Chapter 34: Vaccine trials

Introduction

34.1 The Commission's Terms of Reference require it to establish the extent of compliance with relevant regulatory and ethical standards of the time of systemic vaccine trials found to have been conducted on children in one or more of the institutions being investigated by the Commission during the relevant period.

Sources

34.2 GlaxoSmithKline provided the Commission with extensive documentation about vaccine trials and clinical trials conducted in children's residential institutions in Ireland in the period 1930 to 1973. These trials all involved either the Wellcome Foundation or Glaxo Laboratories. These companies are today part of the same pharmaceutical corporation - GlaxoSmithKline - but were separate commercial entities when the trials described here were being conducted. The archives of both companies, although now merged, evolved separately. The Wellcome Foundation retained extensive documentation while Glaxo Laboratories's available documentation was quite sparse. Most of the documentation quoted below, particularly the protocols for the tests and the correspondence between the companies and the researchers, came from the GlaxoSmithKline archives.

34.3 The institutional records of the mother and baby homes involved, which were provided to the Commission by the Child and Family Agency (TUSLA), were then used to establish the identity of the children involved where possible and to establish what, if any, involvement or knowledge the authorities in these institutions had about the trials. These institutional records are described in the individual chapters on the institutions.

34.4 Relevant documentation was also provided by the HSE and the Department of Health (see Part 5: Archives).

Regulatory Standards

34.5 The legislation governing clinical research and the importation of vaccines into Ireland during the period under review was the *Therapeutic Substance Act* 1932,[1] and the *Control of Clinical Trials Act* 1987.[2] None of the trials described here took place after the enactment of the latter Act.

34.6 The *Therapeutic Substance Act* 1932 aimed to regulate the manufacture, import and sale of therapeutic prophylactic and diagnostic substances. Its primary purpose was to ensure that imported vaccines, sera, toxins, antitoxins and antigens complied with standards of strength, quality and purity as prescribed by an advisory committee. The act also made provision for the Minister for Local Government and Public Health/Minister for Health to grant Manufacturer's Licences, Import Licences, Import Permits and Research Licences to suitably qualified applicants.

34.7 Researchers undertaking clinical trials were obliged to get a Research Licence from the Minister for Local Government and Public Health (the Department of Health from 1947). A Research Licence granted the holder ministerial approval to import therapeutic substances covered by the *Therapeutic Substance Act* for the purpose of scientific research. The terms and constraints of a Research Licence were clearly defined. Firstly, the licence applied to the licensee only. Secondly, scientific research could be undertaken only at the address stated on the licence; if the licence holder wanted to conduct clinical research in a location other than that stated on the licence, the holder was obliged to get the authorisation of the minister to do so.

34.8 The Act did not specifically provide for a regulatory body or mechanism to oversee its implementation. The Act required that a Therapeutic Substances Advisory Committee be established to advise and assist the minister in the making of orders and regulations under the Act. This was not done until 1939 when the events surrounding the Ring College immunisation problems in 1936, and the associated High Court case in 1939, forced the government of the day to establish such a

[1] http://www.irishstatutebook.ie/eli/1932/act/25/enacted/en/print.html.
[2] http://www.irishstatutebook.ie/eli/1987/act/28/enacted/en/html.

committee.[3] It has been stated that there was widespread non-compliance with the Act and that the code was not enforced by the department.[4]

34.9 The National Drugs Advisory Board (NDAB) was established in 1966. It was set up to organise and administer a service for obtaining, assessing and disseminating information about the safety of new and reformulated drugs and of drugs already in use, and to advise the Minister for Health on matters relating to the safety and quality of drugs.[5] As its name makes clear, it was an advisory and not an implementation board. A voluntary agreement was entered into by the NDAB with the pharmaceutical industry and the medical profession whereby the prior approval of the NDAB would be sought before the undertaking of clinical trials. This did not change the law in any way.

Ethical Standards

34.10 Ethical standards relating to clinical trials in human research subjects, and especially the critical issue of consent, applicable during the period 1922-1998 were set out in the *Nuremberg Code* (1947), *Report of the Medical Research Council (UK)* (1962) and the *Declaration of Helsinki* (1964). The main points of each are as follows:

Nuremberg Code (1947)[6]

34.11 The *Nuremberg Code* was drawn up by American judges sitting in judgment of Nazi doctors accused of conducting murderous and torturous human experiments in the Nazi concentration camps.[7] It states:

> The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient

[3] In 1936, an immunisation accident at Ring College, County Waterford, caused twenty children to develop tuberculosis and the death of a 12 year old girl. See Michael Dwyer, *Strangling Angel: Diphtheria and childhood immunisation in Ireland*, (Liverpool, 2018), 101-43.
[4] This view was expressed by Mr Thomas McGuinn, chief pharmacist at the Department of Health to the Lindsay Tribunal and accepted at p. 210 of the *Report of the Tribunal of Inquiry into the Infection of Persons with Haemophilia* and Related Matters Dublin: Government Publications, 2002.
[5] SI 163/1966: *The National Drugs Advisory Board (Establishment) Order* 1966. http://www.irishstatutebook.ie/eli/1966/si/163/made/en/print
[6] https://history.nih.gov/research/downloads/nuremberg.pdf.
[7] Evelyne Shuster, *Fifty years later: The significance of the Nuremberg Code*, The New England Journal of Medicine, 13 November 1997: https://www.rcsi.ie/files/research/docs/20151204040235_nuremberg-code.pdf

knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

'Clinical Research', *Report of the Medical Research Council*, 1962/63.[8]

34.12 In its report for 1962/63, the British Medical Research Council (MRC) published a series of recommendations aimed at clinicians engaged in clinical research. The MRC subsequently published a statement on 'Responsibility in investigations on human subjects' in the *British Medical Journal*.[9] The principal recommendation echoed that of the *Nuremburg Code* in relation to the obtaining of consent - that it is 'both considerate and prudent to obtain a patient's agreement before using a novel procedure'. The second MRC recommendation was that clinical researchers must ensure that

> it is clearly within the competence of a parent or guardian of a child to give permission for procedures intended to benefit the child when he is not old or intelligent enough to be able himself to give valid consent.
>
> It should be understood that the possibility or probability that a particular investigation will be of benefit to humanity or posterity would afford no defence in legal proceedings. The individual has rights that the law protects, and nobody can infringe those rights for the public good. In investigations of this type it is therefore always necessary to ensure that the true consent of the subject is explicitly obtained.
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> The need for obtaining of consent in this type of investigation has been generally recognised, but there are some misunderstandings as to what constitutes evidence. In general, the investigator should obtain the consent

[8] Medical Research Council, 'Clinical Research', *Report of the Medical Research Council for 1962-63*, 248-51.
[9] Medical Research Council, 'Responsibility in investigations on human subjects; Statement by the Medical Research Council', *British Medical Journal*, 18 July 1964, 178-80.

himself in the presence of another person. Written consent unaccompanied by other evidence that an explanation has been given, understood, and accepted, is of little value.

In the opinion of the Council, the head of a department where investigations on human subjects take place has an inescapable responsibility for ensuring that practice by those under his direction is irreproachable.

Declaration of Helsinki (1964)[10]

34.13 This states:

The nature, the purpose and the risk of clinical research must be explained to the subject by the doctor.

Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

The subject of clinical research should be in such a mental, physical and legal state as to be able to exercise fully his power of choice.

Consent should, as a rule, be obtained in writing. However, the responsibility for clinical research always remains with the research worker; it never falls on the subject even after consent is obtained.

Consent for children

34.14 Common law recognised that medical procedures could not generally be carried out without the consent of the person affected. Legally, children do not, and did not at the time of these trials, have the capacity to consent to participation in the trials. In general, the parent(s) or guardians had the authority to consent to medical procedures involving the child. The situation in respect of illegitimate children was unclear before the enactment of the *Guardianship of Children Act 1964.* This Act provided, for the first time, that an unmarried mother was automatically the guardian of her child. The notion that either parent (if married) or the mother (if unmarried) could give consent on behalf of the child to medical treatment was assumed to be part of the parent's custody rights and responsibilities with respect to the child.[11] In more recent years, case-law has qualified the legal capacity of parents to give consent to experimental or

[10] World Medical Assembly, *Declaration of Helsinki: Recommendations guiding doctors in clinical research*. Adopted by the WMA, June 1964.

[11] Skegg, "Consent to Medical Procedures on Minors" (1973) 36 M.L.R. 370 at 375.

investigative treatment in the absence of a *direct medical benefit* to the child.[12] For the purposes of the trials that occurred before 1964, the mother's consent, in the case of 'illegitimate' children who remained in their mother's custody, was required prior to medical treatment or vaccination unless some other legal guardian was appointed or an order had been made placing the child formally in the care of the State under the *Children Acts 1908-1941* or in the context of wardship proceedings.

34.15 The common law view of the mother as custodian of the illegitimate child was strengthened over the years by the application of provisions of the Irish Constitution. In *State (Nicolau) v. An Bord Uchtala* (1966),[13] the Supreme Court reasoned that the mother had a personal constitutional right to the custody of her child born out of wedlock, by virtue of Article 40.[14] This view deepened in *G. v. An Bord Uchtala* (1979),[15] where it was found that the right to custody 'is clearly based on the natural relationship which exists between a mother and child'. The Supreme Court in *G*. considered that s. 6(4) of the *Guardianship of Infants Act 1964*, deeming the unmarried mother automatically the guardian of her child, was construed merely to 'constitute a compliance by the State with its obligation, in relation to the mother of an illegitimate child, to defend and vindicate in its laws this right to custody' - in other words, that this was a right which predated the *Guardianship of Infants Act 1964*.

34.16 It seems clear that, in cases where the children who were subjected to vaccine trials were accompanied in the institutions by their mothers, the mother was the person whose consent should have been sought. The issue is a bit more complex in the cases of children whose mothers were not with them in the institutions. If the mother's whereabouts were known, it is strongly arguable that she should have been contacted and her consent requested. In cases where mothers could not be contacted, the guardian of the children could be either the authorities in the institution or the health authority which was paying to maintain them in the institution. Precisely who was the guardian is, however, largely irrelevant as no attempt seems to have been made to seek the consent of parents or guardians.

[12] Sommerville, *Consent to Medical Care* Ottawa: Law Reform Commission, 1980, at p.71. See generally: Nicholson, *Medical Research with Children* Oxford: O.U.P., 1985; and Nicholson, "The Ethics of Research with Children", in Brazier & Lobjoit (eds.), *Protecting the Vulnerable* London: Routledge, 1991.
[13] [1966] I.R. 567 (S.C.).
[14] The father of the 'illegitimate' child did not have a similar constitutional right to custody or guardianship of the child, though, since the passing of the Guardianship of Infants Act in 1964, he has a statutory right to apply for either.
[15] [1980] I.R. 32 (S.C.).

Confirmed Vaccine Trials

34.17 The Commission has identified a total of 13 vaccine trials which took place in the period covered by the Commission's remit 1922-1998; seven of these were conducted in the institutions under investigation and were conducted in the period 1934-1973. There is a further suspected trial in 1965 but it has not been confirmed.

1930: J C Saunders, Wellcome's APT anti-diphtheria vaccine Cork.[16]

34.18 In 1930, Dr J C Saunders, Chief Medical Officer, Cork City, administered Wellcome's experimental Alum Precipitated Toxoid (APT) anti-diphtheria vaccine to 142 children in two unidentified orphanages and to 436 children aged between eight months and 14 years among the general child population in Cork city. This was backed by the Department of Local Government and Public Health, the South Cork Board of Public Assistance and the Irish National Teachers' Organisation. It was regarded as an important public health response to one of the worst diphtheria epidemics ever recorded in Europe.[17] The Commission has been unable to definitively identify the children's institutions referred to in Dr Saunders's published report of the trial. Records relating to Cork County Home give no indication that the trial was conducted there. The institutional records of the only other Cork institution which comes under the Commission's remit, Bessborough, do not indicate any involvement in this trial. Accordingly, there is no evidence to suggest that this vaccine trial was conducted in an institution under the Commission's remit.

1934-36: JC Saunders, Wellcome's APT anti-diphtheria vaccine Cork.[18]

34.19 In the mid-1930s, Dr J C Saunders partnered with Wellcome Research Laboratories to develop a 'one-shot' anti-diphtheria vaccine to protect infants and children from diphtheria, the most dreaded childhood disease at that time. Between 1934 and 1936, Dr Saunders administered Wellcome's still experimental APT anti-diphtheria antigen to 250 children in an unidentified residential institution for boys and to 2,541 children among the general population. Again, this was backed by the Department of Local Government and Public Health as well as the South Cork Board of Public Assistance. It was regarded as an important public

[16] J.C. Saunders, 'Alum-Toxoid as an immunizing agent against diphtheria', *Lancet*, Vol.229, No. 5931 (12 November 1932), 1047-50.
[17] Michael Dwyer, *Strangling Angel: Diphtheria and childhood immunization in Ireland*, (Liverpool University Press, 2018), 82-90.
[18] J.C. Saunders, 'Alum precipitated toxoid in diphtheria prevention', *Lancet*, 1 May 1937, 1064-68.

health intervention against endemic diphtheria.[19] It was not possible to identify the children's institution referred to in Dr Saunders's published report of the trial. Records from Cork County Home and from Bessborough give no indication that the trial was conducted in either institution. Accordingly, there is no evidence to suggest that this vaccine trial was conducted in an institution under the Commission's remit.

1935: Denis F Hanley, Wellcome's APT anti-diphtheria vaccine Dublin.

34.20 In 1934, Dr Denis Hanley, Assistant Medical Officer for the City of Dublin, administered Wellcome's APT anti-diphtheria vaccine to 24 children, varying in age from seven months to 14 years, resident in the Dublin Union. In 1935, Dr Hanley administered Wellcome's APT vaccine to a further 46 children, aged four to 15 years, resident in St Vincent's Industrial School, Goldenbridge,[20] St Joseph's School for Deaf Boys, Cabra,[21] and St Saviour's Orphanage, Lower Dominick Street, Dublin. Dr Hanley also administered Wellcome's APT vaccine to 39,267 Dublin school children before it had been made commercially available. The Dublin Union comes under the Commission's remit and the trial is described under Trial A below.

