Mother and Baby Home Commission of Investigation

Trial summaries 1934-1973

Information in this document has been compiled from GSK internal records and published clinical trial data.
This information is provided in summary form and does not claim to be complete.

Introduction

These summary documents include information on nine separate trials - vaccine trials A to G, as they are referred to in the Commission of Investigation's report and two infant milk formula trials.

The documentation has been collated from our archives as well as other published sources to evaluate, as far as possible, the history of the vaccine or milk products after their trials were conducted by researchers in mother and baby homes.

Each summary outlines the following information:

- What the trial was for, for example, if it was trialling a treatment for infectious diseases such as diptheria, tetanus or measles;
- What date the trial took place;
- The location where it took place;
- The number of participants in the trial;
- The name of those organising the trial;
- The ingredients in the vaccine;
- The dosage;
- How the vaccine was administered;
- Any side effects observed in the trial and side effects observed in later trials;
- The follow up process with trial participants after vaccination and any other comments;
- Further commercialisation and/or licensing of the product.

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Trial A
Wellcome's APT anti-diphtheria vaccine

Date
1935
Trial organiser
Dr Denis F Hanley
Locations
- Dublin Union
- St Vincent's Industrial School, Dublin
- St Joseph's School for Deaf Boys, Dublin
- St Saviour's Orphanage, Dublin

Participant numbers
70

Purpose
To reduce the incidence of diphtheria (a serious infection that can lead to difficulty breathing, heart failure, paralysis and death) and associated child mortality in Dublin. Diphtheria was endemic at this time and outbreaks were common.

Vaccine(s) used
- Alum Precipitated Toxoid (APT) anti-diphtheria vaccine

Usage (doses)
One dose only.

Administration
Injection into the muscle in the upper arm.

Observed side effects
Reactions included: local inflammation around the injection site; localised cold abscesses (abscesses without the usual signs of inflammation); stiffness; headache; and temperature. These reactions occurred three days after vaccination and typically disappeared four or five days after vaccination. No reactions were observed among the first 24 infants. The second 46 were noted to develop a painless pea-sized lump at the injection site, which gradually disappeared.

Side effects observed in other published clinical trials using these vaccines
Local injection site reactions (swelling, redness, tenderness) and general reactions including headache and malaise (generalised weakness/feeling unwell).

Follow-up after vaccination
All children were observed every second day for two weeks following vaccination. The second 46 were Schick tested nine weeks after vaccination. Schick testing is a specific skin test to determine if a person is susceptible to diphtheria. A small (0.1ml) injection of diluted diphtheria toxin is injected under the skin to provoke a reaction. If there is no reaction, this indicates immunity (that the immune system will be able to defend against the disease). Of the 46 children who were Schick tested, 45 had no reaction and one child did have a reaction. After vaccination, 12 children were also randomly chosen for blood testing in addition to the Schick testing that all the children underwent. The one child that had the positive Schick test result also had a low level of antitoxic units in their blood indicating that they had a poor response to the vaccine.

Other
This vaccine was also given to 39,267 Dublin school children before it was commercially available. This was done with support from Dublin municipal health authorities as part of an immunisation scheme to address the public health need of the time. The vaccine became commercially available in the UK in February 1935.

Trial B
Wellcome's '*Quadrivax*' vaccine

Date
1960/61
Trial organisers
Professor Patrick Meenan and Dr Irene Hillary
Locations
- Bessborough, Cork
- Pelletstown/St Patrick's, Dublin
- Manor House Castlepollard, Westmeath
- Ard Mhuire Dunboyne, Meath
- St Clare's Home Stamullen, Meath
- Mount Carmel Industrial School, Moate, Westmeath

Participant numbers
58

Purpose
To compare the antibody responses generated by the body after vaccination with a quadruple vaccine (diphtheria, tetanus, pertussis (whooping cough) - known as DTP - and polio combined) with the standard vaccines in use at the time, which consisted of DTP and polio administered separately. A combined vaccine would reduce the number of vaccinations required to be given to infants.

Vaccines used
- DTP
- Polio IPV (Inactivated polio vaccine - *Polimylex*)
- DTP and polio combined (*Quadrivax*)

Usage (doses)
Three doses with 28-day intervals.

Administration
- **Group A (30 children):** DTP (right arm), *Polimylex* (left arm)
- **Group B (28 children):** *Quadrivax* (left arm)

Observed side effects
In January 1961, 18 infants became ill with vomiting and mild diarrhoea at Bessborough. Of these, 15 were involved with the vaccine trial and comprised infants from both groups A and B who had just received their second doses. One infant had been adopted from the home and subsequently did not receive his second dose. The other two infants were not involved with the trial at all.

