ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Infanrix Penta, Suspension for injection
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) vaccine (adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit

[1]adsorbed on aluminium hydroxide, hydrated (Al(OH)3) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate (AlPO4) 0.2 milligrams Al^{3+}
[4]propagated in VERO cells

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection
Infanrix Penta is a turbid white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Infanrix Penta is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B and poliomyelitis.

4.2 Posology and method of administration

Posology

Primary vaccination:

The primary vaccination schedule consists of three doses of 0.5 ml (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (such as 3, 5 months). There should be an interval of at least 1 month between doses.

The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained.

Where a dose of hepatitis B vaccine is given at birth, Infanrix Penta can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of six weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

Booster vaccination:

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix Penta a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix Penta a booster dose must be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations.

Infanrix Penta can be considered for the booster if the composition is in accordance with the official recommendations.

Paediatric population

There is no relevant use of Infanrix Penta in children over 36 months.

Method of administration

Infanrix Penta is for deep intramuscular injection, preferably at alternating sites for subsequent injections.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients or neomycin and polymyxin.

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis, hepatitis B or polio vaccines.

Infanrix Penta is contraindicated if the infant has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination should be continued with diphtheria-tetanus, hepatitis B and polio vaccines.

As with other vaccines, administration of Infanrix Penta should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication.

4.4 Special warnings and precautions for use

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give further doses of pertussis-containing vaccines should be carefully considered:

- Temperature of ≥ 40.0 C within 48 hours, not due to another identifiable cause;

- Collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination;
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination;
- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

As for any vaccination, the risk-benefit of immunising with Infanrix Penta or deferring this vaccination should be weighed carefully in an infant or in a child suffering from a new onset or progression of a severe neurological disorder.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Infanrix Penta should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Infanrix Penta should under no circumstances be administered intravascularly or intradermally.

Infanrix Penta will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus or poliovirus. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

As with any vaccine, a protective immune response may not be elicited in all vaccinees (see section 5.1).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute a contraindication for the use of Infanrix Penta. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

HIV infection is not considered as a contraindication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity.
As the benefit of the vaccination is high in this group of infants, vaccination should not be withheld or delayed.

4.5 Interaction with other medicinal products and other forms of interaction

Clinical studies have demonstrated that Infanrix Penta can be administered simultaneously with *Haemophilus influenzae* type b vaccines. In these clinical studies, the injectable vaccines were given at different injection sites.

There are no data with regard to the efficacy and safety of simultaneous administration of Infanrix Penta and Measles-Mumps-Rubella vaccine.

As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy an adequate response may not be achieved.

4.6 Fertility, pregnancy and lactation

As Infanrix Penta is not intended for use in adults, adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

- Clinical trials

The safety profile presented below is based on data from more than 10,000 subjects. In virtually all instances, Infanrix Penta was administered at the same time as a Hib vaccine.

As has been observed for DTPa and DTPa-containing combinations, an increase in local reactogenicity and fever was reported after booster vaccination with Infanrix Penta with respect to the primary course.

- Tabulated summary of adverse reactions (clinical trials):

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequencies per dose are defined as follows:

Very common: (≥ 1/10)
Common: (≥1/100 to <1/10)
Uncommon: (≥1/1,000 to <1/100)
Rare: (≥1/10,000 to <1/1,000)
Very rare: (<1/10,000)

Nervous system disorders:
Uncommon: somnolence
Very rare: convulsions (with or without fever)

Respiratory, thoracic and mediastinal disorders
Uncommon: cough

Gastrointestinal disorders:
Common: diarrhoea, vomiting

Skin and subcutaneous tissue disorders
Uncommon: dermatitis, rash
Very rare: urticaria

Metabolism and nutrition disorders
Very common: appetite lost

General disorders and administration site conditions:
Very common: fever ≥ 38°C, local swelling at the injection site (≤ 50 mm), fatigue, pain, redness
Common: fever >39.5°C, local swelling at the injection site (> 50 mm)*, injection site reactions, including induration
Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint*