1935: Naughten, White, Foley, Wellcome's APT anti-diphtheria vaccine Tipperary.[22]

34.21 In 1935, medical officers trialled Wellcome's APT antigen in children's residential institutions in Tipperary. In an article in the *British Medical Journal*, Dr Martin Naughten, County Medical Officer for Tipperary South Riding, Dr J.H. White and Dr A. Foley reported that they had trialled Wellcome's APT anti-diphtheria vaccine among 370 children in three residential institutions. The trial was limited to children aged ten years and older. Although the institutions involved are not named in the article the number of children involved, and their age range, suggests that the trial was undertaken in the three industrial schools in Tipperary South: St Bernard's Industrial School, Fethard; St Francis's Industrial School, Cashel; and St Joseph's Industrial School, Ferryhouse, Clonmel. These institutions are outside the Commission's remit.

[19] Dwyer, *Diphtheria*, (Liverpool, 2018), 94-110.
[20] See Ryan Commission Report: http://www.childabusecommission.ie/rpt/02-07.php
[21] See Ryan Commission Report: http://www.childabusecommission.ie/rpt/01-13.php
[22] Naughten, White, Foley, 'Prevention of diphtheria by the "one-shot" method using alum-precipitated toxoid', *British Medical Journal* (9 November 1935), 893.

1960/61: Professor Patrick Meenan and Dr Irene Hillery, Wellcome's 'Quadrivax' vaccine.

34.22 In 1960 and 1961, Professor Patrick Meenan and Dr Irene Hillery, both of the Department of Medical Microbiology, University College, Dublin, trialled Wellcome Laboratories Quadruple (4 in 1) vaccine 'Quadrivax' on 58 infants and children resident in a number of institutions, four of which come under the Commission's remit: Bessborough, St Patrick's Home, Navan Road (Pelletstown); Dunboyne; and Castlepollard. The other institutions involved were St Clare's Home, Stamullen and Mount Carmel Industrial School, Moate. This trial is described under Trial B below.

1963: Professor Patrick Meenan, Oral Polio Vaccine Carrig-on-Barrow, County Wexford.

34.23 In 1963, Professor Meenan conducted a field-trial of Wellcome Laboratories Oral Polio Vaccine (OPV) in Carrig-on-Barrow, County Wexford. Professor Meenan received permission from the Department of Health to undertake the trial in conjunction with the Wexford health authorities. The extant documentation suggests that the trial was undertaken among the general community in Carrig-on-Barrow. There is no evidence to suggest that this trial was conducted in an institution under the Commission's remit.

1964: Professor Meenan and Dr Hillery, Wellcome 'Wellcovax' Measles Vaccine Sean Ross, Roscrea.

34.24 In 1964, Dr Hillery conducted a trial of Wellcome Laboratories 'Wellcovax' measles vaccine on 12 children living in Sean Ross. This institution comes under the Commission's remit and the trial is described under Trial C below.

1964/65 Professor Meenan and Dr Hillery, Glaxo Laboratories 'Mevilin-L' measles vaccine Dublin.

34.25 In 1964/65 Professor Meenan and Dr Hillery conducted a vaccine trial of Glaxo Laboratories 'Mevilin-L' measles vaccine in Dublin. There is evidence that this trial was undertaken on children living in two of the institutions under the Commission's remit - Bessborough and St Patrick's, Navan Road (Pelletstown). This trial is described under Trial D below.

1965: Professor Meenan and Dr Hillery, Glaxo Laboratories 'Quintuple' 5 in 1 vaccine.

34.26 In 1965, Dr Hilery conducted a trial of Glaxo Laboratories 'Quintuple' (5 in 1) vaccine on children resident in two institutions under the Commission's remit - Bessborough and St Patrick's, Navan Road (Pelletstown). This trial is described under Trial E below.

1968: Dr Victoria Coffey, Glaxo Laboratories measles vaccine St Patrick's.

34.27 In December1968/January 1969, Dr Victoria Coffey, Trinity College, Dublin, conducted a trial of Glaxo Laboratories 'Mevilin-L' measles vaccine on at least 30 children resident in St Patrick's, Navan Road (Pelletstown). This trial is described under Trial F below.

1969: Professor Meenan and Dr Hillery, Wellcome Rubella vaccine trial, Westmeath.[23]

34.28 In 1969, Dr Hillery and Professor Meenan undertook a field-trial of Wellcome's Rubella vaccine involving 81 children living in the general community in Westmeath. The County Medical Officer for Westmeath facilitated the trial. The published trial results and associated documentation examined by the Commission suggest that this trial was not undertaken in a children's residential institution and is not covered under the Commission's remit.

1970: Dr Hillery, Wellcome Rubella vaccine, Dublin.[24]

34.29 In 1970, Dr Hillery conducted a field trial of Wellcome's Rubella vaccine on 72 children living in the general community and 69 children aged between two and 18 years old 'resident in an orphanage in a suburb of Dublin'. The Commission has not been able to identify the orphanage but the age range of the institutional children involved suggests that this institution is not covered under the Commission's remit.

1973: Professor Meenan, Dr Hillery and Dr Margaret Dunleavy, Wellcome Diphtheria, Tetanus and Pertussis (DTP) Trial, Dublin.

34.30 In 1973, Dr Hillery and Dr Margaret Dunleavy undertook a trial of Wellcome's modified DTP vaccine on 65 children in the general community and 53 children resident in St Patrick's, Navan Road (Pelletstown) and in three residential

[23] Hillery, Meenan et al, 'Rubella vaccine trial in children', *British Medical Journal*, 1969, 2, 531-32
[24] Hillery, I.B., 'Trials of intranasal administered rubella vaccine', *Journal of Hygiene* (1971), 69, 547-52.

children's homes - Madonna House, The Cottage Home and Bird's Nest Home. It was also conducted in another location which the Commission has been unable to identify. This trial is described under Trial G below.

Unconfirmed vaccine trial

34.31 There may have been an oral polio vaccine trial in St Patrick's, Navan Road (Pelletstown) in 1965.

Milk trials

34.32 The Commission has identified two clinical milk trials both of which were conducted in institutions being investigated by the Commission - Pelletstown and Bessborough - in 1968/69. These were not vaccine trials and so do not come under the Commission's specific vaccine trials remit. However, the Commission considers that they are relevant to other Terms of Reference, in particular in relation to conditions within the institutions and to the involvement of mothers in relation to decisions about their children. These trials are described below under Milk Trials.

Trial A: 1935: Denis F Hanley, Wellcome's APT anti-diphtheria vaccine Dublin.[25]

34.33 In 1934, the Dublin municipal health authorities introduced an anti-diphtheria immunisation scheme in city schools. Dr Denis Hanley, Assistant Medical Officer for the City of Dublin, conducted the childhood immunisation scheme under the supervision of Dr Matt Russell, Chief Medical Officer to the City of Dublin. Dr Hanley reported that, while children were presented willingly for the first injection, each successive visit met with increasing reluctance resulting in a reduced uptake of the subsequent vaccination injections. In the 1930s, diphtheria was one of the deadliest diseases of childhood. In Cork, Dr Jack Saunders, Chief Medical Officer for the City of Cork, definitively demonstrated the benefits of utilising Wellcome Laboratories experimental one-shot Alum Precipitated Toxoid (APT) anti-diphtheria vaccine in reducing the incidence of diphtheria and associated child mortality there. Before Dr Saunders's intervention, Wellcome's APT vaccine had not previously been tested on children. In 1935, the APT vaccine was not commercially available and was still considered by Wellcome to be in the experimental stage. However,

[25] Denis F Hanley, 'Anti-diphtheria immunization', *Irish Journal of Medical Science*, Vol. 12, No. 9 (1937).

Dr Saunders's application of the APT vaccine in Cork convinced the Department of Local Government and Public Health of its efficacy and safety and urged Dublin health authorities to adopt an anti-diphtheria scheme along the lines of the Cork model. Considering the endemic nature of diphtheria in the city, the Dublin public health authorities decided to explore the possibility of substituting the generally used three-shot vaccine with Wellcome's APT vaccine in Dublin.

34.34 In January 1935, with the 'consent and co-operation of the medical superintendent and staff' of the Dublin Union, Dr Denis Hanley administered Wellcome's APT vaccine to 24 children, varying in age from seven months to 14 years, resident in the institution. Satisfied that the trial had not produced 'an unduly high percentage' of reactions, Dr Hanley took further steps to ascertain the immunising power of the vaccine.

34.35 Early in 1935, Dr Hanley 'sought and was readily granted' permission to test Wellcome's APT vaccine from the authorities at three children's residential institutions: St Vincent's Industrial School, Goldenbridge; St Joseph's School for Deaf Boys, Cabra; and St Saviour's Orphanage, Lower Dominick Street, Dublin. A combined 360 children, varying in age from four to 15 years were selected for inclusion in the trial. However, Dr Hanley found that 314 of the children selected had a natural immunity to diphtheria and were subsequently excluded from further tests. Forty six children drawn from the three institutions were subsequently included in the trial. Working on the results of his own investigations, and with the full support of the Dublin municipal health authorities, Dr Hanley administered Wellcome's still experimental, and not commercially available, one-shot APT vaccine to 39,267 schoolchildren in Dublin.

Compliance with regulatory and ethical standards

34.36 In the 1930s, diphtheria took a heavy toll on child health and life expectancy. The Department of Local Government and Public Health (DLGPH) promoted childhood immunisation as the most effective means to tackle 'this most deadly disease of childhood'. Dublin health authorities had long struggled to arrest the spread of diphtheria among school children and the disease had persisted in endemic form for over 25 years. Traditional methods of disease control had failed to stem the spread of the disease and Dublin health authorities were eager to embrace any option, however radical, to protect the lives of children. The DLGPH report for 1935/6 reported that, in the years 1933-35, 2,991 diphtheria cases were recorded

in Dublin and 277 associated child deaths ensued. In this context, the decision to introduce Wellcome's APT one-shot vaccine may be considered to have been an appropriate response to a pressing public health crisis. The fact that the DLGPH had authorised the Dublin public health authorities to import and use Wellcome's APT vaccine suggests that Dr Hanley's intervention in Dublin complied with the regulatory framework in existence at that time.

34.37 An examination of the institutional records of the Dublin Union and Pelletstown failed to identify the 24 children involved in Dr Hanley's initial APT trial. However, it is more than likely that the children selected for inclusion were 'illegitimate' and unaccompanied children as most children resident there at the time were categorised as such. Children living in institutions were routinely used as research subjects in vaccine trials in the United Kingdom, the United States and several other jurisdictions at this time. In the United States, William Park and the New York Department of Public Health undertook vaccine trials in the Israel Orphan Asylum, the New York Foundling Asylum and the Howard Coloured Orphan Asylum.[26] In the United Kingdom Wellcome Laboratories, in conjunction with the London County Council health authorities undertook vaccine trials in the Holborn and Lambeth Poor Law Schools and in Dr Barnardo's Girls' Homes, Ilford.[27] Although the utilisation of institutional children as research subjects would not now be regarded as acceptable, these vaccine trials, along with the Dublin APT trials, pre-dated any formal codification of ethical practices in relation to clinical trials involving human subjects and may not have been in breach of any ethical guidelines in place at that time.

34.38 However, in the local authority anti-diphtheria immunisation scheme, overseen by Dr Hanley in Dublin schools during 1935, health authorities insisted on obtaining written parental consent before inoculating children. This applied to children treated in the city schools and to children treated in municipal public health clinics. In his published report on the matter, Dr Hanley emphasised the importance of obtaining written consent prior to treatment and provided a breakdown of the number of consent forms returned in each school. No child was immunised unless a written parental consent form was produced. However, Dr Hanley made no mention of consent, written or otherwise, in respect of institutional children. If the

[26] See Evelyn Maxine Hammonds, *Childhood's deadly scourge: The campaign to control diphtheria in New York city, 1880-1930* (Baltimore, 1999).
[27] See H.J. Parish, *Victory with vaccines: The story of immunisation* (London, 1968)

children resident in the Dublin Union/Pelletstown were unaccompanied, and/or under the guardianship of the Dublin Board of Public Assistance, then Dr Hanley may have taken the 'consent and co-operation' of the medical superintendent as the consent of the children's guardians.

34.39 The Dublin APT trial was part of a wider DLGPH initiative to reduce the negative impact of diphtheria on the health and life expectancy of Dublin school children. It was undertaken by the municipal health authority with ministerial approval and the vaccine was of direct benefit to those children resident in institutions as well as those among the public. The trial was not an academic or commercial exercise to assess the efficacy, or otherwise, of a new vaccine. Dublin health authorities had already decided to adopt Wellcome's APT vaccine as the primary anti-diphtheria vaccine in the municipal childhood immunisation scheme and they had a duty of care to ensure that institutional children, as well as children among the general population, were afforded protection from diphtheria. The decision to undertake initial tests of the vaccine among vulnerable institutional children before rolling it out to the general population would not be regarded as acceptable practice today. However, even a cursory perusal of the most respected medical journals demonstrates that such practices were accepted in all jurisdictions in the early twentieth century and predated any codification of ethical standards pertaining to clinical research in human subjects.

