

1

Hib

2

Haemophilus b
Conjugate Vaccine
(Tetanus Toxoid Conjugate)
ActHIB®



3

4 **DESCRIPTION**

5 ActHIB®, Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate), produced by Sanofi
6 Pasteur SA, is a sterile, lyophilized powder which is reconstituted with either saline diluent (0.4%
7 Sodium Chloride) or Tripedia®, Sanofi Pasteur Inc. Diphtheria and Tetanus Toxoids and Acellular
8 Pertussis Vaccine Adsorbed (DTaP) (when reconstituted known as TriHIBit®) for intramuscular
9 administration only. The vaccine consists of the Haemophilus b capsular polysaccharide
10 (polyribosyl-ribitol-phosphate, PRP), a high molecular weight polymer prepared from the
11 *Haemophilus influenzae* type b (Hib) strain 1482 grown in a semi-synthetic medium, covalently
12 bound to tetanus toxoid. (1) The lyophilized ActHIB vaccine powder and saline diluent contain no
13 preservative. The tetanus toxoid is prepared by extraction, ammonium sulfate purification, and
14 formalin inactivation of the toxin from cultures of *Clostridium tetani* (Harvard strain) grown in a
15 modified Mueller and Miller medium. (2) The culture medium contains milk derived raw

1 materials (casein derivatives). Further manufacturing process steps reduce residual formaldehyde
2 to levels below 0.5 micrograms (mcg) per dose by calculation. The toxoid is filter sterilized prior
3 to the conjugation process. Potency of ActHIB vaccine is specified on each lot by limits on the
4 content of PRP polysaccharide and protein in each dose and the proportion of polysaccharide and
5 protein in the vaccine which is characterized as high molecular weight conjugate.

6

7 When ActHIB is reconstituted with saline diluent (0.4% Sodium Chloride), each 0.5 mL dose is
8 formulated to contain 10 mcg of purified capsular polysaccharide conjugated to 24 mcg of
9 inactivated tetanus toxoid, and 8.5% of sucrose.

10

11 When ActHIB is reconstituted with Tripedia vaccine to formulate TriHIBit vaccine, each 0.5 mL
12 dose contains 10 mcg of purified capsular polysaccharide conjugated to 24 mcg of inactivated
13 tetanus toxoid, 8.5% of sucrose, 6.7 Lf of diphtheria toxoid, 5 Lf of tetanus toxoid, and 46.8 mcg
14 of pertussis antigens. Tripedia vaccine (vial presentation 0.6 mL) is formulated without
15 preservatives but contains a trace amount of thimerosal [(mercury derivative), (≤ 0.3 mcg
16 mercury/dose)] from the manufacturing process. (*Refer to product insert for Tripedia vaccine.*)

17

18 **CLINICAL PHARMACOLOGY**

19 *H influenzae* type b was the leading cause of invasive bacterial disease among children in the
20 United States prior to licensing of Haemophilus b conjugate vaccines.

21

1 The response to ActHIB vaccine is typical of a T-dependent immune response to antigen. The
2 prominent isotype of anti-capsular PRP antibody induced by ActHIB vaccine is IgG. (3) A
3 booster response for IgG has been demonstrated in children 12 months of age or older who
4 previously received two or three doses of ActHIB vaccine. Bactericidal activity against *H*
5 *influenzae* type b was demonstrated in serum after immunization and correlated with the anti-PRP
6 antibody response induced by ActHIB vaccine. (4)

7

8 Antibody to *H influenzae* capsular polysaccharide (anti-PRP) titers of >1.0 mcg/mL following
9 vaccination with unconjugated PRP vaccine correlated with long-term protection against invasive
10 *H influenzae* type b disease in children older than 24 months of age. (5) Although the relevance of
11 this threshold to clinical protection after immunization with conjugate vaccines is not known,
12 particularly in light of the induced, immunologic memory, this level continues to be considered as
13 indicative of long-term protection. (6) In clinical studies, ActHIB vaccine induced, on average,
14 anti-PRP levels ≥ 1.0 mcg/mL in 90% of infants after the primary series (2, 4, and 6 months) and
15 in more than 98% of infants following a booster dose given at 15 to 19 months of age. (4)

