10 mIU/ml occurred in 8% (10 mcg dose) and 11% (20 mcg dose) of vaccine recipients at this time. Among mentally retarded individuals with a minimum titer of S/N $\geq$2.1, the geometric mean titers were 8.7 mIU/ml (10 mcg dose) and 13.7 mIU/ml (20 mcg dose). Geometric mean titers for responders with antibody levels of mIU/ml $\geq$10 were 19.9 mIU/ml (10 mcg dose) and 38.7 mIU/ml (20 mcg dose).

Clinical data are available on 201 mentally retarded individuals after two injections of vaccine. The vaccine has been very well tolerated in this population with very few clinical complaints reported. No injection site reactions were reported following either the first or second injection. Systemic complaints were reported in 2% of vaccine recipients following the initial 10 mcg dose and 1% vaccine recipients following the initial 20 mcg dose of vaccine. No systemic complaints were reported after the second injection.

MENTALLY RETARDED INDIVIDUALS

Study 815 - The Netherlands - Dr. S. Schalm

The study population consists of institutionalized mentally retarded individuals and health care personnel. Mentally retarded individuals and health care personnel receive either three 10 or 20 mcg doses of yeast recombinant hepatitis B vaccine lot 993/C-K937 or three 20 mcg doses of plasma-derived vaccine lot 2277K at 0, 1, and 6 months. Vaccination and clinical follow-up continues in progress.

Study 889 - St. Louis, MO - Dr. R. Perrillo

The study population consists of institutionalized mentally retarded individuals and health care personnel. Mentally retarded individuals receive three 10 or 20 mcg doses of yeast recombinant hepatitis B vaccine lot 993/C-K937 at 0, 1, and 6 months. Health care personnel receive 10 mcg doses of vaccine according to the same regimen.

One hundred mentally retarded individuals have received three 10 mcg doses of vaccine. At one month 19% (19/101) participants seroconverted (S/N $\geq$2.1) and 8% (8/101) developed protective levels of antibody (mIU/ml $\geq$10). The geometric mean titer for responders with antibody $\geq$10 mIU/ml was 19.9 mIU/ml.

One hundred mentally retarded individuals have received three 20 mcg doses of vaccine. At one month the seroconversion rate (S/N $\geq$2.1) was 20% (20/100) with 11% (11/100) developing protective levels of antibody (mIU/ml $\geq$10). Responders with titers of at least 10 mIU/ml had a geometric mean titer of 38.7 mIU/ml.

No serious or alarming adverse reactions attributable to vaccine have been reported. The study continues in progress.

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

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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.

PROGRAM:	Alum-Adsorbed Yeast Recombinant Hepatitis B Vaccine, Study 889
PURPOSE:	To evaluate antibody and clinical responses to yeast recombinant 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:	Yeast Recombinant Hepatitis B Vaccine Lot 993/C-K937 (20 mcg/HBsAg/ml)
PRIMARY INVESTIGATOR:	Robert P. Perrillo, M.D. Director, Gastroenterology Veterans Administration Medical Center St. Louis, Missouri 63125
SECONDARY INVESTIGATOR:	Oliver H. Lowry, M.D. Department of Pharmacology Washington Univ. School of Medicine St. Louis, Missouri 63110
STUDY LOCATION:	Beverly Farms Foundation Godfrey, Illinois 62035 Veterans Administration Medical Center St. Louis, Missouri 63125
DATE STUDY INITIATED:	June 19, 1985
DATE STUDY COMPLETED:	In progress
STUDY POPULATION:	The study population consists of approximately 250 mentally retarded individuals, above 5 years of age, and 50 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 889

STUDY PROCEDURE:

Mentally retarded individuals are randomly assigned to one of two groups, stratified by sex and age. Health care personnel constitute a third group.

Mentally retarded individuals receive a 0.5 ml (10 mcg HBsAg) or a 1.0 ml (20 mcg HBsAg) intramuscular injection of vaccine at 0, 1, and 6 months. Health care personnel receive a 0.5 ml (10 mcg HBsAg) intramuscular injection of vaccine according to the same regimen.

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 two weeks before the first injection of vaccine. Post-vaccination blood samples are obtained at 1, 3, 6, 10 and 24 months.

All serum samples are assayed for HBsAg, anti-HBc and anti-HBs. The pre-vaccination and 3 month post-vaccination samples are also tested for 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:

MENTALLY RETARDED INDIVIDUALS

10 mcg Lot 993/C-K937 at 0, 1, and 6 months
20 mcg Lot 993/C-K937 at 0, 1, and 6 months

1. Number Vaccinated:

Dose (mcg)	Injection No. 1	2	3
10	101	101	100
20	101	100	100

Study 889

RESULTS: (Contd)

2. Serologic Results:

Serologic data at 1 month are available for 101 mentally retarded individuals who received a 10 mcg dose and 100 mentally retarded individuals who received a 20 mcg dose of vaccine.