Trial B: 1960/61 Professor Patrick Meenan and Dr Irene Hillery, Wellcome's 'Quadrivax' vaccine.[28]

34.40 In 1959, Wellcome Laboratories considered developing a Quadruple (4 in 1) vaccine combining the Salk-type Polio vaccine with their commercially available Triple (Diphtheria, Tetanus, Pertussis) vaccine. The rationale was that Quadruple vaccine would reduce the number of injections necessary to confer immunity in infants. Wellcome considered that such a vaccine would be potentially beneficial to infants presented for immunisation as well as being 'highly desirable administratively'. In early 1960, Wellcome produced 'Quadrivax'; a quadruple vaccine. Dr Neville Butler, Health Department, Swindon, field-trialled 'Quadrivax'

[28] Irene B Hillery, P. N. Meenan: Department of Medical Microbiology, University College Dublin; A.P. Goffe, G.J. Knight, A.D. Kanarek: The Wellcome Research Laboratories; T.M. Pollock, Medical Research Department: The Wellcome Foundation *Antibody Response in Infants to the Poliomyelitis Component of a Quadruple Vaccine', British Medical Journal, 21 April 1962, 1098-1102.*

and found that the vaccine had poor antigenic effect.[29] By October 1960, Wellcome had produced two further batches of the Quadrivax vaccine. Dr Tom Pollock, Wellcome Research Laboratories, contacted Professor Patrick Meenan, Head of the Department of Medical Microbiology, University College, Dublin, asking if he would be willing to conduct a clinical trial to compare the antigenic effect of Quadrivax with the standard Triple vaccine plus Polio immunisation schedule.

34.41 Professor Meenan had previously written to Dr David Long, Chief Medical Adviser to The Wellcome Foundation, regarding the prospect of conducting clinical trials of Wellcome products in Ireland. Professor Meenan stated that he had made discreet inquiries regarding children's homes and asked Dr Long his views on conducting part of the proposed Quadrivax trial in children's residential institutions in Ireland. Professor Meenan cautioned that, if the proposed trial was undertaken in conjunction with Irish public health authorities, it would be confined to infants who had already received some form of vaccination. Professor Meenan informed Dr Long that he would gather 'some information on other field possibilities first'. In November 1960, Dr Pollock acknowledged that Professor Meenan had found 'suitable participants for the Quadrivax studies' and suggested to him that the clinical trial should be started immediately 'if the infants are available now and you feel it is most convenient to begin'.

34.42 In December 1960, Dr Pollock drew up a Trial Protocol, 'Comparison of Quadruple Antigen and Triple Antigen plus Polio Vaccine in Infants in Eire', and forwarded it to Professor Meenan. The trial sought to study:

- The antibody response in infants to Salk polio vaccine when given in combination with Diphtheria toxoid, Tetanus toxoid and Pertussis vaccine (Quadrivax), and Salk polio vaccine given concurrently but not in combination with Diphtheria toxoid, Tetanus toxoid and Pertussis vaccine (DTPP)
- The individual influence upon these antigenic responses of (i) age and (ii) maternal antibody
- The co-relation of the antigenic responses obtained in (a) with those obtained in the [laboratory] chick.

[29] Neville Butler, et al, 'Immunization with Quadruple antigen', Publication unknown.

34.43 The Trial Protocol stated that participants in the investigation would be infants aged between three and twelve months, 'resident in children's homes in Eire'. Children were to be immunised with either DTPP in one arm and Polio vaccine (Type I, II, III) in the other, or with Quadrivax.

34.44 The allocation of infants to each group due to receive the DTPP plus Polio vaccine regime, or to the group to receive Quadrivax, was done through random selection at the Wellcome Research Laboratories based on the age of the selected infants. Allocation of infants to the DTPP plus Polio vaccine group or to the Quadrivax group was arranged as follows:

> Professor Meenan sent a list of the children's homes concerned and the names and dates of birth of the infants who are to be vaccinated with their pre-vaccination blood samples. The Statistical Section at the Wellcome Research Laboratories, Beckenham, allocated the infants as due to receive one of the two regimes (Regime A or Regime B) in a way as to ensure that within each home each group contained equal numbers of children of the same age. At Beckenham, the name and date of birth of the child was entered on a Clinical Record Card labelled appropriately A or B. The Clinical Record Cards were sent to Professor Meenan. At the vaccination sessions the infants were immunised from ampoules marked A or B or B1 according to the Clinical Record Card held.

34.45 The Wellcome Immunological and Virological Departments, Beckenham, drew up a brief description of the vaccine trial suitable for inclusion in a published report. The Quadrivax, DTPP and Polio vaccines were each packed in 1 ml. containers and transported by air to Professor Meenan in an insulated box and kept refrigerated until use. The Polio vaccine component in the Quadrivax group and the Polio vaccine given concurrently with the DTPP were drawn from the same batch of vaccine. As an external check on this batch of Polio vaccine it was to be administered to a third group of infants aged seven months or older: an age when the antibody response was unlikely to be affected either by immaturity or by the presence of maternal antibody. A sample of six A, B and B1 ampoules used in the trial were returned by air to London where a potency test for Polio was estimated using chicks at Wellcome Research Laboratories. These levels were compared with the levels obtained from trial infants and children in Ireland.

34.46 In all cases, children received intramuscular injections into the deltoid area. Either 1 ml. of Quadrivax or 1 ml. of DTPP plus 1 ml. of Polio vaccine was administered according to the Clinical Record Card associated with the infant. Quadrivax or Polio vaccine was always administered in the left deltoid and DTTP in the right deltoid of the appropriate infants. Each infant received three injections at intervals of 28 days. Blood samples were taken (1) within 14 days of the first immunising session and (2) approximately 14 days after the third immunisation. The blood samples were forwarded by air in refrigerated containers to Dr Alan Goffe, Department of Virology at the Wellcome Research Laboratories, London. Professor Meenan held the clinical record cards of each child until the final blood sample was withdrawn. They were then returned to Dr Pollock, Wellcome Research Laboratories, for statistical analysis.

34.47 In April 1962, the *British Medical Journal* published the results of this quadruple vaccine trial. Dr Hillery and Professor Meenan were named as lead investigators. The stated rationale for the trial was that a satisfactory quadruple vaccine (Diphtheria, Tetanus, Pertussis, and Polio) would reduce the number of injections necessary to immunise a child in early childhood. The authors stated that quadruple vaccine had been used in the USA and Canada but that it was not in routine use in Ireland or the UK.

34.48 The trial of Wellcome's quadruple vaccine was undertaken between December 1960 and November 1961. It involved 58 infants living in five children's homes and 10 children living in an industrial school in Ireland. Documentation made available by GSK shows that 25 children were living in Bessborough; 14 were in Pelletstown; nine in Dunboyne; six in Castlepollard; these are all institutions being investigated by the Commission. Four children were living in St Clare's, Stamullen. The third group of children in the control group 'Regime B1' were 10 children, aged between two and 12 years, living in Mount Carmel Industrial School, Moate. The Commission has identified all 68 children involved in this trial.

The trial in Bessborough

34.49 The Bessborough institutional records show that 25 children living there were selected for involvement in the polio vaccine trial in 1960. They received their first inoculation on 9 December 1960; the second on 6 January 1961 and the third on 10 February 1961. In February 1961, Dr Hillery returned to Bessborough and extracted blood samples from the trial children.

34.50 Bessborough's institutional records show that 12 children were assigned to Regime A and were administered Wellcome's Quadrivax 4 in 1 combined vaccine (Diphtheria, Pertussis, Tetanus and Polio combined). Thirteen children were assigned to Regime B and were administered Wellcome's Polio, Diphtheria, Pertussis and Tetanus vaccines following standard procedure used in the national childhood immunisation programme. The 13 infants assigned to Regime B were inoculated with commercially available vaccines and the method of inoculation employed did not deviate from that employed in the general childhood immunisation programme.

34.51 In Bessborough, 23 of the 25 children involved in the quadruple vaccine trial were living with their mothers in Bessborough at the time of this trial. One child involved in the trial was an abandoned child resident in the institution. The child had been placed in Bessborough by the Cork Board of Public Assistance who paid the Congregation of the Sacred Hearts of Jesus and Mary for the child's maintenance. The institutional records show that 24 of the 25 children involved were public patients maintained there by Boards of Public Assistance.

34.52 The Bessborough institutional records show that at least five mothers of children resident in Bessborough who participated in the trial had mental health issues. Another mother was 17 years old.

The trial in Pelletstown

34.53 Fourteen children living in Pelletstown were involved in the 1960/61 Quadrivax quadruple vaccine trial. Dr Hillery administered the vaccines on 1 December 1960, 30 December 1960 and 27 January 1961. She administered the Quadrivax 4 in 1 combined vaccine to six children and the remaining eight were inoculated using routine vaccine and procedure. She returned in August and September 1961 and drew blood samples from the trial children.

34.54 The Pelletstown institutional records show that 13 of the 14 children involved were described as 'illegitimate'. Nine were accompanied by their mothers at the time of the trial and five were unaccompanied.[30] Three had been born in Grangegorman Mental Hospital and admitted to Pelletstown unaccompanied. Another was

[30] It should be noted that unaccompanied children were among the 'Schedule A' and 'Schedule B' groups.

described as an ‘abandoned’ child admitted unaccompanied. Two children were described as ‘mixed-race’.

The trial in Dunboyne

34.55 Nine children resident in Dunboyne were involved in the 1960/61 Quadrivax vaccine trial. All were ‘illegitimate’. Eight of the children were accompanied by their mothers. The mother of one child was under treatment in Mullingar Mental Hospital when Dr Hillery administered the first and second vaccinations and was present in Dunboyne on the date of the third vaccination. Dr Hillery conducted the inoculations on 1 December 1960, 29 December 1960 and 26 January 1961. She administered the Quadrivax 4 in 1 combined vaccine to five children and the other four were inoculated using routine vaccine and procedure. Dr Hillery returned to Dunboyne in February 1961 to extract blood samples from the trial children.

The trial in Castlepollard

34.56 Six children resident in Castlepollard were involved in the quadruple vaccine trials. The institutional records do not record the dates involved but it seems likely that Dr Hillery administered the vaccine there on dates between 1 December 1960 and 10 February 1961. All children were ‘illegitimate’, and all were accompanied by their mothers. Dr Hillery administered the Quadrivax vaccine to three children at Castlepollard and the remaining three were inoculated with a routine vaccine and procedure. She returned to Castlepollard in September 1961 to extract blood samples from the trial children.

Compliance with regulatory and ethical standards

34.57 The Commission understands the stated rationale for the trial of Quadrivax and recognises that there is no evidence that any child who participated in the trial was harmed in any way. However, it is abundantly clear that Trial B did not comply with the regulatory and ethical standards in place at the time:

- There was no import licence in place for the vaccine.
- The researchers did not have a research licence which covered research carried out in the children’s institutions.
- There is no evidence that consent was properly sought or received.

Import licence

34.58 Although the Quadrivax vaccine was composed of the same four commercially available Polio, Diphtheria, Pertussis and Tetanus vaccines used in the general childhood immunisation programme the product itself 'Quadrivax' was prepared by Wellcome Research Laboratories specifically for the purpose of a vaccine trial and, according to Dr James Kiely, former Chief Medical Officer, Department of Health, was not a commercially available vaccine. In his *Report on 3 Clinical Trials*, Dr Kiely concluded that, although the individual components of the quadruple Quadrivax vaccine were each covered by Wellcome Research Laboratories import licence, the Quadrivax vaccine itself was not.[31] In January 1999, the Acting Head of Glaxo Wellcome's Medical Department confirmed that Wellcome's Quadrivax vaccine 'was not used or licensed for use in the UK.' In his 1997 report on the quadruple vaccine trial, Thomas McGuinn, Chief Pharmacist, Department of Health, confirmed that Wellcome's quadruple Quadrivax vaccine administered to Group A 'was clearly not licensed' for use in Ireland under the *Therapeutic Substances Act 1932*.[32]

34.59 The Commission has not seen any evidence that Professor Meenan sought or received an import licence to import Wellcome's Quadrivax vaccine used in this clinical trial.

Research licence

34.60 In July 1958, the Minister for Health granted a research licence to Professor Meenan. The research licence issued under the provisions of the *Therapeutic Substances Act* 1932, licensed Professor Meenan to import therapeutic substances for the purpose of scientific research. The terms of the licence specified that it applied only to Professor Meenan and to scientific research conducted only at the Department of Medical Microbiology, University College, Dublin, or 'in such other place or places as the said Minister may from time to time authorise'.[33]

34.61 No documentary evidence has been produced to suggest that Professor Meenan sought ministerial approval to conduct the quadruple vaccine trial outside of University College, Dublin, or to conduct the quadruple vaccine trial in children's

[31] Dr James Kiely, Department of Health, *Report on 3 clinical trials involving babies and children in institutional settings 1960/61, 1970 and 1973*, 1997.
[32] Department of Health file: MED-IMP-0-135205.
[33] *Therapeutic Substance Act*, 1932. Research Licence: Licence No.216; issued 29 July 1958.

residential institutions. Dr Hillery did not hold a research licence and appears to have not been aware of the requirement to have one. In her formal statement to the Department of Health in 2000, she stated that, to her understanding, there were no statutory controls relating to vaccine trials in place at the time and that 'the issue of non-compliance does not arise'. Dr Hillery told the Department of Health that she conducted all vaccine trials under the direction of Professor Meenan, and with his full knowledge. When, in 1990, Professor Meenan was asked about his involvement in vaccine trials in children's residential institutions he stated that he presided over 'several drug tests' between about 1960 and 1975' and that the clinical work associated with them was supervised by Dr Hillery.[34] However, the fact that her work was supervised by Professor Meenan does not explain why she was not aware of the statutory requirements which were in place.