16

17 Two clinical trials supported by the National Institutes of Health (NIH) have compared the anti-
18 PRP antibody responses to three Haemophilus b conjugate vaccines in racially mixed populations
19 of children. These studies were done in Tennessee (7) (**TABLE 1**) and in Minnesota, Missouri,
20 and Texas (8) (**TABLE 2**) in infants immunized with ActHIB vaccine and other Haemophilus b
21 conjugate vaccines at 2, 4, and 6 months of age. All Haemophilus b conjugate vaccines were
22 administered concomitantly with Poliovirus Vaccine Live Oral and whole cell DTP vaccines at

1 separate sites. Neither Poliovirus Vaccine Live Oral nor whole cell DTP vaccines are licensed or
2 distributed in the US.

3

4 **TABLE 1: Anti-PRP Antibody Responses Following a Two or Three Dose Series of a**
5 **Haemophilus b Vaccine at 2, 4, and 6 Months of Age - Tennessee (7)**

VACCINE	N ^a	GEOMETRIC MEAN CONCENTRATION (GMC) (mcg/mL)			Post Third Immunization % ≥1.0 mcg/mL
		Pre-Immunization at 2 months	Post Second Immunization at 6 months	Post Third Immunization at 7 months	
PRP-T ^b (ActHIB vaccine)	65	0.10	0.30	3.64	83%
PRP-OMP ^c (PedvaxHIB®)	64	0.11	0.84	N/A	50% ^d
HbOC ^e (HibTITER®)	61	0.07	0.13	3.08	75%

6 a N = Number of Children

7 b Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)

8 c Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)

9 d Seroconversion after the recommended 2-dose primary immunization series is shown

10 e Haemophilus b Conjugate Vaccine (Diphtheria CRM₁₉₇ Protein Conjugate)

11 N/A Not applicable in this comparison trial although third dose data have been published (7)

12

1 **TABLE 2: Anti-PRP Antibody Responses Following a Two or Three Dose Series of a**
2 **Haemophilus b Vaccine at 2, 4, and 6 Months of Age - Minnesota, Missouri, and Texas (8)**

VACCINE	N ^a	GEOMETRIC MEAN CONCENTRATION (GMC) (mcg/mL)			Post Third ^b Immunization % ≥1.0 mcg/mL
		Pre Immunization at 2 months	Post Second Immunization At 6 months	Post Third ^b Immunization At 7 months	
PRP-T ^c (ActHIB vaccine)	142	0.25	1.25	6.37	97%
PRP-OMP ^d (PedvaxHIB)	149	0.18	4.00	N/A	85% ^e
HbOC ^f (HibTITER)	167	0.17	0.45	6.31	90%

3 a N = Number of Children

4 b Sera were obtained after the third dose from 86 and 110 infants, in PRP-T and HbOC vaccine groups,
5 respectively

6 c Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)

7 d Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)

8 e Seroconversion after the recommended 2-dose primary immunization series is shown

9 f Haemophilus b Conjugate Vaccine (Diphtheria CRM₁₉₇ Protein Conjugate)

10 N/A Not applicable in this comparison trial although third dose data have been published (8)

11

12 Native American populations have had high rates of *H influenzae* type b disease and have been
13 observed to have low immune responses to Haemophilus b conjugate vaccines. In a clinical study
14 enrolling Alaskan Native Americans, following the administration of a three dose series of
15 ActHIB at 6 weeks, 4 months, and 6 months of age, 75% of subjects achieved an anti-PRP
16 antibody titer of ≥1.0 mcg/mL at 7 months of age (1 month after the last vaccination). (9)

17

18 In four separate studies, children 12 to 24 months of age who had not previously received
19 Haemophilus b conjugate vaccination were immunized with a single dose of ActHIB vaccine

1 (TABLE 3). GMC anti-PRP antibody responses were 5.12 mcg/mL (90% responding with ≥ 1.0
2 mcg/mL) for children 12 to 15 months of age and 4.4 mcg/mL (82% responding with ≥ 1.0
3 mcg/mL) for children 17 to 24 months of age. (10)

4

5 **TABLE 3: Anti-PRP Antibody Responses in 12- to 24-month-old Children Immunized with**
6 **a Single Dose of ActHIB (10)**

