***William A. Rutala, PhD; Karen K. Hoffmann, RN, MS; and David J. Weber, MD, were asked to respond to this letter.***

In a single sentence in the discussion section of our original article (1989; 10:511-514), we recommended that bronchoscopes should be high-level disinfected between patients by immersing them in a 2% glutaraldehyde (or other high-level disinfectant) for at least 20 minutes. We felt it was inappropriate in this article to provide an exhaustive description of the efficacy of disinfectants and factors that influence their antimicrobial activity.

In regard to the need for longer exposure times and higher temperatures for certain 2% glutaraldehydes, our original article only suggested that a minimum exposure time of 20 minutes should be employed, and this should not be construed as precluding the use of longer exposure times and higher temperatures for disinfecting semicritical items (e.g., 45 minutes at 25°C). As we stated in an earlier letter (1990; 11:334, 336) in response to comments from Marian Kennedy (Director, Professional Services, Sporicidin International) "we do not believe it is necessary to indicate which 2% glutaraldehyde was used because there is no evidence in the scientific literature that identifies differences in the tuberculocidal activity when the disinfectants are used as recommended by the Association for Practitioners in Infection Control (APIC) draft guideline (i.e., ⩾ 20 minutes at room temperature)."[1] Mr. Schattner (Vice President, Sporicidin International) has not referenced any articles published in the scientific literature that suggests disinfection as we have recommended would result in the survival of mycobacteria.

Mr. Schattner also expresses concern about the tuberculocidal activity of acid glutaraldehydes. We think the APIC Guideline is correct in stating "that neutral or alkaline glutaraldehydes possess superior microbiocidal and anticorrosion properties compared with acid glutaraldehydes."[2] This statement is based on published reports, including the paper by Masferrer and Marquez referred to by Mr. Schattner.[3] However, both a 2% acid glutaraldehyde and a 2% alkaline glutaraldehyde, when employed for a 20-minute immersion time as recommended in the APIC Guideline, demonstrate tuberculocidal activity[4,5]

Mr. Schattner implies that manufacturers' registered label claims are always accurate. It should be recognized that Environmental Protection Agency (EPA) registration claims are based only on microbiocidal efficacy data submitted by the manufacturer. Pre- and post-registration efficacy testing are no longer performed by the EPA. In 1987, Rutala and Cole submitted identical samples of six EPA-registered, hospital-grade disinfectants to 18 laboratories.[6] These disinfectants failed in 20% to 62% of the trials. Interestingly, four laboratories unknowingly tested their own products, and three of the four failed their products against one or more of the test organisms.

A similar survey using mycobacteria has not been performed. However, recent studies have explored the effect of modifying the AOAC tuberculocidal activity test to improve the test's sensitivity to detect the failure of disinfectants to inactivate mycobacteria. Substitution of Middlebrook 7H9 broth as the primary subculture media, rather than modified Proskauer-Beck medium, and neutralization by dilution improve the ability to detect small numbers of viable and sublethally damaged mycobacteria.[5] In a number of trials, the standard AOAC test passed a disinfectant (0 positive penicylinders per 10 replicates); while using the modified AOAC test, the same disinfectant demonstrated no mycobactericidal activity (10 positive penicylinders per 10 replicates). This questions the ability of currently used testing methodology to assure that disinfectants are in fact mycobactericidal.

We believe that the peer-reviewed papers by Ascenzi and coworkers[7] and Collins[8] used sound methodology and produced valid data. Since the APIC Guideline appeared, another paper was published that further supports the Guideline recommendation of at least a 20-minute exposure time at room temperature.[5] We believe that three independent investigators obtaining similar data using different methods, especially in the absence of conflicting published studies, is Sufficient support for the APIC Guideline.