Consent

34.62 The requirement to get consent for vaccine trials was very well known and respected in the conduct of such trials in the UK. Authors of published reports relating to two contemporaneous Wellcome-sponsored vaccine trials, (which reference the same scientists from the Wellcome Research Laboratories who were involved in Professor Meenan and Dr Hillery's quadruple vaccine trial), suggest that the practice of getting parental consent for a child's participation in a vaccine trial was common practice. In a published report of a measles vaccine trial involving 85 institutional British children, the authors, who included Dr Goffe and Dr Pollock of the Wellcome Foundation, explicitly stated that 'parental consent for the vaccination of these children was obtained'.[35] Similarly, the published report of clinical trials of a Wellcome measles vaccine involving 90 children in Ibadan and Ilesha, Nigeria, in 1960, (which also involved Drs Goffe and Pollock) also explicitly stated that 'parental consent for vaccination was received for each child'.[36]

34.63 It was accepted best practice in general immunisation schemes at the time in Ireland that the consent of the relevant person should be in writing. Written parental consent was a prerequisite for children receiving immunisation under a local authority immunisation scheme since at least 1935. School children who did not produce a written consent form were not eligible for immunisation.[37]

[34] *Sunday Tribune*, 28 October 1990.
[35] I.R. Aldous, et al, 'Part III. Clinical trial in British children', *British Medical Journal*, 11 November 1961, 1250-53.
[36] P. Collard, et al, 'Part II. Clinical trial in Nigerian children', *British Medical Journal*, 11 November 1961, 1246-50.
[37] Denis F. Hanley, 'Anti-diphtheria immunization', *Irish Journal of Medical Science*, Vol. 12, No.9 (1937), 578-85.

34.64 In the case of Trial B, it appears that the researchers proceeded with a vaccine trial based on a loose arrangement with the institutional medical officers who themselves may not have been fully informed about the nature of the work. There is no evidence that the consent of mothers was sought or received; similarly, there is no evidence that the consent of possible guardians was sought or received. Professor Meenan has always asserted that consent was obtained from institutional medical officers.[38] He has said that he did not secure parental permission from women in residential institutions.[39] Dr Hillery has stated that she obtained consent from medical officers in charge of the children's institutions but her public statements about getting consent from mothers are conflicting. On one occasion she said that she had received consent from 'those mothers who requested information'.[40] She has also stated that she did not consult the mothers so that they could 'maintain their anonymity'[41]. On another occasion she has stated that she consulted all parents where available.[42] She was quoted in a *Sunday Tribune* article as saying, 'I never got them to sign anything as there was no requirement for consent forms'.[43]

34.65 The first draft of the *British Medical Journal* (BMJ) article in which this trial was reported named all five children's homes in which Professor Meenan and Dr Hillery trialled the quadruple vaccine. This section was subsequently withdrawn prior to publication. In the published article, the authors, Dr Hillery and Professor Meenan, named and thanked five medical officers who they stated 'had granted them permission to carry out this investigation on infants under their care' but did not name the institutions involved.

34.66 There is nothing in the institutional records or any other documentation seen by the Commission that suggests that the institutional medical officers named in the published report discussed the question of vaccine trials or any attendant issues with either the mothers who were present in the institution or the owners or administrators of the institutions or with any local or national health authorities.

[38] Department of Health file: ENV-1NA-0-532733
[39] *Sunday Tribune*, 28 October 1990.
[40] *ibid*
[41] CICA, Irene Hillery, Statement on media reports on clinical trials, 11 July 1997.
[42] Irene Hillery, Response to the draft Report of the Chief Medical Officer into vaccine trials in the 60s and 70s, 4 May 2000.
[43] *Sunday Tribune*, 28 October 1990.

34.67 One of the medical officers named in the publication is Dr R Sutton. At the time of the quadruple vaccine trial, he was the medical officer to Bessborough. The Bessborough institutional records do not include any documentary evidence to suggest that Dr Sutton discussed the matter with or informed either the mothers who were resident there at the time or the Congregation of the Sacred Hearts of Jesus and Mary or the Boards of Health/Public Assistance who were paying for the children involved. In an affidavit drawn up for the Commission to Inquire into Child Abuse in 2002, Sister Sarto said that, to the best of her knowledge, information and belief,[44] the trial was conducted by Professor Hillery, acting with the authority of the Department of Health and in co-operation with Dr Sutton. She said that the local health authority attended annually to administer vaccines to the children. She said that the vaccines administered in 1961 were part of the annual programme. Former residents of Bessborough have insisted to the Commission that they were unaware that their children had been part of a vaccine trial and have remained equally insistent that their consent was never sought for their children's involvement. It appears that Dr Sutton, in his capacity as medical officer, independently granted access to Bessborough and to the children under his medical care there.

34.68 Dr Hillery stated that the children in Pelletstown were presented to her by the medical officer 'who was responsible for the assessment of the children's health and their suitability for vaccination'. Dr Victoria Coffey was the medical officer when Dr Hillery undertook the quadruple vaccine trials there. In a letter to Dr W L Burland, Glaxo Laboratories, in October 1968, Dr Coffey confirmed that she was aware that Dr Hillery was conducting vaccine trials on children in her care in Pelletstown and that she had assisted Dr Hillery in doing so.

34.69 The Pelletstown institutional records show that it was the matron who gave written consent for all medical procedures which unaccompanied children underwent. When infants from the institution were presented for standard routine vaccination at municipal public health clinics written consent was obtained from either a parent or guardian. This was usually the matron. Pelletstown was a local authority institution and the matron was a local authority employee. The local authority may have been the guardian of unaccompanied children in Pelletstown.

[44] Sister Sarto was not in Bessborough when this trial was conducted.

34.70 The Commission has seen no documentary evidence to suggest that the researchers informed the matron or the Dublin Health Authority that children resident in Pelletstown were to be used as research subjects in a vaccine trial. It would appear that Dr Coffey may have been solely responsible for providing Professor Meenan and Dr Hillery with access to Pelletstown.

34.71 The Dunboyne institutional records contain completed written consent forms relating to instances where infants resident there were presented for immunisation at the public health clinic. These consent forms were signed by either the mother or the matron. The Commission has not found any evidence of written consent forms relating to the quadruple vaccine trial. The Good Shepherd Sisters who ran Dunboyne adamantly refute claims that they knowingly allowed 'vaccine studies or trials' to be carried out on children resident there. It appears that Dr Hillery was given access to Dunboyne by the medical officer as he was one of those named in the published report.

34.72 As with the other institutions involved no written consent forms have been produced to indicate that Dr Hillery obtained parent or guardian consent in Castlepollard.

Adverse consequences

34.73 In January 1961, several children involved in the quadruple vaccine trial in Bessborough fell ill. All afflicted children experienced vomiting and mild diarrhoea after receiving the second inoculation. In her report on the matter to Dr Pollock, Dr Hillery stated that 15 of the 22 infants who received the second inoculation at Bessborough subsequently fell ill. Two children resident in Bessborough who were not involved in the trial also fell ill with the same symptoms. The remaining three children from the original group of 25 had been discharged from the home for adoption. Two of these children were administered the second inoculation in their foster homes and, as far as Dr Hillery was aware, had not become ill. Another child, who had been discharged for adoption the day before the second inoculation was due, had also fallen ill with vomiting and diarrhoea although he had not received the second inoculation.

34.74 Thirty-three children resident in the four other institutions involved in the Quadrivax trials, and ten older children in Moate Industrial School, had all received the second inoculation from the same batch of vaccines and none had fallen ill.

Analysis of the Bessborough medical records show that infants inoculated under both Regime A and Regime B had fallen ill. As both groups had been administered different vaccines it is not possible to say with any certainty that the illness experienced by the infants at Bessborough was caused by one of the vaccines. All affected infants fully recovered from their illness and all were presented for the third inoculation without any further complications.

34.75 At Wellcome, Dr Pollock was anxious to know if the vaccine could have been in any way responsible for causing the illness at Bessborough. Professor Meenan undertook bacteriological examination of faecal specimens taken from the afflicted children and reported that 'nothing had shown up' to suggest that Wellcome's vaccines were responsible. In a letter to Dr Goffe, Professor Meenan conceded that he 'had not yet got to the bottom of the Cork episode after the second injection' but he suspected that the second inoculation had coincided with an outbreak of influenza in the institution.

34.76 There is no documentary evidence of any adverse consequences among the Pelletstown, Dunboyne or Castlepollard children.

Claims that the Bessborough vaccine trial documentation was 'altered'

34.77 On 15 November 2016, the *Irish Examiner* reported that files relating to children involved in the quadruple vaccine trial in Bessborough had been altered. The claim was based on a one page document listing 16 changes to information collated by staff at Bessborough on foot of a discovery order issued by the Commission to Inquire into Child Abuse (CICA) in 2002. The *Irish Examiner* article caused great distress among former Bessborough residents who called for 'a full criminal investigation' into the matter. One former resident who was directly involved in the quadruple trial in Bessborough told the Commission that she filed a criminal complaint with An Garda Síochána and also complained to the Data Protection Commissioner.

34.78 The Commission has examined the document on which the *Irish Examiner* based its claim. This was not an original document from the institutional records but rather a document compiled by Bessborough staff for the Commission to Inquire into Child Abuse. The Commission has concluded that there were no alterations made to any original institutional document. The alterations that were made

involved corrections to the information previously supplied to CICA which had been found to be incorrect.

34.79 Most of the changes made were minor. In the case of the complaint filed with An Garda Síochána, the 'altered' information related to the county of origin of the complainant's mother: the word 'Dublin' was correctly inserted instead of 'All Counties'.

34.80 The changes which caused most controversy related to instances where the discharge dates of three women were extended by periods of four months, twelve months and two years, respectively. The Commission has cross-referenced these dates with the original documents and can state that the amended dates of discharge were, in fact, correct. The original dates recorded by staff at Bessborough related to the discharge of the three women from the Bessborough Maternity Hospital. The amended dates related to the final discharge of the women from the Bessborough Home. (see Chapter 18).

Trial C: 1964: Professor Meenan and Dr Hillery, Wellcome 'Wellcovax' Measles Vaccine Sean Ross[45]

34.81 In August 1964, Dr Hillery trialled a Wellcome Laboratories Measles Vaccine at Sean Ross Abbey. The stated objective of the trial was to compare the anti-body response and reaction after vaccination with 1 ml. of Measles Vaccine 27 and 0.1 ml. MV27.

34.82 In Wellcome's Trial Protocol, Dr Pollock, Wellcome Research Laboratories, stated:

> The trial will be made in appropriate infant homes in Eire under the direction of Professor Meenan and Dr Hillery will carry out the field work. The infants concerned will be those without a previous history of measles, aged eight months or more. About thirty infants will be concerned. As soon as the infants' ages and names are known, a list will be sent by Dr Hillery to Mr Knight [Wellcome Laboratories] who will allocate children to receive either the small or large dose. The trial will begin about the middle of August.

34.83 Dr Hillery selected 32 children resident in Sean Ross for inclusion in a field-trial of Wellcome's MV27 measles vaccine. The MV27 vaccine was not a licensed or

[45] *Wellcome Measles Vaccine (MV27) Trial, Sacred Heart Home, Sean Ross, August 1964. (Unpublished)*

commercially available measles vaccine. When it transpired that 20 of the selected children had previously had measles, Dr Hillery removed them from the trial. She took pre-vaccination serum samples from the remaining 12 children aged between eight and 18 months. Later she administered the Wellcome measles vaccine to all 12 children. She then took post-vaccination serum samples from ten of the 12 children and sent them to the Wellcome Research Laboratories, Beckenham. Dr Hillery stated that she had made arrangements with 'the sister in charge' at Sean Ross to take a rectal temperature from each child before vaccination and every day for the following fourteen days.

34.84 In a letter to Professor Meenan in March 1965, Dr Goffe, Wellcome Research Laboratories, concluded that although the measles vaccine trial at Sean Ross had been disappointing it had produced 'very useful results'. The measles vaccine failed to confer immunity in more than half of the trial children and Dr Goffe conceded:

> Retrospectively we have established that this particular batch of vaccine MV 27 was an unstable lot after freeze-drying and this explains the low conversion rate. We have now got a lot more stable vaccine and we should be glad to let you have some if you would like to repeat the exercise.

34.85 It subsequently transpired that Dr Hillery had inadvertently administered 0.1 ml. of Wellcome's Measles vaccine to children at Sean Ross instead of the recommended 0.3 ml. dose. She gave Dr Goffe an undertaking to re-trial the MV 27 measles vaccine at a later date. However, Dr Hillery qualified her offer by informing Dr Goffe that she had recently completed a trial of a measles vaccine for Dr A J Beale of Glaxo Laboratories and that 'this has used up my available sources of small babies for some months'.

The children involved

34.86 The Commission has identified all 12 children involved in this trial. Ten of the 12 children involved were accompanied by their mothers on the date of vaccination. Three of these women were aged under 18 years; two were 17 and one was 16 years old. Another woman was described as 'mentally retarded' by a family member. Another child had been admitted to Sean Ross unaccompanied. In another case it is unclear if the child was accompanied or not on the date of vaccination.

Compliance with regulatory and ethical standards

34.87 It is clear that Trial C did not comply with the regulatory and ethical standards in place at the time:

- There was no import licence in place for the vaccine.
- The researchers did not have a research licence which covered research carried out in the children's institutions.
- There is no evidence that consent was properly sought or received.
- The results of the trial were not published.

Import licence

34.88 While it is clear that new vaccines were developed and produced at Wellcome Laboratories under conditions which complied with contemporary safety standards as they applied to pharmaceutical companies in the UK, Wellcome's MV 27 measles vaccine was not licensed for general use, it was not commercially available and was not covered by Wellcome's Import Licence. There is no evidence that Professor Meenan applied for or received an import licence for the vaccine.

Research license

34.89 As described above, while Professor Meenan did hold a research licence to conduct trials in UCD, this did not permit him to carry out trials elsewhere. At this stage it is clear that Professor Meenan was aware that he needed ministerial permission to conduct clinical research outside of University College, Dublin and that the Department of Health was not willing to approve the conduct of such trials in children's institutions.

34.90 In 1963 Professor Meenan had written to the Department of Health asking permission to import a live polio vaccine for use in a vaccine trial to be conducted among the general population of Carrig-on-Barrow, County Wexford, in conjunction with Dr Aughney, Wexford County Medical Officer. In his letter Professor Meenan stated:

> I am not clear whether my own licence under the Therapeutic Substance Act is sufficient to enable me to import vaccine without any further special licence, but I am writing so that the Department would be aware of what is proposed.