AGE GROUP	N ^a	GEOMETRIC MEAN CONCENTRATION (GMC) (mcg/mL)		% SUBJECTS WITH ≥ 1.0 mcg/mL	
		Pre Immunization	Post Immunization ^b	Pre Immunization	Post Immunization ^b
12 to 15 months	256	0.06	5.12	1.6	90.2
17 to 24 months	81	0.10	4.40	3.7	81.5

7 a N = Number of Children

8 b Post immunization responses measured at approximately 1 month after vaccination

9

10 ActHIB vaccine has been found to be immunogenic in children with sickle cell anemia, a
11 condition which may cause increased susceptibility to Haemophilus b disease. Following two
12 doses of ActHIB vaccine given at two-month intervals, 89% of these children (mean age 11
13 months) had anti-PRP antibody titers of ≥ 1.0 mcg/mL. This is comparable to anti-PRP antibody
14 levels demonstrated in normal children of similar age following two doses of ActHIB vaccine.
15 (11)

16

17 **TriHIBit Vaccine (ActHIB vaccine combined with Tripedia vaccine by reconstitution)**

18 Randomized comparative clinical trials demonstrated that the anti-PRP response achieved in 15-
19 to 20-month-old children 1 month after one dose of TriHIBit vaccine (ActHIB vaccine

1 reconstituted with Tripedia vaccine) was similar to that achieved when the ActHIB and Tripedia
2 vaccines were given concomitantly at different sites with separate needles and syringes (**TABLE**
3 **4**). (10) All children had received three doses of a Haemophilus b conjugate vaccine (HibTITER
4 or ActHIB vaccine) and three doses of a whole-cell DTP vaccine prior to entry into this clinical
5 trial.

6

7 **TABLE 4: Anti-PRP Responses in 15- to 20-month-old Children Following Immunization**
8 **with TriHIBit Vaccine Compared to ActHIB Vaccine and Tripedia Vaccine Given**
9 **Concomitantly at Separate Sites (10)**

	IMMUNOGENICITY			
	Pre-Dose		Post-Dose (1 month post-vaccination)	
	TriHIBit vaccine	Separate Injections ^a	TriHIBit vaccine	Separate Injections ^a
N ^b	88	94	93	98
Anti-PRP (mcg/mL)	0.89	1.15	90.30	80.90
% >1 mcg/mL	45.50	53.20	100.00	100.00

10 a ActHIB and Tripedia administered concomitantly at separate sites
11 b N= Number of Children
12

13 For data on the antibody responses to diphtheria, tetanus and pertussis (PT and FHA) antigens in
14 this study, refer to the Tripedia vaccine product insert.

15

16 INDICATIONS AND USAGE

17 ActHIB vaccine is indicated for the active immunization of infants and children 2 months through
18 5 years of age for the prevention of invasive disease caused by *H influenzae* type b.

19

1 TriHIBit vaccine, ActHIB vaccine combined with Tripedia vaccine by reconstitution, is indicated
2 for the active immunization of children 15 through 18 months of age for prevention of invasive
3 disease caused by *H influenzae* type b and diphtheria, tetanus and pertussis.

4

5 Vaccination with ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or
6 Tripedia vaccine (TriHIBit vaccine) may not protect 100% of individuals.

7

8 **CONTRAINDICATIONS**

9 ActHIB vaccine is contraindicated in children with a history of hypersensitivity to any component
10 of the vaccine and to any component of Tripedia vaccine when it is used to reconstitute ActHIB.

11 Any contraindication for Tripedia vaccine is a contraindication for TriHIBit vaccine, ActHIB
12 vaccine reconstituted with Tripedia vaccine. (*Refer to product insert for Tripedia vaccine.*)

13

14 TriHIBit vaccine (ActHIB reconstituted with Tripedia) is contraindicated in children who have
15 shown symptoms of encephalopathy (e.g., coma, decreased level of consciousness, prolonged
16 seizures) within 7 days of administration of a previous dose of a pertussis-containing vaccine that
17 is not attributable to another identifiable cause. TriHIBit is contraindicated in children who have a
18 progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive
19 encephalopathy. Pertussis-containing vaccines should not be administered to individuals with
20 these conditions until a treatment regimen has been established and the condition has stabilized.