Psychiatric disorders:
Very common: crying abnormal, irritability, restlessness
Uncommon: nervousness

- Post-marketing surveillance

Nervous system disorders:
Collapse or shock-like state (hypotonic-hyporesponsiveness episode)

Respiratory, thoracic and mediastinal disorders:
Apnoea [see section 4.4 for apnoea in very premature infants (≤ 28 weeks of gestation)]

General disorders and administration site conditions:
Swelling of the entire injected limb*

Immune system disorders
Allergic reactions, including anaphylactic and anaphylactoid reactions

- Experience with hepatitis B vaccine:

In extremely rare cases, paralysis, neuropathy, Guillain-Barré syndrome, encephalopathy, encephalitis and meningitis have been reported. The causal relationship to the vaccine has not been established. Thrombocytopenia has been reported with hepatitis B vaccine.

* Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. These reactions resolve over an average of 4 days.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA12

Results obtained in the clinical studies for each of the components are summarised in the tables below:

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix Penta

Antibody (cut-off)	3-5 months N= 168	6-10-14 weeks N= 362	1.5-3.5-6 months N= 55	2-3-4 months N= 326	2-4-6 months N= 1146)	3-4-5 months N= 884	3-4.5-6 months N=554
Anti-diphtheria (0.1 IU/ml) †	97.6	99.2	100	99.7	99.7	99.3	100
Anti-tetanus (0.1 IU/ml) †	99.4	100	100	100	100	99.4	100
Anti-PT (5 EL.U/ml)	100	99.7	100	100	99.7	99.4	100
Anti-FHA (5 EL.U/ml)	100	99.4	100	100	100	99.5	100
Anti-PRN (5 EL.U/ml)	100	100	100	100	99.8	99.5	100
Anti-HBs (10 mIU/ml) †	96.8	98.7*	100	98.4	99.4	98.2	99.6
Anti-Polio type 1 (1/8 dilution) †	97.4	99.4	ND	99.6	99.7	99.5	100

Anti-Polio type 2 (1/8 dilution) †	94.7	99.2	ND	97.1	99.6	99.5	100
Anti-Polio type 3 (1/8 dilution) †	99.3	99.4	ND	99.6	99.9	99.5	100

N = number of subjects
ND = not determined
* in a subgroup of infants not administered hepatitis B vaccine at birth, 80.2% of subjects had anti-HBs titres ≥ 10 mIU/ml
† cut-off accepted as indicative of protection

Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix Penta

Antibody (cut-off)	**Booster vaccination at 11/12 months of age following a 3-5 month primary course N = 168**	**Booster vaccination during the second year of life following a three dose primary course N = 350**
Anti-diphtheria (0.1 IU/ml) †	100	100
Anti-tetanus (0.1 IU/ml) †	100	100
Anti-PT (5 EL.U/ml)	100	99.7
Anti-FHA (5 EL.U/ml)	100	99.7
Anti-PRN (5 EL.U/ml)	100	99.7
Anti-HBs (10 mIU/ml) †	100	98.8
Anti-Polio type 1 (1/8 dilution) †	100	99.7
Anti-Polio type 2 (1/8 dilution) †	100	100
Anti-Polio type 3 (1/8 dilution) †	100	100

N = number of subjects
† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix Penta administration is equivalent to that of Infanrix, the protective efficacy of the two vaccines is expected to be equivalent.

The clinical protection of the pertussis component of Infanrix, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are efficacious in infants when administered according to the 3 and 5 months primary vaccination schedule, with a

booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age with this 3-5-12 months schedule. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this particular schedule.