34.91 The Department of Health, in response, confirmed that his research licence did not cover him to import a live polio vaccine for use outside the confines of University College Dublin. His application to extend the terms of the licence to include Carrig-on-Barrow was approved by the Minister for Health. The minister specified that full details of the application and approval of the vaccine trial were to be sent to the Wexford county medical officer and to the Wexford health authority.

34.92 A Department of Health document dated 30 September 1963 dealing with this application noted that, in April 1962, Professor Meenan had asked to field-trial an Oral Polio Vaccine in Pelletstown. In that instance, it was noted that the Department of Health had no objection to the trial itself but raised concerns regarding the selection of Pelletstown: 'While the procedure proposed appeared to be a safe one, the selection of the group to participate was open to objection and approval was not given on that occasion.'

34.93 There is no documentary evidence to suggest that he subsequently sought or received ministerial permission to conduct clinical trials in children's residential institutions and specifically no such evidence that would have covered this trial. Dr Hillery did not hold a research licence.

Consent

34.94 The Commission has not seen any evidence that consent was sought or received from either the mothers who were present in the institution, or the Congregation of the Sacred Hearts of Jesus and Mary who ran the institution, or from any health authority which may have been a guardian of the children. As already stated, Dr Hillery did arrange with the Sister in charge in Sean Ross to take the children's temperatures before and after the vaccine was administered. There is nothing in the Sean Ross institutional files to indicate that this trial took place. Clearly the Sister in charge must have co-operated with the trial but there is nothing to indicate whether or not she understood its nature. No records which the Commission has seen indicate that the nursing staff at Sean Ross knew that they were monitoring children who were research subjects in a vaccine trial or that the medical officer in Sean Ross was involved in any way.

Non-publication of the results

34.95 The results of the measles vaccine trial in Sean Ross were never published. This was in breach of the researchers' ethical duties as set out in the *Declaration of*

Helsinki. Published in the year in which the vaccine trial in Sean Ross was undertaken, the *Declaration of Helsinki* stated that the results of all clinical trials involving human subjects should be published whether such trials had been successful or not. The declaration stated:

> Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available.

Adverse consequences

34.96 The Commission has not found any evidence that any child involved in the trial suffered any adverse effects as a result of participation in the trial nor that any such trial child was left with no, or a compromised, vaccination status. One infant was recorded as having a 'slight temperature and rash' 14 days after vaccination.

Measles vaccine trials in the UK

34.97 Measles vaccine trials conducted in Ireland were undertaken on different terms to those which governed vaccine trials in the UK. Firstly, vaccine trials in the UK were conducted under the auspices of a professional medical body, the Medical Research Council. Secondly, they were undertaken with the full cooperation of general practitioners and public health authorities. Thirdly, they were undertaken on children from among the general population; they were not undertaken in children's residential institutions. Fourthly and critically, the participating children were included in the UK trial only when the relevant parental consent had been obtained.

34.98 In 1964 the British Measles Vaccine Committee undertook a vaccine trial to compare measles vaccines prepared by Wellcome Laboratories; Glaxo Laboratories and Pfizer Ltd. The vaccines were prepared under the auspices of the British Medical Research Council's Measles Vaccine Committee and involved 242 children attending 38 general practitioners and 108 children attending day nurseries in London. The trial was undertaken with the cooperation of the Chief Medical Officer of London County Council, 38 general practitioners and the administrators of 20 day nurseries. The published findings of this study, which

appeared in the *British Medical Journal* in March 1965, stated that 'the parents were approached and, in each case, agreed to the participation of their children'.[46]

34.99 In late 1964/early 1965, the British Medical Research Council undertook clinical trials to assess the efficacy of the measles vaccine produced by Glaxo Laboratories. The vaccine trial, which included over 47,000 children, was conducted under the auspices of the British Measles Vaccines Committee with the cooperation of Municipal Medical Officers. The children involved were drawn from the general population and parental consent was secured in every case.[47]

Trial D: 1964/65 Professor Meenan and Dr Hillery, Glaxo Laboratories 'Mevilin-L' measles vaccine Dublin [48]

34.100 In 1990, in response to media queries, Professor Meenan and Dr Hillery acknowledged that they had undertaken vaccine trials in children's residential institutions in Ireland. In a statement to the *Sunday Tribune,* Dr Hillery stated that 'Wellcome was the sole sponsor' of vaccine trials undertaken by her and Professor Meenan.[49] However, the Commission has confirmed previously undisclosed vaccine trials in children's residential institutions which were undertaken by Professor Meenan and Dr Hillery and sponsored by Glaxo Laboratories.

34.101 In 1965, Professor Meenan and Dr Hillery trialled a Glaxo Laboratories measles vaccine in Dublin. In May 1964, a Glaxo Clinical Trials Meeting was told that Professor Meenan was anxious to 'do something on measles'. In December 1964, Dr A J Beale, Glaxo Laboratories, forwarded 50 doses of Mevilin-L[50] adjuvant measles vaccine and 50 doses of an adjuvant placebo to Professor Meenan and Dr Hillery. A confidential memorandum relating to biological research activities involving Glaxo products in the period January to March 1965 referred to the clinical trials involving Glaxo measles vaccines which 'were carried out in Dublin by Professor Meenan'.

[46] Medical Research Council Measles Vaccines Committee, 'Vaccination against Measles: a study of clinical reactions and serological responses of young children', *British Medical Journal*, 27 March 1965, 1, 817-23.
[47] Medical Research Council Measles Vaccines Committee, 'Vaccination against Measles: a clinical trial of live measles vaccine given alone and live preceded by killed vaccine', *British Medical Journal*, 19 February 1966, 1, 441-46.
[48] Irene B. Hillery, P.N. Meenan (A.J. Beale, Glaxo Laboratories) *Glaxo Measles Vaccine Trial, January 1965.*
[49] *Sunday Tribune*, 28 October 1990.
[50] Department of Health file: INACT-INA-O-451644.

34.102 The published results of this trial in the *Lancet* do not state when or where the trial was undertaken.[51] It is not clear from the *Lancet* article whether institutional children were used as research subjects for the Dublin measles vaccine trial nor does it give any indication as to where the trial was undertaken. However, the evidence suggest that it was probably undertaken in a children's institution.

34.103 Thirty-four children aged over eight months were the research subjects. Blood samples were taken from children selected for participation in the trial one month before the first measles vaccine, Glaxo's inactivated measles vaccine, was administered to 34 children. A second measles vaccine, Glaxo's attenuated measles vaccine, was administered to one half of this group of children one month later.

34.104 The *Lancet* article outlined the protocol followed by Dr Hillery while undertaking the Dublin measles vaccine trial. Serum samples were taken before and one month after vaccination and children had rectal temperatures taken for 14 days after vaccination. This mirrors the approach adopted by Dr Hillery while undertaking the previously discussed measles vaccine trial in Sean Ross some months earlier (Trial C). Children involved in the Dublin measles vaccine trial had a rectal temperature taken at 6pm each evening; this would probably have been difficult to arrange outside of an institutional setting. In addition, the trial results refer to 'the adults looking after the children' rather than referring to parents.

34.105 There were few institutions in Dublin where 34 children aged between eight and twelve months could be monitored for a period of two weeks. As already discussed, Professor Meenan and Dr Hillery had previously undertaken clinical trials in Pelletstown in 1960/61 and they had done so with the co-operation of the institutional medical officer Dr Victoria Coffey. The Commission considers it likely that children living in Pelletstown were involved in the Glaxo measles vaccine trial but has found no conclusive evidence in this regard. Despite thorough analysis of Pelletstown's institutional records, the Commission did not identify children who may have been involved in the Glaxo measles trial.

34.106 However, there is evidence that Bessborough children may have been involved. Analysis of Bessborough's institutional records identified seven children whose

[51] Irene B. Hillery, P.N. Meenan, A.J Beale, 'Measles Vaccination', *Lancet*, 14 August 1965, 317-18.

medical records suggest that they were involved in a measles vaccine trial conducted in the manner described. Medical records relating to all seven children contained handwritten lines which read 'Blood spec. taken for measles vaccine' and '1st injection for measles'. All seven children were over eight months old and match the age profile of children involved in this measles vaccine trial. All blood specimens were taken on 18 November 1964 and all '1st measles vaccines' were administered to children on 7 December 1964. Glaxo had dispatched a consignment of their inactivated and attenuated measles vaccines to Professor Meenan and Dr Hillery in December 1964. The Commission takes the view that, on the balance of probabilities, the measles vaccine trial may have been undertaken, at least partially, in Bessborough.

Compliance with regulatory and ethical standards

34.107 As so little is known about this trial, it is difficult to know whether or not it complied with the regulatory and ethical standards of the time. It seems unlikely that it was covered by the terms of the research licence which Professor Meenan held. Nothing is known about what consents, if any, were sought or obtained.

Trial E 1965: Professor Meenan and Dr Hillery, Glaxo Laboratories 'Quintuple' 5 in 1 vaccine[52]

34.108 In 1965, Dr Hillery field-trialled Glaxo Laboratories' Quintuple (5 in 1) Measles Vaccine. The stated purpose of the trial was to assess the effectiveness of Glaxo's Quintuple measles vaccine on its own, as compared with the Quintuple vaccine supplemented by a follow-on attenuated measles vaccine. The trial protocol named Dr Hillery, University College, Dublin, as lead investigator and Dr Beale, Glaxo Laboratories, as 'the person responsible for follow-up of the trial'. The vaccine used was Glaxo Quintuple V CT21:

34.109 The immunisation schedule was as follows:

1. Quintuple as primary course (not earlier than 3 months of age)
2. Inactivated Measles (not earlier than 3 months of age).
3. Both groups to receive 5 doses at monthly intervals and to be bled before and one month after the third dose. Six months after primary immunisation half the children to receive a booster dose of inactivated measles and the

[52] *Glaxo Quintuple (5 in 1) Measles Vaccine Trial August 1965. (Unpublished).*

other half an attenuated measles vaccine-the child being bled before and one month later.

34.110 An examination of a contemporaneous published article leads the Commission to the view that the vaccine schedule outlined in this trial of Glaxo's Quintuple vaccine is identical to that outlined in the published results of another trial of Glaxo's Quintuple vaccine carried out by A.J. Beale in association with researchers at the Middlesex Hospital Medical School, London, and the Department of Microbiology, Queens University, Belfast, in 1966.[53]

34.111 On 25 August 1965, Dr Hillery initiated a trial of the Quintuple vaccine in two of the institutions being investigated by the Commission - Pelletstown and Bessborough. Dr Hillery administered the Quintuple vaccine to three infants resident in Pelletstown on 25 August, 22 September and 27 October 1965. She administered the Quintuple vaccine to 16 infants resident in Bessborough on 26 August, 25 September and 23 October 1965. All 19 infants received the first injection; 15 received the second injection and seven infants received all three injections while resident in one of the institutions. Most children involved in the trial were adopted and discharged from their respective institutions during the timeframe of the vaccine trial. Dr Hillery administered the third injection to at least two children in their adoptive homes. The Commission heard evidence that Dr Hillery may have visited all discharged children in their adoptive homes to administer the later injections and, on separate occasions, to take blood samples from children. A former resident of the Bessborough Home produced a letter to the Commission, dated 13 April 1966, from an adoption agency to one foster mother to let her know that 'a lady doctor, Dr Hillery' would be calling to her home to give her foster child an injection. The letter stated: 'She gave [the child] course of inoculations when he was in Bessborough and he is due one further injection and it is necessary that she gives this herself'.

34.112 Further evidence heard by the Commission suggests that there may have been up to 25 infants involved in the Glaxo Quintuple vaccine trial. The Commission has identified 19.

[53] G.W.A. Dick, D.M.S. Dane, E. Moya Briggs, Margaret Haire, A.J. Beale, 'Quintuple Vaccine', *Lancet*, 20 August 1966, 424-25.

The children involved

34.113 Eighteen of the identified 19 infants involved in the Quintuple vaccine trial were in the institution with their mothers at the time of vaccination. The institutional records from Pelletstown and Bessborough show that two of the mothers were under 18 years of age. One woman was described as being of 'very low mentality' and another had suffered a 'nervous breakdown'. One child, described as 'an unaccompanied foundling', was awaiting adoption in Bessborough. Another child was suspected of having Cerebral Palsy and another was referred to as a 'mixed race child'.

Compliance with regulatory and ethical standards

34.114 It is clear that this trial did not conform to the regulatory and ethical standards in place at the time.

Import Licence

34.115 Dr Hillery is named as the sole clinical investigator in this trial. Dr Hillery did not hold a research licence to import vaccines. Furthermore, the vaccine was not covered by Glaxo Laboratories Import Licence. The vaccine was prepared by Glaxo Laboratories specifically for field-trial in Ireland and was not licensed for commercial use in Ireland or the UK.[54]

Research licence

34.116 There is no evidence that Dr Hillery held a research licence to conduct such trials.

Consent

34.117 A former resident of Bessborough has publicly stated that she did not know that her child was part of a vaccine trial and that she was not asked for consent for her child's participation.[55] There is no evidence that consent was sought or received from the mothers who were in the institutions, the authorities in the institutions or the health authorities who may have been the guardians of children in the institutions.

[54] This quintuple vaccine appears to be the same or similar to the quintuple vaccine prepared by Glaxo and trialled by G.W.A Dick et al. See Dick, G.W.A., et al, 'Quintuple vaccine', *Lancet*, 20 August 1966, 424-5.
[55] *Prime Time: Anatomy of a scandal*, RTE, 9 June 2014.

Adverse consequences

34.118 One child died of cardiac and respiratory failure two weeks after receiving the first injection. The available medical records do not suggest that this child's death was in any way linked to the vaccine.