21

22 **WARNINGS**

1 The stopper of the diluent vial contains natural rubber latex which may cause allergic reactions.

2 The lyophilized vaccine vial is not made with natural rubber latex.

3

4 If ActHIB vaccine or ActHIB vaccine reconstituted with Tripedia vaccine (TriHIBit vaccine) is

5 administered to immunosuppressed persons or persons receiving immunosuppressive therapy, the

6 expected antibody responses may not be obtained. This includes patients with asymptomatic or

7 symptomatic HIV infection (12), severe combined immunodeficiency, hypogammaglobulinemia,

8 or agammaglobulinemia; altered immune states due to diseases such as leukemia, lymphoma, or

9 generalized malignancy; or an immune system compromised by treatment with corticosteroids,

10 alkylating drugs, antimetabolites, or radiation. (13) (*Refer to product insert for Tripedia*

11 *vaccine.*)

12

13 **PRECAUTIONS**

14 **GENERAL**

15 Care is to be taken by the health-care provider for the safe and effective use of this vaccine.

16

17 **Epinephrine injection (1:1000) must be immediately available should an anaphylactic or**

18 **other allergic reactions occur due to any component of the vaccine.**

19

20 Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse

21 reactions. This includes a review of the patient's history with respect to possible sensitivity and

22 any previous adverse reactions to the vaccine or similar vaccines, and to possible sensitivity to

23 natural rubber latex, previous immunization history, current health status (see

1 **CONTRAINDICATIONS** and **WARNINGS** sections), and a current knowledge of the literature
2 concerning the use of the vaccine under consideration. (*Refer to product insert for Tripedia*
3 *vaccine.*)

4

5 The health-care provider should ask the parent or guardian about the recent health status of the
6 infant or child to be immunized including the infant's or child's previous immunization history
7 prior to administration of ActHIB vaccine or Tripedia vaccine.

8

9 If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior vaccine containing
10 tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including ActHIB or
11 TriHIBit, should be based on careful consideration of the potential benefits and possible risks.

12

13 Minor illnesses such as upper respiratory infection with or without low-grade fever are not
14 contraindications for use of ActHIB vaccine. (14)

15

16 Immunization with ActHIB vaccine does not substitute for routine tetanus immunization.

17

18 **INFORMATION FOR PARENTS AND GUARDIANS OF VACCINE** 19 **RECIPIENTS**

20 The health-care provider should inform the parent or guardian of the benefits and risks of the
21 vaccine.

22

1 Prior to administration of ActHIB vaccine reconstituted with saline diluent (0.4% Sodium
2 Chloride) or Tripedia vaccine (TriHIBit vaccine), the parent or guardian should be asked about
3 the recent health status of the infant or child to be immunized.

4

5 The health-care provider should inform the parent or guardian of the importance of completing
6 the immunization series.

7

8 The physician should inform the parent or guardian about the significant adverse reactions that
9 have been temporally associated with the administration of ActHIB vaccine reconstituted with
10 saline diluent (0.4% Sodium Chloride) or ActHIB vaccine reconstituted with Tripedia vaccine
11 (TriHIBit vaccine). The parent or guardian should be instructed to report any serious adverse
12 reactions to their health-care provider.

13

14 As part of the child's immunization record, the date, lot number, and manufacturer of the vaccine
15 administered should be recorded. (15) (16) (17)

16

17 The US Department of Health and Human Services has established a Vaccine Adverse Event
18 Reporting System (VAERS) to accept all reports of suspected adverse events after the
19 administration of any vaccine, including but not limited to the reporting of events required by the
20 National Childhood Vaccine Injury Act of 1986. (15) The toll-free number for VAERS forms and
21 information is 1-800-822-7967.

22

1 The National Vaccine Injury Compensation Program, established by the National Childhood
2 Vaccine Injury Act of 1986, requires physicians and other health-care providers who administer
3 vaccines to maintain permanent vaccination records and to report occurrences of certain adverse
4 events to the US Department of Health and Human Services. Reportable events include those
5 listed in the Act for each vaccine and events specified in the package insert as contraindications to
6 further doses of the vaccine. (16) (17)

7

8 The health-care provider should provide the Vaccine Information Statements (VISs), which are
9 required to be given with each immunization.