Protective antibodies against hepatitis B have been shown to persist for at least 3.5 years in more than 90% of children administered four doses of a combined vaccine containing the same HBs antigen as Infanrix Penta. Antibody levels were not different from what was observed in a parallel cohort administered 4 doses of monovalent hepatitis B vaccine.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, specific toxicity, repeated dose toxicity and compatibility of ingredients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride (NaCl)
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

For adjuvants, see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

3 years.

Upon removal from the refrigerator, the vaccine is stable for 8 hours at 21°C.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
Do not freeze.

Store in the original package, in order to protect from light.

6.5 Nature and contents of container

0.5 ml of suspension in a pre-filled syringe (type I glass) with plunger stoppers (butyl).

Pack sizes of 1, 10, 20 and 50 with or without needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage, a white deposit and clear supernatant may be observed. This does not constitute a sign of deterioration.

The syringe should be well shaken in order to obtain a homogeneous turbid white suspension.

The DTPa-HBV-IPV suspension should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

Any unused product of waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBERS

EU/1/00/153/001
EU/1/00/153/002
EU/1/00/153/003
EU/1/00/153/004
EU/1/00/153/005
EU/1/00/153/006
EU/1/00/153/007
EU/1/00/153/008
EU/1/00/153/009
EU/1/00/153/010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 October 2000
Date of latest renewal: 23 October 2005

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substances

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89,
1330 Rixensart
Belgium

Novartis Vaccines and Diagnostics GmbH & Co. KG
Emil-von-Behring-Str. 76,
D-35041 Marburg
Germany

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89,
1330 Rixensart
Belgium

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

- **OTHER CONDITIONS**

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, as described in version 3.06 presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the product is on the market.

PSURs
The holder of marketing authorisation will submit 2-yearly PSURs.

The holder of the marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

Official batch release: in accordance with Article 114 of Directive 2001/83/EC as amended, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
1 PRE-FILLED SYRINGE WITHOUT NEEDLE
10 PRE-FILLED SYRINGES WITHOUT NEEDLES
20 PRE-FILLED SYRINGES WITHOUT NEEDLES
50 PRE-FILLED SYRINGES WITHOUT NEEDLES
1 PRE-FILLED SYRINGE WITH 1 NEEDLE
10 PRE-FILLED SYRINGES WITH 10 NEEDLES
20 PRE-FILLED SYRINGES WITH 20 NEEDLES
50 PRE-FILLED SYRINGES WITH 50 NEEDLES
1 PRE-FILLED SYRINGE WITH 2 NEEDLES
10 PRE-FILLED SYRINGES WITH 20 NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

Infanrix Penta, Suspension for injection
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) vaccine (adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 dose (0.5 ml):

Diphtheria toxoid[1]	≥ 30 IU
Tetanus toxoid[1]	≥ 40 IU
Bordetella pertussis antigens (Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 micrograms
Hepatitis B surface antigen[2]	10 micrograms
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU

[1]adsorbed on $Al(OH)_3$	0.5 milligrams Al^{3+}
[2]adsorbed on AlPO4	0.2 milligrams Al^{3+}

3. LIST OF EXCIPIENTS

Sodium chloride
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
1 pre-filled syringe
1 dose (0.5 ml)

10 pre-filled syringes
10 x 1 dose (0.5 ml)

20 pre-filled syringes
20 x 1 dose (0.5 ml)

50 pre-filled syringes

50 x 1 dose (0.5 ml)

1 pre-filled syringe + 1 needle
1 dose (0.5 ml)

10 pre-filled syringes + 10 needles
10 x 1 dose (0.5 ml)

20 pre-filled syringes + 20 needles
20 x 1 dose (0.5 ml)

50 pre-filled syringes + 50 needles
50 x 1 dose (0.5 ml)

1 pre-filled syringe + 2 needles
1 dose (0.5 ml)