Trial F 1968/69 1968: Dr Victoria Coffey, Glaxo Laboratories measles vaccine, Pelletstown[56]

34.119 GlaxoSmithKline supplied the Commission with a list of vaccine trials conducted worldwide in the period November 1963 to December 1968. One of the listings was a trial of a Glaxo measles vaccine involving Dr Victoria Coffey, Trinity College, Dublin. Dr Coffey was also institutional medical officer to Pelletstown. At a meeting of Glaxo's 25th Biological Clinical Trials Committee in January 1968, Dr W L Burland, Head of clinical research at Glaxo Laboratories, stated that he had recently visited Ireland and that 'both the Public Health Department in Cork and Dr Coffey, Trinity College, Dublin, had indicated that they would be prepared to undertake trials'.

34.120 In June 1968, Dr Coffey informed Dr Burland that she had spoken to 'the Chief Medical Advisor to the Government' who had informed her that he was very interested in the proposed measles survey and that he wished to be kept informed of the results. Dr Coffey suggested that the measles vaccine trial should involve 50 trial children and an equal number of control children. In return for conducting the measles trial, Glaxo promised Dr Coffey a grant to assist towards the purchase of laboratory equipment. Dr Coffey asked that the grant would be sent to the Medical Research Council of Ireland. In July 1968 Glaxo issued a cheque to the value of £230 to Dr Coffey made payable in her own name. Dr Burland wrote to Dr Coffey suggesting that 100 trial children and 100 control subjects would be a more suitable number for the proposed measles trial and requested more details of Dr Coffey's plans. Dr Coffey informed Dr Burland that she did not wish to discuss the proposed measles trial by post and suggested that they discuss the details in person on his visit to Dublin in August 1968.

34.121 Following their meeting in Dublin, Glaxo forwarded Dr Coffey a Trial Protocol relating to a field trial of Glaxo's Measles vaccine in Dublin. The Trial Protocol named Dr Victoria Coffey as lead clinical researcher and Dr W L Burland was

[56] *Dr Victoria Coffey/Glaxo Measles (BT 58) Vaccine Trial Dublin December 1968. (Unpublished)*

assigned to follow up on the trial on behalf of Glaxo Laboratories. The Trial Protocol also stated that Dr Hillery, Dublin, would carry out Measles HA titres. The Trial Protocol read as follows:

- Measles Vaccine Trial
- Final Protocol
- Clinician: Dr V. Coffey
- Glaxo Laboratories: Dr W.L. Burland
- Purpose of Trial: 1. Establish the form and rate of reactions in children to a single dose of live further attenuated measles vaccine prepared from the Schwarz strain of virus. 2. To estimate the effectiveness of vaccination as measured (a) by post-vaccination antibody levels and (b) by protection from the natural infection after sibling contact.
- Materials/Vaccine: Live further attenuated measles vaccine (Schwarz strain). Each dose contained in 0.5ml for subcutaneous injection.
- Population: 250 healthy, susceptible children aged 12 months or more with an older susceptible sibling living at home. Some children in St Patrick's Home, Dublin, will be vaccinated and each paired with a susceptible child of like age as control. (Exclude children with a personal history of convulsions, or allergy, asthma and eczema, or strong family history of same).
- Method: Each of the children should be vaccinated and then these and their sibling controls observed for any symptoms such as fever, rash, Coryza, pharyngitis, cough, conjunctivitis, vomiting, diarrhoea, anorexia and others during the following three week period.
- Every 5th child will be bled immediately prior to vaccination and again 4 weeks later. Paired sera should be separated and assayed for measles HI antibody titres.
- The children will be followed up and the incidence of measles in the susceptible sibling contacts and the vaccinated children recorded after twelve months or after the next measles epidemic.
- Assays: Measles HA titres will be carried out by Dr Hillery, Dublin.

34.122 On 5 September 1968, Dr Coffey told Dr Burland that she had come up against 'the usual complications' while trying to arrange to field-trial Glaxo's measles vaccine in Dublin. Dr Coffey had planned to conduct the trial in association with the Dublin Child Welfare Service. However, she said that the Dublin health

authorities refused to facilitate her on the basis that the risk of convulsions and other adverse reactions were too high and they were not prepared to accept responsibility for this. In response, Dr Burland advised Dr Coffey to liaise with Dr Hillery as 'she may be able to suggest a way in which you could overcome the problems you have encountered'. On 3 October 1968, Dr Coffey replied:

> Thank you for your letter of 23 September concerning the measles vaccine trial. I agree that Dr Hillery was able to follow-up her cases easily because most of her trials were carried out in St Patrick's Home and only necessitated the children being detained there for six weeks. In this I was able to assist her whereas in the measles trial it would necessitate detaining them for twelve months. However, with your offer for financial assistance in the follow-up trial this would be much simpler. I could carry out the trial in St Patrick's and arrange the follow-up by a junior doctor. By this means I could easily trial at least 250 children and we could start as soon as you would be agreeable to let me have the material.

34.123 On 30 October 1968, Dr Burland sent a cheque for £250 to Dr Coffey 'to meet the expenses involved in your proposed measles trial' and notified her that the supply of vaccine for use in the trial had been dispatched to Dublin. The minutes of Glaxo's 31st Biological Clinical Trials Meeting, held on 27 November 1968, confirmed that 250 doses of Glaxo's 'Mevilin L' vaccine had been supplied to Dr Coffey and that the 'B.T. 58 Measles Vaccine Trial' was underway. A Glaxo Laboratories memorandum written in February 1969 noted that Dr Coffey had vaccinated 30 children with Glaxo's trial vaccine and that she was 'actively searching for suitable families' to take part in the trial. The Commission has not been able to identify the children involved in this trial.

Compliance with regulatory and ethical standards

34.124 It is clear that this trial did not conform to the ethical and regulatory standards in place at the time. There is no evidence that Dr Coffey applied for or received a research licence under the *Therapeutic Substances Act*. There is no evidence that the relevant consents were sought or given. Glaxo's Mevilin-L (live attenuated) Measles Vaccine appears to have been commercially available in Ireland since 1966 and is presumed to have been covered for importation under Glaxo's Import Licence.

Adverse consequences

34.125 As the Commission has not been able to identify the children involved, there is no information available on any possible adverse consequences for them.

Trial G: 1973 Professor Meenan, Dr Hillery and Dr Margaret Dunleavy, Wellcome Diphtheria, Tetanus and Pertussis (DTP) Trial, Dublin.[57]

34.126 The stated purpose of this study was to compare the reactogenicity[58] of commercially available combined Diphtheria/Tetanus/Pertussis (DTP) vaccines, Trivax and Trivax AD, developed and marketed by Wellcome, with a new modified combined DTP vaccine containing a 'two-phase' pertussis component developed by the Wellcome Research Laboratories, Beckenham, Kent. In their Protocol for Clinical Trial of the modified DTP vaccine, Wellcome stated that commercially available DTP vaccines contained 20,000 million killed pertussis organisms and were known to cause 'minor disturbances' in up to 50% of children after inoculation. The new modified DTP vaccine contained 15,000 million killed pertussis organisms and in theory this would attenuate post-vaccination reactions in children without lowering the potency of the vaccine.

34.127 Wellcome was a commercial company and, not surprisingly, there was a significant commercial impetus behind this trial. In the late 1960s and early 1970s Wellcome's Trivax and Trivax AD vaccines competed with similar commercially available vaccines developed, licenced and marketed by Glaxo Laboratories and the Lister Institute. Trials designed to assess and compare different brands of commercially available DTP vaccines were previously undertaken by the municipal health authority in Cardiff and by clinicians at Guy's Hospital, London. It is evident from Wellcome documentation that pharmaceutical companies eagerly anticipated results which would give their product a marketable edge over their competitors. Trial results, however, revealed no discernible difference between the commercially available DTP vaccines. It was within this milieu that the idea of a modified Wellcome DTP vaccine emerged. Wellcome's stated aim was to produce a modified DTP vaccine with 'a real possibility of reduced reactions and increased potency'. According to contemporaneous documentation surrounding the project,

[57] *The Wellcome Foundation Ltd: Clinical trial to compare the reactogenicity of commercially available batches of the combined Diphtheria/Tetanus/Pertussis (DTP) vaccines Trivax and Trivax AD with a modified combined DTP vaccine containing a 'two-phase' Pertussis component. (Unpublished) 1973.*

[58] Reactogenicity of a vaccine relates to its capacity to produce adverse reactions.

however, internal exchanges of memoranda as well as records of minutes of meetings regarding the modified DTP vaccine appear to show that Wellcome's primary motivation for producing an improved DTP vaccine was a desire to cut production costs, to increase sales and to turn their DTP vaccine from a 'loss-making product' into a 'moderately profitable' one.

34.128 In August 1971, Wellcome Research Laboratories began production of their modified DTP vaccine. A Wellcome Laboratories memorandum revealed that, at this juncture, Wellcome had already made arrangements to conduct clinical trials of the modified DTP vaccine in Ireland. In August 1972, five separate batches of the modified 'two-phase' vaccine were bulked and laboratory tested and Wellcome submitted laboratory reports to the British Committee on Safety of Drugs for approval. Documentation produced by the Wellcome Foundation shows that the modified DTP vaccine complied with standards prescribed by *British Pharmacopoeia* (1968), the *Therapeutic Substances Act* 1956 [UK], the World Health Organisation Technical Report Series and the *European Pharmacopoeia* (1971) Vol. II. As a further precaution, Wellcome recruited adult volunteers working at their research laboratory at Beckenham to participate in a trial which closely modelled the proposed trial due to be undertaken in Ireland. Acknowledging that their commercially available and modified DTP vaccines were normally given exclusively to infants, researchers at Wellcome were anxious to compare the effects of the new formulation vaccine with those produced by Trivax and Trivax AD 'before proceeding to infant trials'.

34.129 In a Wellcome Laboratories memorandum dated October 1972, Dr A H Griffith, Head of the Department of Clinical Microbiology, Wellcome Research Laboratories, outlined the necessity to carry out clinical trials of Wellcome's modified DTP vaccine. Dr Griffith stated that it was 'difficult to arrange meaningful trials of any medicinal products in young children' and that Professor Meenan, Department of Medical Microbiology, University College, Dublin, was willing to carry out the trials. Dr Griffith said that Professor Meenan, and his senior lecturer Dr Hillery, had a long association with Wellcome and had been 'good collaborators on other lines'. He said that Professor Meenan had 'appealed' for a grant to employ a laboratory technician and recommended that Wellcome sanction a 'non-renewable grant' of £1,650. He also recommended that a 'personal grant' of £650 be put in place for Dr Hillery to draw down while undertaking the Dublin trials. Professor Meenan requested that the cheque for £1,650 be made payable in his

own name stating that he would endorse and forward it to the Secretary, Bursar, University College, Dublin. Wellcome's grant to Professor Meenan was renewed in 1973 and again a cheque for £1,650 was made payable to him personally.

34.130 In October 1972, Dr Griffith forwarded draft protocols for clinical trials of Wellcome's modified DTP vaccines to Dr Hillery and to Dr Margaret Dunleavy, Deputy Chief Medical Officer, Eastern Health Board, Dublin. Dr Hillery and Dr Dunleavy were asked to consider and comment on the draft protocols with a view to informing an application to the National Drug Advisory Board of Ireland, which had been established in 1966, for a clinical trial certificate. In February 1973, Dr Griffith forwarded a final draft of the application to Dr Hillery's home address in Dublin with a handwritten note which read 'Cheque for £300 enclosed'. Dr Hillery received the balance (£350) of Wellcome's £650 'personal grant' in November 1973.

34.131 In October 1972, Wellcome Research Laboratories authorised clinical trials of Wellcome's modified DTP vaccine in Dublin with the proviso that an initial group of five subjects would be studied at least one week before the main study and that the main trial should proceed on the basis that there were no adverse side effects.

34.132 In February 1973, The Wellcome Foundation Ltd made an application for a Clinical Trial Certificate to the National Drugs Advisory Board. The four vaccines to be compared were:

- Trivax: Normal commercial preparation.
- Trivax AD: Normal commercial preparation.
- New DTP Plain: Batch No. PX 296 (in manufacturing Batch A) at 15,000 million organisms per dose.
- New DTP Adsorbed: Batch No. PX 297 (in manufacturing Batch A) at 15,000 million organisms per dose.

34.133 Wellcome's finalised Trial Protocol proposed that clinical trials to compare all four vaccines for reactogenicity and antigenicity[59] would be carried out 'under existing practices' in an institution and a day nursery among children who were due to receive routine immunisation with a standard DTP vaccine. Participants were required to be under 12 months old and either in care at an institution in Dublin or

[59] Antigenicity: The property of being able to produce a specific immune response.

attending a day nursery in the city. Children were allocated to receive one of the four vaccines (a 0.5.ml. dose on two occasions, separated by an interval of six weeks).

34.134 Only children without previous history of immunisation or whooping cough were deemed suitable for inclusion in the vaccine trial. Blood samples were to be taken one week after the second dose was administered and sent to Wellcome Laboratories to assess diphtheria and tetanus antitoxin levels and for slide pertussis agglutinin tests. Temperatures were to be taken at the time of vaccination and four to six hours later. The number of children in the trial was not to exceed 120 with up to 30 in each group. Reactions were to be assessed by a nurse or a doctor who would 'call on the mother' on the morning after vaccination and complete a reaction form. The site of the vaccine was to be examined on this occasion and seven days later when a second reaction form was to be completed. The reactogenicity of the vaccine was to be assessed according to the data on these completed forms. Dr Hillery and Dr Dunleavy were named as lead investigators.

34.135 In April 1973, Dr Aileen Scott, Medical Director, National Drugs Authority Board, approved the Wellcome Foundation Ltd application to conduct a comparative trial of the reactogenicity of commercial Trivax and Trivax AD, and the corresponding new DTP vaccines (Batch No. PX 296 and PX 297) made with an improved 'two-phase cultured' pertussis component in Ireland. This approval came with a caveat - the proviso was to the effect that the results of the investigation were to be forwarded to the National Drugs Advisory Board on completion. On receipt of a clinical trial certificate for the Dublin DTP trials Wellcome forwarded 100 doses of Batch No. PX 296 and PX 297 to Dr Irene Hillery, University College, Dublin.