10

11 **DRUG INTERACTIONS**

12 When Tripedia vaccine is used to reconstitute ActHIB vaccine (TriHIBit vaccine) and
13 administered to immunosuppressed persons or persons receiving immunosuppressive therapy, the
14 expected antibody response may not be obtained.

15

16 Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic
17 drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune
18 response to vaccines. Short-term (<2 weeks) corticosteroid therapy or intra-articular, bursal, or
19 tendon injections with corticosteroids should not be immunosuppressive. Although no specific
20 studies with pertussis vaccine are available, if immunosuppressive therapy will be discontinued
21 shortly, it is reasonable to defer vaccination until the patient has been off therapy for one month;
22 otherwise, the patient should be vaccinated while still on therapy. (14)

23

1 If ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or ActHIB vaccine
2 reconstituted with Tripedia vaccine (TriHIBit vaccine) has been administered to persons receiving
3 immunosuppressive therapy, a recent injection of immunoglobulin or having an
4 immunodeficiency disorder, an adequate immunologic response may not be obtained.

5

6 In clinical trials, ActHIB vaccine was administered, at separate sites, concomitantly with one or
7 more of the following vaccines: DTP, DTaP, Poliovirus Vaccine Live Oral (OPV), Measles,
8 Mumps and Rubella vaccine (MMR), Hepatitis B vaccine and occasionally Inactivated Poliovirus
9 Vaccine (IPV). No impairment of the antibody response to the individual antigens, diphtheria,
10 tetanus and pertussis, was demonstrated when ActHIB vaccine was given at the same time, at
11 separate sites, with IPV or MMR. (10) In addition, more than 47,000 infants in Finland have
12 received a third dose of ActHIB vaccine concomitantly with MMR vaccine with no increase in
13 serious or unexpected adverse events. (10)

14

15 No significant impairment of antibody response to Measles, Mumps and Rubella was noted in 15-
16 to 20-month-old children who received TriHIBit vaccine, ActHIB vaccine reconstituted with
17 Tripedia vaccine, concomitantly with MMR. No data are available to the manufacturer concerning
18 the effects on immune response of OPV, IPV or Hepatitis B vaccine when given concurrently
19 with ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or Tripedia
20 vaccine (TriHIBit vaccine). (10)

21

22 Use with caution in patients on anticoagulant therapy.

1

2 **CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY**

3 ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or Tripedia vaccine
4 (TriHIBit vaccine) has not been evaluated for its carcinogenic, mutagenic potential or impairment
5 of fertility.

6

7 **PREGNANCY CATEGORY C**

8 Animal reproduction studies have not been conducted with ActHIB vaccine reconstituted with
9 saline diluent (0.4% Sodium Chloride) or Tripedia vaccine (TriHIBit vaccine). It is also not
10 known whether ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or
11 Tripedia vaccine (TriHIBit vaccine) can cause fetal harm when administered to a pregnant woman
12 or can affect reproduction capacity. ActHIB vaccine reconstituted with saline diluent (0.4%
13 Sodium Chloride) or Tripedia vaccine (TriHIBit vaccine) is not approved for use in pregnant
14 women.

15

16 **PEDIATRIC USE**

17 Safety and effectiveness of ActHIB vaccine reconstituted with saline diluent (0.4% Sodium
18 Chloride) in infants below the age of 6 weeks have not been established. (See **DOSAGE AND**
19 **ADMINISTRATION** section.)

20

21 Safety and effectiveness of TriHIBit vaccine, ActHIB vaccine reconstituted with Tripedia
22 vaccine, in infants below the age of 15 months have not been established. (See **DOSAGE AND**
23 **ADMINISTRATION** section.)

1

2 **ADVERSE REACTIONS**

3 More than 7,000 infants and young children (≤ 2 years of age) have received at least one dose of
4 ActHIB vaccine during US clinical trials. Of these, 1,064 subjects 12 to 24 months of age who
5 received ActHIB vaccine alone reported no serious or life threatening adverse reactions.