10 pre-filled syringes + 20 needles
10 x 1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
Intramuscular use
Shake before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/153/001 - 1 pre-filled syringe without needle
EU/1/00/153/002 - 10 pre-filled syringes without needles
EU/1/00/153/003 - 20 pre-filled syringes without needles
EU/1/00/153/004 - 50 pre-filled syringes without needles
EU/1/00/153/005 - 1 pre-filled syringe with 1 needle
EU/1/00/153/006 - 10 pre-filled syringes with 10 needles
EU/1/00/153/007 - 20 pre-filled syringes with 20 needles
EU/1/00/153/008 - 50 pre-filled syringes with 50 needles
EU/1/00/153/009 - 1 pre-filled syringe with 2 needles
EU/1/00/153/010 - 10 pre-filled syringes with 20 needles

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Infanrix Penta
Suspension for injection
DTPa-HBV-IPV
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

LOT:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Infanrix Penta, Suspension for injection
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) vaccine (adsorbed)

Read all of this leaflet carefully before your child receives this vaccine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This vaccine has been prescribed for your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT INFANRIX PENTA IS AND WHAT IT IS USED FOR

Infanrix Penta is a vaccine used to protect your child again five diseases:
- **Diphtheria -** a serious bacterial infection that mainly affects the airways and sometimes the skin. The airways become swollen causing serious breathing problems and sometimes suffocation. The bacteria also release a poison. This can cause nerve damage, heart problems, and even death.

- **Tetanus** - tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are more likely to get tetanus infection are burns, fractures, deep wounds or wounds that have soil, dust, horse manure or wood splinters in them. The bacteria release a poison. This can cause muscle stiffness, painful muscle spasms, fits and even death. The muscle spasms can be strong enough to cause bone fractures of the spine.

- **Whooping cough (Pertussis)** - a highly infectious illness that affects the airways. It causes severe coughing that may lead to problems with breathing. The coughing often has a "whooping" sound. The cough may last for one to two months or longer. Whooping cough can also cause ear infections, chest infections (bronchitis) which may last a long time, lung infections (pneumonia), fits, brain damage and even death.

- **Hepatitis B -** is caused by the hepatitis B virus. It makes the liver swollen. The virus is found in body fluids such as in the vagina, blood, semen, or spit (saliva) of infected people.

- **Polio -** a viral infection. Polio is often only a mild illness. However, sometimes it can be very serious and cause permanent damage or even death. Polio can make the muscles unable to move (paralysis). This includes the muscles needed for breathing and walking. The arms or legs affected by the disease may be painfully twisted (deformed).

How the vaccine works
- Infanrix Penta helps your child's body make its own protection (antibodies). This will protect your child against these diseases.
- As with all vaccines, Infanrix Penta may not fully protect all children who are vaccinated.
- The vaccine cannot cause the diseases that it protects your child from.

2. BEFORE YOUR CHILD RECEIVES INFANRIX PENTA

Infanrix Penta should not be given if:

- your child is allergic (hypersensitive) to
  - Infanrix Penta, or any ingredients in Infanrix Penta (listed in Section 6)
  - neomycin or polymyxin (antibiotics).

  Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- your child has had an allergic reaction to any vaccine against diphtheria, tetanus, whooping cough, hepatitis B or polio.
- your child has had problems of the nervous system within 7 days after previous vaccination with a vaccine against whooping cough.
- your child has a severe infection with a high temperature (over 38°C).
  A minor infection such as a cold should not be a problem, but talk to your doctor first.

Infanrix Penta should not be given if any of the above apply to your child. If you are not sure, talk to your doctor or pharmacist before your child is given Infanrix Penta.

Take special care with Infanrix Penta

Check with your doctor or pharmacist before your child is given this vaccine if:

- after previously having Infanrix Penta or another vaccine against whooping cough, your child had any problems, especially:
  - a high temperature (over 40°C) within 48 hours of vaccination
  - a collapse or 'shock-like' state within 48 hours of vaccination
  - persistent crying lasting 3 hours or more within 48 hours of vaccination
  - fits with or without a high temperature within 3 days of vaccination
- your child has an undiagnosed or progressive disease of the brain or epilepsy which is not controlled. After control of the disease the vaccine can be given.
- your child has a bleeding problem or bruises easily
- your child tends to have fits when they have a fever, or if there is a history of this in the family.