34.136 A Wellcome Research Laboratories memorandum of a phone call from Dr Hillery in July 1973 suggests that the Dublin DTP trials had been initiated in June 1973. Documents made available by the Wellcome Foundation confirmed that the Dublin DTP trials among the control group, who were administered Wellcome's commercially available Trivax and Trivax AD by Dr Margaret Dunleavy, had commenced in January 1973. The first doses of the new modified DTP vaccine were administered some months later in June 1973. Minutes of the Sixth Meeting of the Department of Clinical Immunology, Wellcome Research Laboratories, held

in June 1973, also confirmed that the Dublin trials of Trivax and the modified DTP vaccines were underway at that time.

34.137 In June 1973, Wellcome became aware that there had been a setback in the Dublin DTP trials. A significant number of adverse reactions were reported among children involved in the trial and two children had been hospitalised due to severe adverse reactions. A letter from Dr Dunleavy in August 1973 confirmed that post-inoculation reactions 'were occurring with greater frequency' and that all reactions were associated exclusively with Wellcome's commercial 'off the shelf' Trivax and Trivax AD vaccines. Dr Dunleavy reported that most cases had 'resolved themselves after a few days' but noted that two children remained in hospital suffering 'infantile spasms'.

34.138 One hundred and sixteen children were involved in the Dublin DTP trials. Fifty three institutional children were administered Wellcome's modified APT vaccines. The remaining children, drawn from the general population, were administered Wellcome's commercially available Trivax and Trivax AD DTP vaccines as part of routine immunisation procedure in public health clinics in Dublin.

34.139 Of the 53 institutional children 20 were resident in Pelletstown; 19 were in Madonna House, Blackrock, Dublin; seven were in Cottage Home, Dun Laoghaire; six were in Mrs Smyly's Bird's Nest Home, Dun Laoghaire and one lived in an institution which the Commission has been unable to identify. Pelletstown is the only one of these institutions which comes under the Commission's remit. The Commission has identified all 20 infant residents of Pelletstown involved in this trial.

34.140 Dr Hillery administered Wellcome's modified APT vaccine to the 20 children resident in Pelletstown on dates between 16 August 1973 and 30 April 1974; 14 were given the New DTP Plain (Batch No. PX 296) vaccine and six were given the New DTP Adsorbed (Batch PX 297) vaccine.

34.141 Thirteen children were administered vaccines on the same three dates: 16 August 1973; 27 September 1973 and 14 January 1974. Of these, five received three doses of antigen. The remaining seven received two inoculations; five had been discharged for adoption after the second inoculation.

34.142 Four children were administered vaccines on the same three dates: 22 January; 7 March and 30 April 1974. Of these, three received all three doses and the remaining child received two doses. The remaining three children received all three shots on 23 November 1973; 4 January 1974 and 11 March 1974.

The children involved

34.143 The Pelletstown institutional records show that all 20 children were unaccompanied 'illegitimate' children aged between three and nine months old. Seven had been admitted unaccompanied by their mothers; in the remaining 13 cases, mothers had discharged themselves. Two of the children were recorded as having Downs' Syndrome; another had Crouzon Syndrome (Facial Deformity); another had Congenital Talipes Equino-Varus (Club Foot) and another had Congenital Heart Disease. Another was described as a 'mixed race child'. Institutional records note that at least seven of the mothers had psychiatric disorders or were recorded as being 'mentally handicapped'. Another mother was 15 years old.

Compliance with regulatory and ethical standards

34.144 In July 1997, the Minister for Health gave an undertaking to make enquiries into media allegations that vaccine trials had been undertaken in children's residential institutions in Ireland. In his subsequent report on the matter Dr James Kiely, Chief Medical Officer, Department of Health made the following observations:

> The prevention and control of infectious disease was still considered to be of major public health importance at the time of the trial. The use of effective and safe vaccines was a major element in disease control and, given that the minimisation of adverse reactions was a major factor in the acceptance of vaccines by the general population, research which would result in the production of vaccines which had a lower incidence of reaction and were, therefore, considered to be safer, was an appropriate and reasonable subject for clinical trials.[60]

34.145 Wellcome's application to the National Drugs Advisory Board stated that the purpose of the trial was to develop a less reactogenic and, in theory, safer DTP vaccine and as Dr Kiely concluded, this would have been 'an appropriate and

[60] Dr James Kiely, *Report on 3 Clinical Trials involving babies and children in institutional settings 1960/61, 1970 and 1973*, Department of Health, 1997.

reasonable subject for clinical trials'. As already noted, there were also significant commercial considerations involved in this trial.

34.146 A public statement issued by the Wellcome Foundation in July 1997 stated that the context in which the Dublin DTP trials were undertaken was a response to a request issued in August 1973 by the Eastern Health Board, through its Deputy Chief Medical Officer, Dr Dunleavy, to investigate the increased occurrence of adverse reactions to Wellcome's commercial DTP vaccines, Trivax and Trivax AD - vaccines then in use in the Eastern Health Board's Immunisation Programme. A public statement issued by Dr Hillery in July 1997 also stated that this was the reason for her involvement in the Dublin DTP trials:

> When in 1973 it appeared there were more than the expected number of adverse reactions (such as soreness at the site of the injection, raised temperature and irritability) possibly associated with the triple (DTP) vaccine in use at vaccination clinics in Dublin, I agreed to undertake an investigation involving the vaccine on behalf of Wellcome.

34.147 In September 1973, Dr Dunleavy contacted Wellcome Laboratories 'regarding the possibility of reducing or altering the pertussis element in their [DTP]vaccine'. As noted earlier, documents made available by the Wellcome Foundation clearly show that arrangements for the Dublin DTP trials had been made two years earlier, in August 1971. Furthermore, draft copies of the proposed Dublin DTP Trial Protocol were sent to both Dr Hillery and Dr Dunleavy in October 1972. One draft Trial Protocol explicitly stated that the vaccines would be trialled on 'in-care children' and on 'infants under the care of Dr Dunleavy'.

34.148 In April 1973 the National Drugs Advisory Board issued a clinical trial certificate for the Dublin DTP trials naming Drs Hillery and Dunleavy as lead clinical investigators. In addition, DTP Reaction Forms made available by the Wellcome Foundation unequivocally show that children administered the commercial Wellcome DTP vaccines, Trivax and Trivax AD, received their first inoculations in January 1973. Similarly, the same records show that children administered Wellcome's modified APT vaccine received their first inoculations in June 1973. Thus, it appears to the Commission that the extant documentary material does not support the claim by the Wellcome Foundation and Dr Hillery that the Dublin DTP trials were initiated on foot of an Eastern Health Board request to investigate the cause of increased reactions to Wellcome's DTP vaccines in August 1973. The

documents provided to the Commission show that the Dublin DTP trials were planned, sanctioned and initiated well before this date.

34.149 Dr Aileen Scott of the National Drugs Advisory Board, who approved Wellcome's application for a Clinical Trial Certificate, has stated that she was not aware that any vaccine trial involving institutional children had been undertaken on foot of a general trial approval issued by the NDAB. However, Wellcome's application for a Clinical Trial Certificate clearly stated: 'All the participants will be under twelve months of age and be either in care at an institution in Dublin or attending a day nursery in the City.' Despite Dr Scott's assertions, the unambiguous wording of Wellcome's application clearly stated that the subjects of the Dublin DTP trial could potentially have involved institutional infants. This, in fact, turned out to be the case. The Commission assumes, therefore, that the NDAB was fully aware of this when it granted Wellcome a Clinical Trial Certificate to undertake the Dublin DTP trials. There is no documentary evidence to suggest that Dr Scott, or any other person from the NDAB, consulted the Department of Health before approving Wellcome's application for the trial certificate.

Import licence

34.150 The arrangement whereby applications were made to the National Drugs Advisory Board was a voluntary one and did not change the law in relation to import licences. It is clear that the issue of a Clinical Trial Certificate to Wellcome from the NDAB related exclusively to the supply of materials for the purpose of clinical trials and certified that the vaccines used conformed to specifications prescribed by *British Pharmacopoeia* 1968,[61] the *Therapeutic Substance Act* [UK]1956,[62] the World Health Organisation Technical Report Series[63] and by *European Pharmacopeia* (1971) Vol. II.[64] The NDAB Clinical Trial Certificate did not sanction the importation of the trial vaccines nor did it sanction their use in an institutional setting.

34.151 The Wellcome Foundation and Dr Scott of the National Drugs Advisory Board have stated that Wellcome's modified DTP vaccine, administered to the 53 institutional

[61] General Medical Council, *British Pharmacopoeia 1968*, (The Pharmaceutical Press, 1968).
[62] *Therapeutic Substances Act 1956* (United Kingdom), http://www.legislation.gov.uk/ukpga/Eliz2/4-5/25/enacted
[63] World Health Organization Expert Committee on Biological Standardization, *Technical Report Series No. 274* (World Health Organization, Geneva, 1964).
http://apps.who.int/iris/bitstream/handle/10665/40582/WHO_TRS_274.pdf;jsessionid=218CA9AC788A53B494C8A6A218D1C892?sequence=1
[64] Council of Europe, *European Pharmacopoeia, Vol.II*, (Rittenhouse, Philadelphia, 1972).

children, was not a 'new vaccine'. Glaxo Wellcome Ltd , however, has acknowledged that the modified DTP vaccine used in the Dublin DTP trials was an unlicensed product. It was not licensed for commercial use in the UK or Ireland and was not covered under Wellcome's Import Licence, issued under the *Therapeutic Substances Act*, 1932. Thomas McGuinn, Chief Pharmacist, Department of Health, has also confirmed that 'none of the modified vaccines used in this [DTP] trial were licenced under the *Therapeutic Substances Act*, 1932'.[65]

Research licence

34.152 As already set out, Professor Meenan did have a research licence but its use was limited to research carried out in UCD. Professor Meenan does not seem to have taken an active part in this particular trial. Drs Hillery and Dunleavy were the only named clinical investigators in the trial protocol.

34.153 The Department of Health had been made aware in 1969 that Professor Meenan had conducted trials in breach of his research licence. The Department of Health Chief Medical Officer, Dr Daly, raised concerns within the department about the published results of a clinical trial 'Rubella Vaccine in Children' undertaken by Professor Meenan and Dr Hillery in Westmeath.[66] This trial appears to have been undertaken on behalf of Wellcome Laboratories and the rubella vaccine was trialled among 'mothers of large isolated families' at their family homes in Westmeath. Dr Daly pointed out that Professor Meenan had not asked the department for permission to conduct a trial in Westmeath and that Professor Meenan's research licence did not cover the importation of the rubella vaccine used in that trial. Dr Daly also highlighted the fact that Professor Meenan had sought and received ministerial approval for the Carrig-on-Barrow trial in 1963 and was well aware of his obligation to secure approval from the Department of Health to undertake the Westmeath trials, but had failed to do so.[67] The department resolved to pursue the matter and insisted that, in the future, Professor Meenan was to give it advance notice of any scientific research with therapeutic substances undertaken outside University College, Dublin.

[65] Department of Health file: MED-IMP-0-135205.
[66] Hillery I.B., Meenan P.N. et al, 'Rubella vaccine trial in children', *British Medical Journal*, 31 May 1969; 2 (5656): 531-2
[67] Dept of Health file: B136/216.

34.154 There is no evidence that Dr Hillery or Dr Dunleavy ever had a research licence. There is no documentation to suggest that ministerial approval was sought or obtained.

Consent

34.155 In her statement issued on 11 July 1997, Dr Hillery stated that the children were presented to her by the medical officer to the home who she claimed, 'was responsible for the assessment of the children's health and their suitability for vaccination'. Dr Coffey was the medical officer at this time. There is no evidence that the mothers or the authorities in Pelletstown were asked for or gave consent. The Commission has not seen any evidence that anyone in the Eastern Health Board, other than Dr Dunleavy, knew about or was involved in this trial.

34.156 All 116 children involved in the Dublin DTP trials were due to be vaccinated as part of the general National Childhood Immunisation Programme. For the 63 children among the general population, acting as the control group, the immunisation treatment and vaccine administered to them did not deviate from the standard procedures associated with routine immunisation treatment. These children were presented by parents for vaccination at Dublin public health clinics and on that basis, it may be reasonable to assume, by virtue of such presentation, that parental consent was obtained. These children were inoculated with licenced, commercially available prophylactics - Trivax and Trivax AD. These were the DTP vaccines used by the Eastern Health Board in their childhood immunisation programme at that time.

Adverse consequences

34.157 DTP vaccine reaction files, produced by the Wellcome Foundation, record one instance where a Pelletstown child had a 'moderate reaction' after the second inoculation and was given Aspirin.[68] No adverse reactions were recorded among the remaining 19 children. Wellcome concluded that the results of the DTP trials in Ireland had been 'quite satisfactory' and considered obtaining a product license to make the modified vaccine commercially available. It is not clear if the new vaccine ever came to market.

[68] 'Moderate Reaction': defined as a baby so upset as to require extra attention or nursing.

34.158 There is medical and scientific consensus that Wellcome's modified DTP vaccine was less reactogenic, and therefore safer, than Wellcome's commercially available DTP vaccines. The available evidence suggests that, in practice, this was proven to be the case. Adverse reactions recorded by Dr Dunleavy, and reported to the Wellcome Research Laboratories in August 1973, all occurred in children who were administered commercially available Trivax and Trivax AD vaccines in Dublin Public Health Clinics.

Veterinary Vaccine Controversy

34.159 In 2001, the *Irish Independent* reported that one child presented for DTP vaccination at a Dublin public health clinic during the Dublin DTP trial was unwittingly administered Wellcome's Tribovax T, a veterinary vaccine, rather than Wellcome's Trivax DTP vaccine. This controversial story quickly escalated and media reports 'confirming the widespread use of a cattle and sheep vaccine to inject babies at Dublin health clinics during 1973' became a cause for concern.[69] There is no documentary or clinical evidence to support the claim that the veterinary vaccine Tribovax T was ever administered to a child, inadvertently or otherwise in a Dublin clinic or in any children's residential institution.