6

7 Adverse reactions commonly associated with a first ActHIB vaccine immunization of children 12
8 to 15 months of age who were previously unimmunized with any Haemophilus b conjugate
9 vaccine, include local pain, redness, and swelling at the injection site. Systemic reactions include
10 fever, irritability, and lethargy. (4) (10)

11

12 Adverse reactions associated with ActHIB vaccine generally subsided after 24 hours and usually
13 do not persist beyond 48 hours after immunization.

14

15 In a US trial, safety of TriHIBit vaccine, ActHIB vaccine combined with Tripedia vaccine by
16 reconstitution, in 110 children aged 15 to 20 months was compared to ActHIB vaccine given with
17 Tripedia vaccine at separate sites to 110 children. All children received three doses of
18 Haemophilus b conjugate vaccine (ActHIB vaccine or HibTITER) and three doses of whole-cell
19 DTP at approximately 2, 4, and 6 months of age.

1 **Table 5: Local and Systemic Reactions at 6, 24, and 48 Hours Following Immunization with**
 2 **ActHIB and Tripedia Vaccines Given Concomitantly at Separate Sites Compared to**
 3 **TriHIBit^a Vaccine in Children 15- to 20-months-old (10)**

Adverse Event	6 Hrs. Post-dose		24 Hrs. Post-dose		48 Hrs. Post-dose	
	Separate Injections ^b N = 110	TriHIBit vaccine N = 110	Separate Injections ^b N = 110	TriHIBit vaccine N = 110	Separate Injections ^b N = 110	TriHIBit vaccine N = 110
Local (%)						
Tenderness	17.3/20.0	19.1	8.2/8.2	10.0	1.8/0.9	1.8
Erythema >1”	0.9/0.0	3.6	2.7/0.9	3.6	0.9/0.0	1.8
Induration ^c	3.6/5.5	2.7	2.7/3.6	8.2	4.5/0.9	3.6
Swelling	3.6/3.6	3.6	2.7/1.8	5.5	0.9/0.0	4.5
Systemic (%)	N = 103-110	N = 102-109	N = 105-110	N = 103-108	N = 104-110	N = 103-109
Fever >102.2°F (39.0°C)	0	2.0	1.0	1.9	1.9	0
Irritability	27.3	22.9	20.9	17.6	12.7	10.1
Drowsiness	36.4	30.3	17.3	13.9	12.7	11.0
Anorexia	12.7	9.2	10.0	6.5	6.4	2.8
Vomiting	0.9	1.8	0.9	1.9	0.9	2.8
Persistent Cry	0	0	0	0	0	0
Unusual Cry	0	0	0	0	0	0.9

4 a TriHIBit vaccine, ActHIB vaccine combined with Tripedia vaccine by reconstitution

5 b Tripedia vaccine injection site/ActHIB vaccine injection site

6 c Induration is defined as hardness with or without swelling

7

8 TriHIBit vaccine, ActHIB vaccine combined with Tripedia vaccine by reconstitution, was

9 administered to approximately 850 children, aged 15 to 20 months. All children received three

1 doses of a Haemophilus b conjugate vaccine (ActHIB vaccine or HibTITER) and three doses of
2 whole-cell DTP at approximately 2, 4, and 6 months of age. Local reactions were typically mild
3 and usually resolved within the 24 to 48 hour period after immunization. The most common local
4 reactions were pain and tenderness at the injection site. Systemic reactions occurring were usually
5 mild and resolved within 72 hours of immunization. The reaction rates were similar to those
6 observed in **TABLE 5** when TriHIBit vaccine, ActHIB vaccine reconstituted with Tripedia
7 vaccine, was administered and when Tripedia vaccine was administered alone as a booster. (10)
8
9 The number of subjects studied with TriHIBit vaccine, ActHIB vaccine combined with Tripedia
10 vaccine by reconstitution, was inadequate to detect rare serious adverse events.