At 1 month, anti-HBs responses among mentally retarded individuals 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
10	19 (19/101)	8 (8/101)	0.5	8.7	19.9
20	20 (20/100)	11 (11/100)	0.6	13.7	38.7

3. Clinical Results:

Clinical follow-up data are available for 101 (10 mcg dose) and 101 (20 mcg dose) mentally retarded individuals following the first injection of vaccine and 101 (10 mcg dose) and 100 (20 mcg dose) individuals following the second injection. Clinical complaints and maximum temperatures reported following each injection are provided in Tables 1-4. In summary:

Clinical Complaint	Dose (mcg)	% Frequency by Injection No. 1	2	3
Injection Site	10	0 (0/101)	0 (0/101)	NA
	20	0 (0/101)	0 (0/100)	NA
Systemic	10	2 (2/101)	0 (0/101)	NA
	20	1 (1/101)	0 (0/100)	NA

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

Table 1

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: RETARDED

CLINICAL COMPLAINTS	TOTAL VACCINEES (101 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)		2 (2.0%)
WHOLE BODY/GENERAL	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
HEADACHE	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
RESPIRATORY	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)		2 (2.0%)
RHINITIS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)		2 (2.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)		2 (2.0%)
PERSONS WITH NO COMPLAINTS	101 (100.0%)	100 (99.0%)	101 (100.0%)	100 (99.0%)	101 (100.0%)	101 (100.0%)		99 (98.0%)
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 1 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: RETARDED

CLINICAL COMPLAINTS	TOTAL VACCINEES (101 PATIENTS) - DOSE 2							
	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	101 (100.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)	100 (100.0%)		101 (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%)

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Table 2

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: RETARDED

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (101 PATIENTS) - DOSE 1 — DAYS POST VACCINATION								NUMBER WITH MAX TEMP
	0	1	2	3	4	5			
< 99	82 (81.2%)	84 (83.2%)	90 (89.1%)	81 (81.8%)	88 (88.0%)	89 (88.1%)			56 (55.4%)
99 - 99.9	15 (14.9%)	16 (15.8%)	11 (10.9%)	16 (16.2%)	11 (11.0%)	12 (11.9%)			38 (37.6%)
100 - 100.9	4 (4.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	0 (0.0%)			6 (5.9%)
101 - 101.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)			1 (1.0%)
TEMPERATURE TAKEN	101 (100.0%)	101 (100.0%)	101 (100.0%)	99 (98.0%)	100 (99.0%)	101 (100.0%)			101 (100.0%)
TEMPERATURE NOT TAKEN	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	1 (1.0%)	0 (0.0%)			0 (0.0%)

Table 2 (cont.)

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 10 MCG
PATIENT CLASS: RETARDED

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (101 PATIENTS) - DOSE 2								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	88 (88.0%)	96 (95.0%)	93 (92.1%)	85 (84.2%)	86 (86.0%)	90 (90.0%)			69 (68.3%)
99 - 99.9	10 (10.0%)	5 (5.0%)	6 (5.9%)	14 (13.9%)	13 (13.0%)	10 (10.0%)			28 (27.7%)
100 - 100.9	1 (1.0%)	0 (0.0%)	2 (2.0%)	1 (1.0%)	1 (1.0%)	0 (0.0%)			3 (3.0%)
101 - 101.9	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)
102 - 102.9	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)			1 (1.0%)
TEMPERATURE TAKEN	100 (99.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)	100 (99.0%)	100 (99.0%)			101 (100.0%)
TEMPERATURE NOT TAKEN	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)			0 (0.0%)

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Table 3

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 20 MCG
PATIENT CLASS: RETARDED

CLINICAL COMPLAINTS	TOTAL VACCINEES (101 PATIENTS) - DOSE 1							NUMBER WITH COMPLAINTS
	DAYS POST VACCINATION							
	0	1	2	3	4	5		
SYSTEMIC	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
WHOLE BODY/GENERAL	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
HEADACHE	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
PERSONS WITH COMPLAINTS	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)
PERSONS WITH NO COMPLAINTS	101 (100.0%)	101 (100.0%)	100 (99.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)		100 (99.0%)
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 3 (cont.)

PATIENT COUNT CLINICAL COMPLAINTS
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 20 MCG
PATIENT CLASS: RETARDED

CLINICAL COMPLAINTS	TOTAL VACCINEES (100 PATIENTS) - DOSE 2						
	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	100 (100.0%)	100 (100.0%)	100 (100.0%)	100 (100.0%)	100 (100.0%)	100 (100.0%)	100 (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 4

PATIENT COUNT MAXIMUM TEMPERATURES
RECOMBINANT HEPATITIS B VACCINE

STUDY : 0889
TREATMENT :
LOT NUMBER : CK937
DOSE : 20 MCG
PATIENT CLASS: RETARDED

MAX TEMPERATURE (DEG F, ORAL)	TOTAL VACCINEES (101 PATIENTS) - DOSE 1								NUMBER WITH MAX TEMP
	DAYS POST VACCINATION								
	0	1	2	3	4	5			
< 99	88 (88.0%)	93 (92.1%)	89 (88.1%)	83 (82.2%)	85 (84.2%)	86 (86.0%)			62 (61.4%)
99 - 99.9	11 (11.0%)	8 (7.9%)	11 (10.9%)	17 (16.8%)	14 (13.9%)	13 (13.0%)			33 (32.7%)
100 - 100.9	1 (1.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	2 (2.0%)	1 (1.0%)			6 (5.9%)
TEMPERATURE TAKEN	100 (99.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)	101 (100.0%)	100 (99.0%)			101 (100.0%)
TEMPERATURE NOT TAKEN	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)			0 (0.0%)