**William A. Rutala, PhD;**
**David J. Weber, MD;**
**Karen K. Hoffmann, RN, MS**
Chapel Hill, North Carolina

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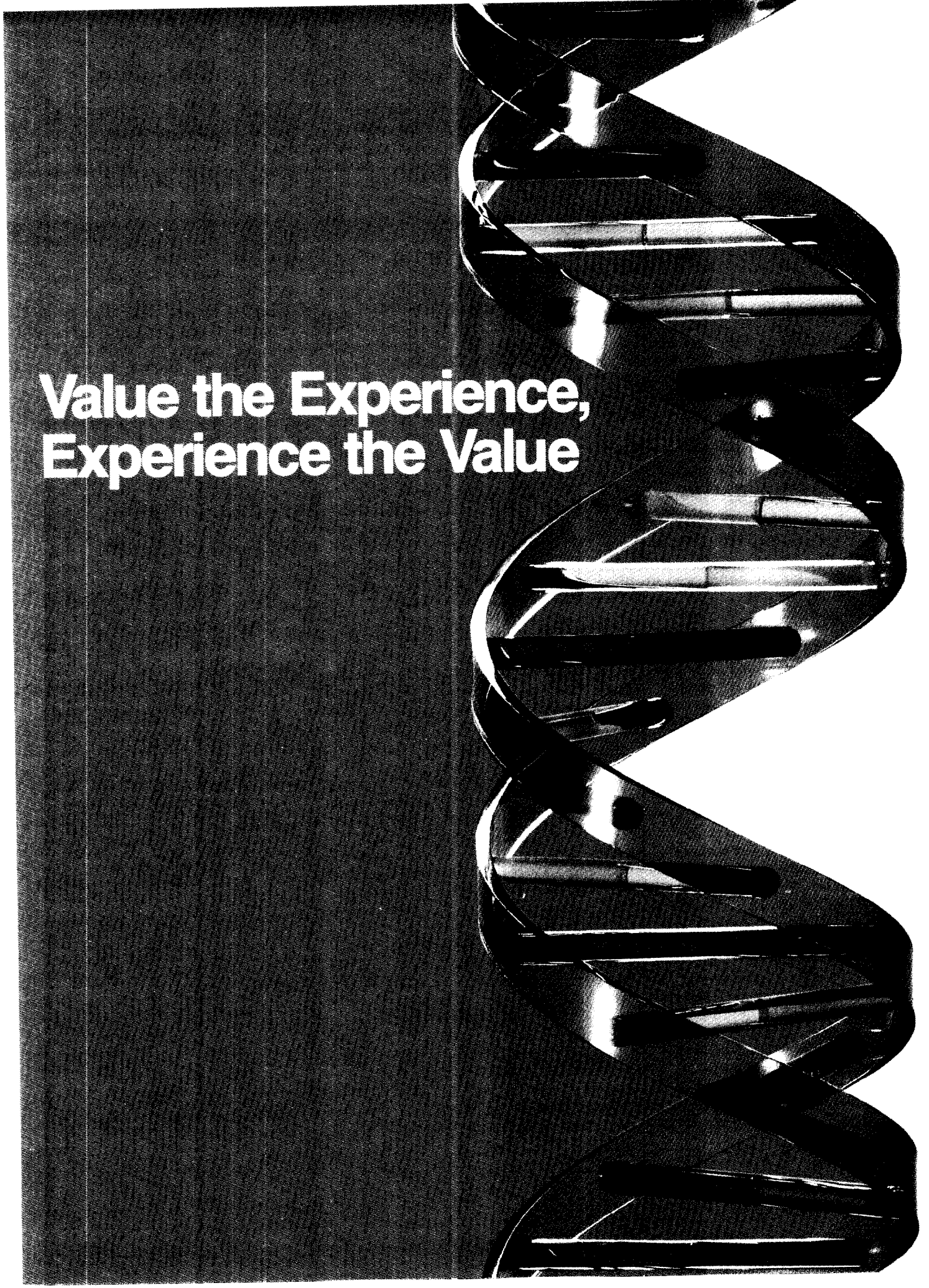

## Value the Experience

- Over 2.6 million doses distributed in the United States
- In clinical trials, three IO-mcg doses induced protective levels of antibodies in 96% of healthy adults
- Contains no detectable yeast DNA and not more than 1% yeast protein
- Generally well tolerated in over three years of clinical use

## Experience the Value

- Innovative services to help support your vaccination program
- Wide range of doses includes 40-mcg/mL Dialysis Formulation
- Now a 2.5-mcg pediatric dose may reduce vaccine costs by 50%
- Available in convenient multidose vials direct from MSD

# Recombivax HB™

**(Hepatitis B Vaccine [Recombinant] | MSD)**

RECOMBWAX HB is contraindicated in the presence of hypersensitivity to yeast or to any component of the vaccine.

Please see the following page for a Brief Summary of Prescribing Information for RECOMBIVAX HB.

MSD
MERCK SHARP & DOHME

# Value the Experience, Experience the Value

**Recombivax HB**
(Hepatitis B Vaccine [Recombinant] [MSD])

INDICATIONS AND USAGE

RECOMBIVAX HB is indicated for vaccination against Infection caused by all known subtypes of hepatitis B virus. RECOMBIVAX HB Dialysis Formulation is indicated for vaccination of adult predialysis and dialysis patients against infectron caused by all known subtypes of hepatitis B virus.