12 **Reporting of Adverse Events**

13 Reporting by the parent or guardian of all adverse events occurring after vaccine administration
14 should be encouraged. Adverse events following immunization with vaccine should be reported
15 by the health-care provider to the US Department of Health and Human Services (DHHS)
16 Vaccine Adverse Event Reporting System (VAERS). Reporting forms and information about
17 reporting requirements or completion of the form can be obtained from VAERS through a toll-
18 free number 1-800-822-7967. (15) (16) (18)

20 **Health-care providers also should report these events to Sanofi Pasteur Inc., Discovery**
21 **Drive, Swiftwater, PA 18370 or call 1-800-822-2463.**

1 **Post-Marketing Experience**

2 The following events have been spontaneously reported during the post-approval use of ActHIB.

3 Because these events are reported voluntarily from a population of uncertain size, it is not always
4 possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

5

6 • *Immune System Disorders*: Anaphylaxis, other allergic/hypersensitivity reactions (including
7 urticaria, angioedema)

8 • *Nervous System Disorders*: Convulsions

9 • *General Disorders and Administration Site Conditions*: Extensive limb swelling, peripheral
10 edema, pruritus, and rash

11

12 **DOSAGE AND ADMINISTRATION**

13 **For intramuscular injection only**

14

15 The ActHIB vaccine, reconstituted with saline diluent (0.4% Sodium Chloride), appears clear and
16 colorless. TriHIBit vaccine, the reconstituted vaccine using Tripedia vaccine, is a homogenous
17 white suspension.

18

19 Parenteral drug products should be inspected visually for particulate matter and/or discoloration
20 prior to administration, whenever solution and container permit. If these conditions exist, the
21 vaccine should not be administered.

22

1 **RECONSTITUTION**

2 ActHIB is to be reconstituted only with the accompanying saline diluent (0.4% Sodium Chloride)
3 or Tripedia vaccine to formulate TriHIBit vaccine. TriHIBit vaccine, ActHIB vaccine combined
4 with Tripedia vaccine by reconstitution, should not be administered to infants younger than 15
5 months of age.

6

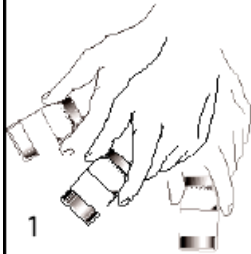
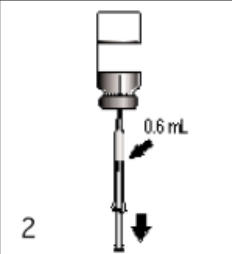
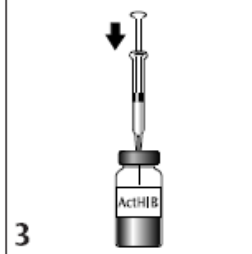
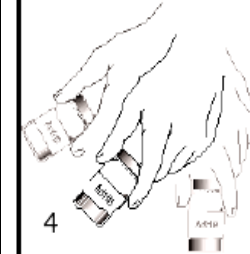
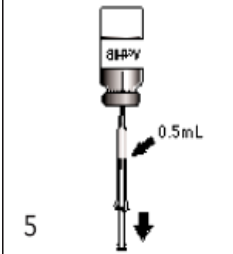
7 To prepare ActHIB vaccine, withdraw 0.6 mL of saline diluent (0.4% Sodium Chloride) and
8 inject into the vial of lyophilized ActHIB vaccine. Agitate the vial to ensure complete
9 reconstitution. The vaccine will appear clear and colorless. Withdraw a 0.5 mL dose of the
10 reconstituted vaccine and inject intramuscularly. After reconstitution with saline diluent (0.4%
11 Sodium Chloride), ActHIB vaccine should be administered promptly or stored refrigerated
12 between 2° to 8°C (35° to 46°F) and administered within 24 hours. If the vaccine is not
13 administered promptly, agitate the vial again before injection. Refer to Figures 1, 2, 3, 4, and 5.

14

15 To prepare TriHIBit vaccine, thoroughly agitate the vial of Sanofi Pasteur Inc. Tripedia vaccine
16 then withdraw 0.6 mL and inject into the vial of lyophilized ActHIB vaccine. After reconstitution
17 and thorough agitation, the combined vaccines will appear whitish in color. Withdraw a 0.5 mL
18 dose of the combined vaccines and inject intramuscularly. TriHIBit vaccine (ActHIB
19 reconstituted with Tripedia vaccine) should be administered within 30 minutes of reconstitution.
20 Refer to Figures 1, 2, 3, 4, and 5.