If any of the above apply to your child (or you are not sure), talk to your doctor or pharmacist before your child is given Infanrix Penta.

Using other medicines or vaccines
Please tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently had any other vaccine.

Important information about some of the ingredients of Infanrix Penta
This vaccine contains neomycin and polymyxin (antibiotics). Please tell your doctor if your child has had an allergic reaction to these ingredients.

3. HOW INFANRIX PENTA IS GIVEN

How much is given
- Your child will have a total of two or three injections with at least 1 month between each injection.
- You will be told by the doctor or nurse when your child should come back for their next injections.
- If additional injections (boosters) are necessary, the doctor will tell you.

How the vaccine is given
- Infanrix Penta will be given as an injection into a muscle.
- The vaccine should never be given into a blood vessel or into the skin.

If your child misses a dose
- If your child misses an injection which is due, it is important that you make another appointment.
- **Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against the diseases.**

4. POSSIBLE SIDE EFFECTS

Like all medicines, Infanrix Penta can cause side effects, although not everybody gets them. The following side effects may happen with this vaccine:

Allergic reactions
If your child has an allergic reaction, see your doctor straight away. The signs may include:
- rashes that may be itchy or blistering
- swelling of the eyes and face
- difficulty in breathing or swallowing
- a sudden drop in blood pressure and loss of consciousness.

These signs usually start very soon after the injection has been given. Talk to a doctor straight away if they happen after leaving the doctor's surgery.

See your doctor straight away if your child has any of the following serious side effects:
- collapse
- times when they lose consciousness or have a lack of awareness
- fits – this may be when they have a fever

These side effects have happened very rarely with other vaccines against whooping cough. They usually happen within 2 to 3 days after vaccination.

Other side effects include:

Very common (these may occur with more than 1 in 10 doses of the vaccine)
- feeling tired
- loss of appetite
- high temperature of 38°C or higher
- swelling, pain and redness where the injection was given
- unusual crying
- feeling irritable or restless.

Common (these may occur in with up to 1 in 10 doses of the vaccine)
- diarrhoea
- being sick (vomiting)
- high temperature of more than 39.5°C
- swelling larger than 5 cm or hard lump where the injection was given.

Uncommon (these may occur in up to 1 in 100 doses of the vaccine)
- feeling sleepy
- cough
- itching (dermatitis), rash
- large swelling at the injected limb
- feeling nervous.

Very rare (these may occur with up to 1 in 10,000 doses of the vaccine)
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination
- temporarily stopping breathing (apnoea)

- lumpy rash (hives)
- swelling of the whole injected limb.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HHOW TO STORE INFANRIX PENTA

- Keep out of the reach and sight of children.
- Do not use Infanrix Penta after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C – 8°C).
- Store in the original package in order to protect from light.
- Do not freeze. Freezing destroys the vaccine.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Infanrix Penta contains

The active substances are:

Diphtheria toxoid[1]	not less than 30 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (Saccharomyces cerevisiae) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.2 milligrams Al^{3+}
[4]propagated in VERO cells

The other ingredients in Infanrix Penta are: sodium chloride (NaCl), medium 199 containing principally amino acids, mineral salts, vitamins and water for injections.

What Infanrix Penta looks like and contents of the pack

- Infanrix Penta is a white, slightly milky liquid presented in a pre-filled syringe (0.5 ml).
- Infanrix Penta is available in packs of 1, 10, 20 and 50 with or without needles.
- Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last approved in

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: http://www.ema.europa.eu/.

The following information is intended for medical or healthcare professionals only:

Upon storage, a white deposit and clear supernatant can be observed. This does not constitute a sign of deterioration.

The syringe should be well shaken in order to obtain a homogeneous turbid white suspension.

The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) suspension should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the container.