Vaccination with RECOMBIVAX HB is recommended in persons of all ages who are or will be at increased risk of Infection with hepatitis B virus. In areas with high prevalence of infection, most of the population are at risk of acquiring hepatitis B infection at a young age. Therefore. vaccination should be targeted to prevent s&transmission In areas of low prevalence, vaccination should be limited to those who are in groups identified as being at increased risk of infectron.

CONTRAINDICATIONS

Hypersensitivity to yeast or any component of the vaccine.

WARNINGS

Patients who develop symptoms suggestive of hypersensitivity after an injection should not receive further injections of the vaccrne (see CONTRAINDICATIONS).

Because of the long incubation penod for hepatitis B, it is possible for unrecognized infection to be present at the time the vaccrne is given The vaccine may not prevent hepatitis B in such patients.

PRECAUTIONS

General

As with any percutaneous vaccine, epinephrine should be available for immediate use should an anaphylactoid reaction occur

Anyserious active infection is reason for delaying use of the vaccine except when, in the opinion of the physician, withholding the vaccine entails a greater risk.

Caution and appropriate care should be exercised in administering the vaccrne to individuals with severely compromised cardiopulmonary status or to others in whom a febrile or systemic reaction could pose a significant risk.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with the vaccine. It is also not known whether the vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The vaccine should be given to a pregnant woman onlv if clearly needed.

Nursing Mothers

It is not known whether the vaccine is excreted in human milk. Because manv drugs are excreted in human milk, caution should be exercised when the vaccine is administered to a nursing woman.

Pediatric Use

RECOMBIVAX HB has been shown to be usually well tolerated and highly immunogenic In infants and children of all aaes. Newborns also respond well; maternally transferred antibodies do not interfere with the active immune response to the vaccine. See DOSAGE AND ADMINISTRATION for recommended pediatric dosage and for recommended dosage for Infants born to HBsAg-positive mothers.

The safety and effectiveness of RECOMBIVAX HB Dialysis Formulation in children have not been established.

ADVERSE REACTIONS

RECOMBIVAX HB and RECOMBIVAX HB Dialysis Formulation are generally well tolerated. No serious adverse reactions attributable to the vaccine have been reported during the course of clinical trials, No adverse experiences were reported during clinical trials which could be related to changes in the titers of antibodies to yeast. As with any vaccrne. there is the possibility that broad use of the vaccine could reveal adverse reactions not observed in clinical trials

In a group of studies, 3,258 doses of RECOMBIVAX HB were administered to 1,252

**RECOMBIVAX HB®**
(Hepatitis B Vaccine [Recombinant], MSD)

healthy adults who were monitored for 5 days after each dose. Injection-site and systemic complaints were reported following 17% and 15% of the *injections*, respectively

The following adverse reactions were reported,

Incidence Equal to or Greater Than 1% of Injections

LOCAL REACTION (INJECTION SITE)

Injection-site reactions consisting principally of soreness and including pain, tenderness, pruritus, erythema, ecchymosis, swelling, warmth, and nodule formation.

BODY AS A WHOLE

The most frequent systemic complaints include fatigue/weakness; headache: fever (≥100°F); malaise.

DIGESTIVE SYSTEM

Nausea; diarrhea.

RESPIRATORY SYSTEM

Pharyngitis; upper respiratory Infection.

Incidence Less Than 1% of Injections

BODY AS A WHOLE

Sweating, achiness; sensation of warmth; lightheadedness; chills; flushing.

DIGESTIVE SYSTEM

Vomiting; abdominal pains/cramps; dyspepsia; diminished appetite.

RESPIRATORY SYSTEM

Rhinitis; influenza; cough.

NERVOUS SYSTEM

Vertigo/dizziness; paresthesia.

INTEGUMENTARY SYSTEM

Pruritus; rash (non-specified); angioedema; urticaria.

MUSCULOSKELETAL SYSTEM

Arthralgia Including monoarticular; myalgia; back pain; neck pain; shoulder pain; neck stiffness.

HEMIC/LYMPHATIC SYSTEM

Lymphadenopathy.

PSYCHIATRIC/BEHAVIORAL

Insomnia/disturbed sleep.

SPECIAL SENSES

Earache.

UROGENITAL SYSTEM

Dysuria

CARDIOVASCULAR SYSTEM

Hypotension.