Some 43 children resident in the other trial locations had been given a dose of vaccine from the same batches and did not fall ill. Faecal testing of some of the infants that fell ill led the investigators in the trial to conclude the observed illness was an unrelated virus that the infants had caught. No reactions, either at the local injection site or general, occurred in any of the infants after the first or third injections with either group A or group B.

Side effects observed in other published clinical trials using these vaccines
No further information available.

Follow-up after vaccination
Blood samples were taken within 14 days of the first vaccination and 14 days after the third vaccination.

Some months later, 20 children from group A and 16 children from group B received a booster of the polio vaccine.

Other
The DTP vaccine and the polio vaccine used in this trial were both made commercially available in the UK in the late 1950s. Combination vaccines from other manufacturers similar to the one used in this study were already in use in the United States from 1960 and Canada from 1959, respectively.

Trial C
Wellcome '*Wellcovax*' measles vaccine

Date
1964
Trial organisers
Professor Patrick Meenan and Dr Irene Hillary
Location
Sean Ross Abbey, Tipperary

Participant numbers
12

Purpose
To evaluate the antibody response and reaction after vaccination with 0.1ml of measles vaccine (MV27).

Vaccines used
– *Wellcovax*, attenuated measles vaccine (batch MV27)

An attenuated vaccine uses a live virus strain which has been altered to elicit an immune response against the virus but not to cause the disease.

Usage (doses)
One dose only – 0.1ml.

Administration
Arm (deltoid) subcutaneous (injection administered just under the skin) or intramuscular (injection administered deep into the muscle).

Observed side effects
One infant experienced a reaction which was not described.

Side effects observed in other published clinical trials using these vaccines
A proportion of cases: transient (short) fever 6-10 days after vaccination, rash 9-12 days after vaccination.

Occasionally: local injection site reaction, regional adenopathy (swelling of glands), exacerbation (worsening) of pre-existing tonsillitis (inflammation of the tonsils) or otitis media (middle ear infection) 7-12 days after administration.

Follow-up after vaccination
Blood samples were taken before vaccination and two months after vaccination. Rectal temperatures were taken on the day of vaccination and 14 days later.

Other
Wellcovax was licensed in the UK in 1965.

Trial D
Glaxo Laboratories '*Mevilin-L*' measles vaccine

Date
1964/65
Trial organisers
Professor Patrick Meenan and Dr Irene Hillary
Location
Dublin (exact institution is unclear from available records)

Participant numbers
34

Purpose
To determine whether one dose of the inactivated vaccine (vaccine that only contains killed viruses and no live viruses) a month in advance of the attenuated vaccine reduced the incidence of side effects after the attenuated dose.

An attenuated vaccine uses a live virus strain which has been altered to elicit an immune response against the virus but not to cause the disease.

Vaccines used
- Inactivated (Edmonston strain) measles (a measles vaccine using the killed Edmonston strain of the measles virus)
- Placebo (a non-active control vaccine that will have no effect on the recipient)
- Attenuated (Schwartz strain) measles (*Mevilin-L*) (a measles vaccine using the live attenuated Schwartz strain)

Usage (doses)
- **Group A (17 children):** one dose inactivated, followed by one dose attenuated one month later.
- **Group B (17 children):** one dose placebo, followed by one dose attenuated one month later.

Administration
Inactivated given intramuscularly (injected deep into the muscle), attenuated given subcutaneously (injected under the skin).

Observed side effects
- **Group A:** one child developed conjunctivitis (inflamed eyes) and two children had temperatures above 101°F for less than two days.
- **Group B:** three children developed a rash, one child with coeliac disease (intolerance to gluten) vomited and six children had temperatures above 101°F for less than two days.

Side effects observed in other published clinical trials using these vaccines
- **Inactivated measles vaccine**
  - Transient local erythema (short-term redness at the injection site), tenderness and swelling at the injection site, fever, rash (up to 1% of vaccinated children).
- **Attenuated measles vaccine (*Mevilin-L*)**
  - Fever, cough, runny nose, rash
  - Rarely: diarrhoea

Follow-up after vaccination
Blood samples were taken before the first vaccination and one month after the second vaccination. Rectal temperatures were taken daily between six and 14 days after vaccination.

Other
Mevilin-L was licensed in the UK 1965.

Trial E
Glaxo Laboratories '*Quintuple*' 5-in 1-vaccine

Date
1965
Trial organisers
Professor Patrick Meenan and Dr Irene Hillary
Location
unconfirmed

Participant numbers
Unconfirmed, but the Commission identified 19 participants at two locations from its investigations.

Purpose
To assess the effectiveness against measles infection of Glaxo's 5-component vaccine on its own, compared to a weakened live measles vaccine.