21

1 **Instructions for Reconstitution of ActHIB Vaccine with Saline Diluent (0.4% Sodium**
2 **Chloride) or Tripedia Vaccine (TriHIBit Vaccine)**

				
<p>Figure 1. Agitate vial prior to disinfecting the vial stopper to avoid possible contamination.</p>	<p>Figure 2. Withdraw 0.6 mL of 0.4% Sodium Chloride or Tripedia vaccine as indicated.</p>	<p>Figure 3. Cleanse the ActHIB vaccine stopper, insert the syringe needle into the vial, and inject the total volume of diluent.</p>	<p>Figure 4. Agitate vial thoroughly.</p>	<p>Figure 5. After reconstitution, cleanse vial stopper. Using a new needle and syringe, withdraw 0.5 mL of reconstituted vaccine and administer intramuscularly.</p>

3

4 Before injection, the skin over the site to be injected should be cleansed with a suitable germicide.

5

6 Each dose of ActHIB vaccine reconstituted with saline diluent (0.4% Sodium Chloride) or

7 Tripedia vaccine (TriHIBit vaccine) is administered intramuscularly in the outer aspect of the

8 vastus lateralis (mid-thigh) or deltoid. The vaccine should not be injected into the gluteal area or

9 areas where there may be a nerve trunk.

10

11 A 0.5 mL dose of ActHIB is approved for intramuscular administration in infants and children, 2

12 months through 5 years of age as a 4-dose series. The series consists of a primary immunization

1 course of 3 doses administered at 2, 4, and 6 months of age, followed by one booster dose,
2 administered at 15-18 months of age. The booster dose at 15-18 months of age may be given as
3 TriHibit vaccine (ActHIB reconstituted with Tripedia).

4

5 For previously unvaccinated children, the number of doses of Haemophilus b Conjugate Vaccine
6 needed depends on the age at which the immunization series is begun. A previously unvaccinated
7 infant, 7 to 11 months of age, should receive as primary immunizations, two doses of
8 Haemophilus b Conjugate Vaccine at 8-week intervals, followed by a booster dose at 15 to 18
9 months of age. A previously unvaccinated child 12 to 14 months of age should receive one dose
10 of Haemophilus b Conjugate Vaccine followed by a booster dose at 15 to 18 months of age (doses
11 to be separated by an interval of 8 weeks). A previously unvaccinated child 15 months through 5
12 years of age should receive one dose of ActHIB vaccine.

13

14 Preterm infants should be vaccinated according to their chronological age from birth. (19)

15

16 Interruption of the recommended schedule with a delay between doses should not interfere with
17 the final immunity achieved with ActHIB vaccine reconstituted with saline diluent (0.4% Sodium
18 Chloride) or with Tripedia vaccine (TriHIBit vaccine). There is no need to start the series over
19 again, regardless of the time elapsed between doses.

20

21 **HOW SUPPLIED**

22 **ActHIB Vaccine Reconstituted with Saline Diluent (0.4% Sodium Chloride)**

1 Single-dose, lyophilized vaccine vial (NDC 49281-547-58) packaged with single-dose diluent vial
2 (NDC 49281-546-05). Supplied as package of 5 vials each (NDC 49281-545-05).

3

4 **TriHIBit Vaccine, ActHIB Vaccine Reconstituted with Tripedia Vaccine**

5 Single-dose, lyophilized vaccine vial (NDC 49281-545-50) packaged with single-dose diluent vial
6 of Tripedia vaccine (NDC 49281-298-01). Supplied as package of 5 vials each (NDC 49281-597-
7 05).

8

9 **STORAGE**

10 Store lyophilized vaccine packaged with saline diluent (0.4% Sodium Chloride) or Tripedia
11 vaccine at 2° to 8°C (35° to 46°F). DO NOT FREEZE.

12

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18

1 Product Information

2 as of January 2014

3

4 Manufactured by:

5 **Sanofi Pasteur SA**

6 Lyon France

7 US Govt License #1724

8

9 Distributed by:

10 **Sanofi Pasteur Inc.**

11 Swiftwater PA 18370 USA

12 1-800-VACCINE (1-800-822-2463)

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