The following additional adverse reactions have been reoorted with use of the marketed vaccine. In many instances, the relationship to the vaccine was unclear.

*Hypersensitivity*: Anaphylaxis and symptoms of Immediate hypersensitivity reactions including rash, pruritus, urticaria, edema, angioedema, dyspnea, chest discomfort, bronchial spasm, palpitation, or symptoms consistent with a hypotensive episode have been reported within the first few hours after vaccination. An apparent hypersensitivity syndrome (serum-sickness-*like*) of delayed onset has been reported days to weeks after vaccination, including arthralgia/arthritis (usually transient). fever, and dermatologic reactions such as urticaria, erythema multiforme, ecchymoses, and erythema nodosum (see WARNINGS and PRECAUTIONS).

*Nervous* System: Peripheral neuropathy including Bell's Palsy; muscle weakness; Guillain-Barre syndrome.

*Special* Senses: Optic neuritis.

Potential ADVERSE EFFECTS

In addition, a variety of adverse effects not observed in clinical trials with RECOMBIVAX HB or RECOMBIVAX HB Dialysis Formulation have been reported with HEPTAVAX-B® (Hepatitis B Vaccine, MSD)(plasma-derived hepatitis B vaccine). Those listed below are to serve as alerting information to physicians:

Nervous *System:* Neurological disorders such as myelitis including transverse myelitis; acute radiculoneuropathy; herpes zoster.

*Hematologic*: Thrombocytopenia.

Special Senses: Tinnitus; visual disturbances.

**RECOMBIVAX HB®**
(Hepatitis B Vaccine [Recombinant], MSD)

DOSAGE AND ADMINISTRATION

Do not *inject intravenously* or *intradermally.*

RECOMBIVAX HB DIALYSIS FORMULATION (40 mcg/mL) IS INTENDED ONLY FOR ADULT PREDIALYSIS/DIALYSIS PATIENTS.

RECOMBIVAX HB (10 mcg/mL) IS NOT INTENDED FOR USE IN PREDIALYSIS/DIALYSIS PATIENTS.

RECOMBIVAX HB and RECOMBIVAX HB Dialysis Formulation are for intramuscular injection. The *deltoid muscle* is the preferred site for intramuscular injection in adults. Data suggest that injections given in the buttocks are frequently given into fatty tissue instead of into muscle. Such injections have resulted in a lower seroconversion rate than was expected. The *anterolateral thigh* is the recommended site for intramuscular injection in infants and young children.

For persons at risk of hemorrhage following intramuscular injection, RECOMBIVAX HB may be administered subcutaneously. However, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore, subcutaneous administration should be used only in persons (e.g., hemophiliacs) who are at risk of hemorrhage following intramuscular injections.

The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.

The RECOMBIVAX HB vaccination regimen consists of 3 doses of vaccine. The volume of vaccine to be given on each occasion is as follows:

| Age group | Initial | 1 month | 6 months |
|---|---|---|---|
| Birth* through 10 years of age | 0.25 mL (2.5 mcg) | 0.25 mL (2.5 mcg) | 0.25 mL (2.5 mcg) |
| 11-19 years of age | 0.5 mL (5 mcg) | 0.5 mL (5 mcg) | 0.5 mL (5 mcg) |
| ≥20 years | 1 mL (10 mcg) | 1 mL (10 mcg) | 1 mL (10 mcg) |

*Infants born of HBsAg-negative mothers

The recommended RECOMBIVAX HB Dialysis Formulation vaccination regimen for predialysis/dialysis patients is as follows:

| Group | Formulation | Initial | 1 month | 6 months |
|---|---|---|---|---|
| Predialysis and Dialysis Patients | Dialysis 40 mcg/mL | 1 mL | 1 mL | 1 mL |

Whenever revaccination or administration of a booster dose is appropriate, RECOMBIVAX HB may be used.

The recommended regimen for infants born of HBsAg-positive mothers is as follows:

| | Birth | Within 7 days | 1 month | 6 months |
|---|---|---|---|---|
| RECOMBIVAX HB | | 0.5 mL (5 mcg) | 0.5 mL (5 mcg) | 0.5 mL (5 mcg) |
| HEPATITIS B IMMUNE GLOBULIN | 0.5 mL | — | | |

Storage

Store vials at 2°–8°C (36°–46°F). Storage above or below the recommended temoerature mav reduce potency.

*Do not freeze since freezing destroys potency*

For more detailed information, consult your MSD Representative or see Prescribing Information.

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