An attenuated vaccine uses a live virus strain which has been altered to elicit an immune response against the virus but not to cause the disease.

Vaccines used
- Inactivated measles vaccine (using the killed Edmonston strain virus)
- Attenuated (Schwartz strain) measles (*Mevilin-L*) (a measles vaccine using the live attenuated Schwartz strain)
- '*Quintuple*' vaccine, DTP (diphtheria, tetanus, pertussis (whooping cough)) and polio vaccine (*Quadrilin*) combined with inactivated measles (a measles vaccine using the killed Edmonston strain virus)

Usage (doses)
- **Group A:** administered three doses of the '*Quintuple*' vaccine at monthly intervals.
- **Group B:** administered three doses of inactivated measles vaccine at monthly intervals.

Six months after primary vaccination, half the children were given a booster of inactivated measles and the other half were given a booster of attenuated measles.

Administration
Arm (injection)

Side effects observed in other published clinical trials using these vaccines
- **Inactivated measles**
  - Transient local erythema (short term redness at the injection site), tenderness and swelling at the injection site, fever, rash (up to 1% of vaccinated children).
- **Attenuated (Schwartz strain) measles (*Mevilin-L*)**
  - Fever, cough, runny nose, rash
  - Rarely: diarrhoea

Follow-up after vaccination
Blood samples were to be taken before first vaccination and one month after third vaccination. Blood samples were to be taken before the booster and one month after it.

Other
A similar trial was conducted in the UK.

Quadrilin was made commercially available in the UK 1962. It was re-registered with a new formulation, which UK Ministry of Health granted a license for on 11 Feb 1964. *Mevilin-L* was licensed in the UK in 1965.

Trial F
Glaxo Laboratories measles vaccine

Date
1968/69
Trial organiser
Dr Victoria Coffey
Location
Pelletstown/St Patrick's, Dublin

Participant numbers
30

Purpose
To analyse the safety profile in children of a single dose of live further attenuated measles vaccine prepared from the Schwarz strain of the virus and to estimate the effectiveness of vaccination as measured by:
- **(a)** post-vaccination antibody levels, which are markers of an immune response and
- **(b)** protection from the natural infection after sibling contact.

An attenuated vaccine uses a live virus strain which has been altered to elicit an immune response against the virus but not to cause the disease.

Vaccines used
- Attenuated (Schwartz strain) measles vaccine using the live attenuated Schwartz strain (available records indicate the trial vaccine was *Mevilin-L*).

Usage (doses)
One dose only.

Administration
Arm (injection)

Observed side effects
No information available.

Side effects observed in other published clinical trials using these vaccines
- Fever, cough, runny nose, rash
- Rarely: diarrhoea

Follow-up after vaccination
The vaccinated child and their sibling who was not given the vaccine (control partner) were monitored for fever, rash, coryza (nose inflammation), pharyngitis (sore throat), cough, conjunctivitis (inflamed eyes), vomiting, diarrhoea, anorexia (weight loss) during the first three weeks after vaccination.

Every fifth child had a blood sample taken immediately prior to vaccination and again four weeks later. All children were followed up and the incidence of measles in the susceptible sibling and the vaccinated children was recorded after 12 months, or after the next measles epidemic.

Other
Mevilin-L was licensed in the UK 1965.

Trial G
Wellcome diphtheria, tetanus and pertussis (DTP) trial

Date
1973
Trial organisers
Professor Patrick Meenan, Dr Irene Hillary and Dr Margaret Dunleavy
Locations
- Pelletstown/St Patrick's, Dublin
- Madonna House Blackrock, Dublin
- Cottage Home Dun Laoghaire, Dublin
- Ms. Smyly's Bird's Nest Home, Dublin
- One other institution unidentifiable from the records

Participant numbers
118 (53 in mother and baby homes and 65 in the general community)

Purpose
To compare certain expected symptoms associated with vaccination such as pain, redness, or swelling at the injection site of combined DTP (diphtheria, tetanus, pertussis (whooping cough)) vaccines (*Trivax* and *Trivax AD*) with a new modified combined DTP vaccine.

Vaccines used
- *Trivax*, commercially available formulation
- *Trivax AD*, commercially available formulation
- New DTP Plain (vaccine that does not contain additional components to improve the immune response)
- New DTP Absorbed (a vaccine which contains an ingredient called an adjuvant, in this case aluminium hydroxide, which helps to enhance the immune response to the vaccine)

Usage (doses)
Two doses (both doses from same batch) with an interval of six weeks between doses.

Administration
Upper arm or buttock (injection)

Observed side effects
Three severe febrile (fever) reactions (temperature increase, chills, sometimes headache and back pain) following New DTP Absorbed vaccine.

Side effects observed in other published clinical trials using these vaccines
- ***Trivax***
  - Local reaction at the injection site such as swelling, redness and tenderness.
  - Transient (short-term) rise in temperature, restlessness or loss of appetite sometimes seen.
  - Rarely: allergic reactions, including pallor (abnormally pale skin) and dyspnoea (difficulty breathing)
- ***Trivax AD***
  - Erythema (redness at the injection site) may persist for longer than usually encountered with *Trivax.*
  - Transient (short-term) rise in temperature, restlessness or loss of appetite may sometimes occur a few hours after vaccination.
  - Rarely: allergic reactions, including pallor (abnormally pale skin) and dyspnoea (difficulty breathing)

Follow-up after vaccination
Rectal temperatures were taken at the time of vaccination and every three hours after, for a total of twelve hours. Reactions were assessed the mornings after vaccination. Additionally, the children in the community were visited seven days after vaccination for a follow-up reaction assessment. Blood samples were taken a week after the second vaccination.

Other
Before this trial took place, *Trivax* was made commercially available in the UK 1961. *Trivax AD* was licensed in the UK during 1969 and continued to be licensed after the trial.

Milk Trial 1
Glaxo infant milk formula trials

Date
1967
Trial organisers
Dr Victoria Coffey with Dr Eithne Conlon
Locations

- Bessborough, Cork
- Pelletstown/St Patrick's, Dublin

Participant numbers
23

Purpose
To determine whether new formulations of infant milk were well tolerated by babies.

Milks used
- *Ostermilk 1*
- L.14 (half cream milk/half fat)
- L.20 (full cream milk/full fat)

Ingredients/components
The blend proportions were as follows: 90% L.14 or L.20 intermediate base, 0.99% lactose (sugar found in milk) and 0.01% vitamin mix.

Usage (doses)
Use as part of baby's normal feeding schedule (five to seven times per day).

Administration
- **Group A:** every second baby was to receive L.14, the other babies were to receive the standard half cream (half fat) infant milk used by the home as a control. L.14 babies were to be moved onto L.20 as the person in charge of feeding saw fit.
- **Group B:** every second baby was to receive L.20, the other babies were to receive *Ostermilk 1* or the standard full cream infant milk used by the home.
- **Group C:** were to be fed as normal.

Observed side effects
Six out of seven babies on L.14 experienced vomiting and diarrhoea. Those in charge of the infants reverted to the normal feeds used at the homes due to these reactions and reported the reactions to the supervising doctors. The trial was stopped early as a result.

It appears from later testing that the high levels of lactose proved too strong for the babies, as those given diluted L.14 had no similar reported reactions.

Irish L.20 babies were only slightly more reactive to the formula than the control babies, indicating that it was well tolerated, however, in a similar trial in London in 1967/68, L.20 babies experienced vomiting and in one case a rash.

Follow-up
Group A was supervised closely for one month, group B for three months, to include follow-up of the babies' weight, food intake and note any untoward events, both in the trial and control groups (eg. vomiting, diarrhoea, constipation, excess wind, etc.). Follow-up forms were used to record this information. Form A was to be completed after 15 days and Form B was to be completed when the baby left the home.

Other
Trials undertaken on a similar basis were also conducted in the UK, Malaysia and Argentina. *Ostermilk*, which had several different formulations with varying fat content, including *Ostermilk 1*, had been sold in many countries across the world since it was introduced in the 1930s including the UK, Australia, New Zealand, India, Kenya, Argentina and Malaysia. Various re-formulations/improvements were made over the years.

Milk Trial 2
Glaxo infant milk formula trials

Date
1969
Trial organisers
Dr Victoria Coffey with Dr Eithne Conlon and Dr Biddy Foley
Locations:
- Bessborough, Cork
- Pelletstown/St Patrick's, Dublin

Participant numbers
Potentially 80 (40 at each site)

Purpose
To determine whether the new formulations of infant milk were well tolerated by babies.

Milks used
- *Ostermilk 1*
- BY03110 (Pelletstown)
- BY03111 (Bessborough)

Ingredients/components
No information

Usage (doses)
Was to be fed to babies as normal 5-7 times a day.

Administration
Children to be allocated to each group in turn:
- **Group A:** BY-coded milk
- **Group B:** *Ostermilk 1*

Observed side effects
No information

Follow-up
A form was to be completed daily for the first 14 days of the trial. A second form was to be completed weekly until the baby stopped milk feeds or left the home. The urine of the babies at Pelletstown was to be tested weekly and notes made in the second form from resulting chromatography (a laboratory technique used to separate a mixture into its component parts).

Other
The draft protocol is the only information GSK retains regarding this trial. No evidence could be found that this trial was conducted.