34.160 This controversy arose from an entry in a list of children who experienced adverse reactions to the Trivax vaccine which was forwarded by the Wellcome Foundation to the Commission to Inquire into Child Abuse in 2001. In one instance, a child who attended a Dublin clinic is recorded as having been inoculated with a vaccine from 'Batch No.84796'. Batch No. 84796 relates to Wellcome's Tribovax T veterinary vaccine. The claim that children in Dublin clinics were administered a veterinary vaccine rests on this evidence alone. However, one of the Wellcome DTP vaccines in general use in the childhood immunisation programme in Dublin during this period was a vaccine from 'Batch No. 84769'. It seems reasonable to suggest that the recording of Batch No. 84796 was no more than a clerical error. In fact, 21 other children inoculated with vaccine from Batch No. 84769, a commercial Trivax DTP vaccine, also suffered adverse reactions comparable with those suffered by the child who was purportedly administered a veterinary vaccine.

[69] *Irish Independent*, 6 July 2001 and 28 June 2001.

Suspected Oral Polio Vaccine Trial: Pelletstown 1965

34.161 When examining the Pelletstown institutional records in the context of Trial D, the Commission established that nine children were administered immune globulin measles prophylaxis on 30 July 1963 and a further 25 children were administered the measles prophylaxis on 21 June 1964. The Commission understands that immune globulin measles prophylaxis was utilised to confer a level of protection against measles in children who were exposed to the measles virus. The medical records associated with children who were administered immune globulin measles prophylaxis also noted that they were administered an Oral Polio Vaccine on dates between 9 June and 24 August 1965. A trawl of medical records associated with over 800 children admitted to Pelletstown in the years 1962-64 showed that a total of 56 children were administered an oral polio vaccine. All 56 children were administered the first dose of an oral polio vaccine on 9 June 1965. Fifty of the children were administered a second dose on 5 August 1965 and 42 were subsequently administered a third dose over three days in September 1965: 20 September (22 children); 22 September (four children) and 24 September (16 children).

34.162 The 56 children selected to receive a course of oral polio vaccine were all children who were living in Pelletstown unaccompanied. At least 44 of these children had already received a full three-shot vaccination against polio. The institutional records show that 53 of the 56 children selected were 'illegitimate' children and that the three 'legitimate' children involved were either 'abandoned' or had a physical disability. Eight of these children were described as 'mentally retarded'. 'backward' or 'of low intelligence'. Others had physical disabilities and associated notes which read 'child won't walk', 'not lifting head', 'underdeveloped child', 'enlarged heart and partially deaf' and 'no teeth, large head'. In 13 further instances, children were described as 'half-caste' or 'coloured child'.

34.163 As is noted above under Trial C, Professor Meenan sought permission from the Department of Health to import an oral polio vaccine and to field trial it among children living in Pelletstown. Permission was refused. It is clear from the minutes of Glaxo's Clinical Trials Meeting that the company was field trialling its oral polio vaccine in 1964 and a *Lancet* article, authored by Dr Beale of Glaxo Laboratories, showed that Glaxo had evaluated the use of their oral polio vaccine in children

already immunised with the Salk polio vaccine in 1965.[70] The Commission has found no corroborating evidence to confirm that the administration of oral polio vaccine to children living in Pelletstown in 1965 was a vaccine trial. However, considering the methodology employed and the selection criteria as it pertained to the children involved, the Commission takes the view that there is a high probability that it was.

Milk Trials: Glaxo Infant Milk Trials, Bessborough and Pelletstown 1968/69

34.164 Thirty two of the children's files in Bessborough's institutional records include a printed form with the heading 'Clinical Acceptability Trial: Overseas Milk Powders' or 'Clinical Acceptability & Safety Trial: Golden Ostermilk+Lactose'. The forms, produced by Glaxo Laboratories, refer specifically to the 'Bessborough Convent' and name Dr E Conlon as the 'clinician responsible'.

34.165 These forms contained blank sections for completion by an attending clinician or nursing staff. The 32 forms examined by the Commission were blank; none of the forms had been completed nor was there any patient information contained therein. Feeding charts relating to the 32 infants in question demonstrate that 18 of them were fed neither commercially available Ostermilk nor any other Glaxo product. The 14 infants who were fed Glaxo's commercially available Ostermilk lived in Bessborough on various dates between 1969 and 1976. At least four of these infants were not born in Bessborough and were admitted at intervals after birth already weaned on commercially available Ostermilk.

34.166 The name of the 'clinician responsible', Dr E Conlon, which was printed on each Glaxo Milk Trial Form, is taken to be Dr Eithne Conlon who was an assistant to Bessborough's medical officer, Dr Reginald Sutton. The Commission was given access to Dr Conlon's private records by her family. These records contain no documentary evidence that Dr Conlon had either conducted or been involved in any trials conducted in Bessborough. Bessborough's institutional records do not contain any documentary evidence that a Milk Powder Trial was undertaken at Bessborough.

[70] Beale A.J., et al, 'Response to one dose of Trivalent oral polio vaccine in children previously immunised with Salk vaccine: a comparison of liquid vaccine and a capsule presentation, Lancet, 24 April 1965; 1 (7391): 879-81.

34.167 On foot of a specific request from the Commission, however, GlaxoSmithKline archivists located files which confirmed that Glaxo Laboratories had undertaken clinical trials of non-commercial infant milk products in Bessborough and Pelletstown on at least two occasions in 1968 and 1969.

34.168 In November 1967, Dr Burland, Glaxo Laboratories, wrote to a Glaxo representative in Dublin about the possibility of conducting clinical trials with experimental milk food preparations in young infants in Ireland. In his letter, marked 'Highly Confidential', Dr Burland stated:

> I am looking for establishments, such as Homes for illegitimate babies, etc., where these investigations could be set up and where there are sufficient numbers to enable us to have two groups of babies, one fed with experimental milk, and one to act as controls. Do you think it would be possible to set up a trial of this nature in Eire?

34.169 In reply Dr Burland was told that similar trials, which led to the introduction of 'new formula Ostermilk', were previously undertaken by Dr Coffey in Pelletstown as well as by Dr B V (Biddy) Foley, Bacteriologist, and Dr Eithne Conlon, Obstetrician, in Bessborough and it was likely that they would be willing to undertake further Infant Milk Trials.

34.170 Dr Burland visited Ireland in January 1968. Prior to his visit, he drew up a Trial Protocol and forwarded a copy to Drs Coffey, Conlon and Foley. The Trial Protocol, 'Clinical Evaluation of L.14 and L.20 Infant Milk Foods' read as follows:

> L.14 and L.20 are both infant spray-dried infant milk foods. Both milks are already marketed in a non-instantized form and the only change in the milks to be used in the trial is in the method of manufacture. These milks vary from standard milk preparations, such as Ostermilk 1 and 2, in their fat, lactose and vitamin content. L.14 contains 14% fat and L.20 contains 20% fat (Ostermilk 1 contains 20%, Ostermilk 2 contains 26.5%). The fat content of these products has been reduced by 'dilution' with added lactose. L.14 and L.20 have small amounts of thiamine, riboflavin, pyridine, vitamin B12 and nicotinamide added.
>
> <u>Trials:</u>
>
> The trials I have in mind will take the following form: The first study will involve the first 10 to 14 days of feeding. The second, the remaining period of 3 or 4

> months. The plan is to feed alternate babies on L.14-every other baby will receive the normal half-cream employed in the particular institution. Obviously, trials with L.14 and half-cream milks will be limited in time because of the desirability to go to fuller cream milk. Likewise, alternate babies will be fed on L.20-every other one receiving the normal full-cream milk used in the particular institution. It will be necessary to follow the babies' weight and food intake and to note any untoward events, both in the trial and the control groups, e.g. vomiting, diarrhoea, constipation, excess wind, etc.
>
> Centres:
>
> Both Maternity Hospitals and Baby Homes would make ideal trial centres. It is not a trial that will involve a laboratory in any way but will require experienced clinical observation, such as that that can be obtained from experienced nurses.

34.171 In January 1968, Glaxo Laboratories directed Glaxo's Irish representatives to investigate the feasibility of obtaining a license to import 240 kilos of L.20 and L.14 for clinical trials in Ireland. Glaxo acknowledged that the process of obtaining an import licence could take up to three weeks and stated:

> We would therefore be grateful if you could let us know as soon as possible what the chances are of success as it may be necessary to arrange clinical trials in a different area.

34.172 On 15 January 1968, Dr Burland, accompanied by Mrs B M Walker met Dr Coffey in Dublin. Dr Burland stated that Mrs Walker had 'a particular responsibility for nutrition trials' at Glaxo Laboratories. Dr Coffey told Dr Burland that Glaxo's experimental infant milk had arrived at Pelletstown and that the 'Sister in charge of the babies' had prepared some of the milk according to instructions. Dr Coffey planned to start her trial in Pelletstown in March 1968. As reimbursement for her participation, she asked Glaxo for a Chromatography Column (value £170) for her work with 'mentally deficient' children.[71] Dr Coffey stated that she was willing to send copies of the chromatography reports to Glaxo Laboratories along with the Hb levels of babies at 1 month and 3 months.

[71] Dr Coffey had a particular interest in Down's Syndrome children – see Chapter 13.

34.173 On the following day, Dr Burland and Mrs Walker travelled to Cork to meet Dr Conlon at Bessborough. As reimbursement for her work, Glaxo offered to pay Dr Conlon's air fare for a vacation in England. As the proposed milk trials were to compare Glaxo's experimental infant milk with the established feeding regime at Bessborough, Dr Burland stated that he discussed details of the trial with members of the Congregation of the Sacred Hearts of Jesus and Mary involved in preparing infant feeds: Sister Martha, Sister Benedict and Sister Peter.

1968 Trial

34.174 In March 1968, Dr Conlon field-trialled Glaxo's experimental infant milk in Bessborough. Fourteen infants were involved in the trial and were divided into three groups as follows:

Babies fed L14: 4

Babies fed L20: 3

Control group: 7

34.175 The infants in Group A were fed Glaxo's L14 infant milk for 14 days. Dr Conlon reported that infants in this group experienced moderate to severe vomiting, moderate to severe wind, loose stools and green stools. She noted that all infants in this group suffered continuous slight vomiting and regurgitation, that stools were undigested and that vomits contained large curds. She noted that Glaxo's L20 infant feed was tolerated far better and was an acceptable infant feed. She concluded that Glaxo's L14 infant milk, prepared and fed as directed by Glaxo Laboratories, was not well-tolerated by infants.

34.176 Also in March 1968, Dr Coffey conducted trials of Glaxo's experimental infant milk at Pelletstown. Nine infants were involved in the trial and were divided into three groups as follows:

Babies fed L14 (as recommended): 3

Babies fed L14 (diluted): 2

Control babies fed cow's milk: 4

34.177 The three infants in Group A were fed Glaxo's L14 infant milk for five days and several side effects were recorded. Two infants experienced 'severe vomiting' and the third experienced 'moderate vomiting'. Two infants experienced 'severe regurgitation' and all three infants were noted as being 'irritable' and 'loose with

green stools'. The use of Glaxo's L14 infant milk was discontinued due to 'the severity of the side effects'.

34.178 Both infants in Group B were fed a diluted form of Glaxo's L14 infant milk for three days. These infants experienced moderate to severe regurgitation, slight vomiting, green stools and irritability. While Dr Coffey considered that these infants were making 'reasonable progress' she conceded that they were not as satisfactory as infants in the control group.

34.179 The four infants in the control group were fed diluted cow's milk for nine days. One child experience green stools and another experienced slight regurgitation: no other side effects were recorded in this group. Dr Coffey concluded that, due to 'the frequency of undigested stools, frequent vomiting and vomiting of large curds' among trial infants, Glaxo's L14 milk was 'most unsatisfactory'.

34.180 Following the abandonment of the milk trials at Pelletstown and Bessborough, congregational nursing staff involved in infant feeding in both institutions remonstrated that the preparation and feeding instructions which accompanied the experimental feeds, and in some cases the weight of the infants involved in the trials, did not make for a 'fair trial'.

34.181 In April 1968, Mr P M Paterson, Analytical Department, Glaxo Laboratories, travelled to Pelletstown and Bessborough to liaise with the Sisters responsible for infant feeding in both institutions. He reported that the nursing staff (who were Sisters) in both institutions altered the method of preparing Glaxo's experimental infant feeds resulting in a more diluted mixture. Infants selected for inclusion in what Glaxo called the 'Nun's Trial' were over seven pounds in weight and deemed better equipped to process the new feeds. He observed nursing staff in both institutions as they incorporated Glaxo's infant feeds into their already established feeding regimes and reported good results. He reported that the nursing staffs in both institutions were happy to be involved in the development of an improved infant milk product but remonstrated that they had not been told more about the infant milk trials in the beginning and complained that the clinicians involved, Drs Coffey and Conlon, had largely left them in the dark.

1969 Trial

34.182 In consultation with the nursing staff involved in infant feeding at Pelletstown and Bessborough, Glaxo Laboratories produced re-formulated infant milk products with a view to undertaking further clinical trials. Dr Burland once again secured the cooperation of Drs Conlan and Foley in Cork and Dr Coffey in Dublin. On this occasion, he consulted the administrators of both institutions in order to secure their cooperation. In April 1969, Glaxo trialled their new infant milk in Bessborough and Pelletstown whilst undertaking concurrent trials of the same experimental infant milk products in Malaya and Argentina.

34.183 Glaxo's Trial Protocol for the April 1969 infant milk trials 'Overseas Milk Powders: Clinical Acceptability and Safety Trials' named Bessborough and Pelletstown as the Irish trial centres. Drs Conlon, Foley and Coffey were named as the clinicians involved. The stated aim of the clinical trial was to compare Glaxo's new infant milks, BY 0111 and BY 3010, with a control group of infants fed on the commercially available Ostermilk 1. The Trial Protocol called for the inclusion of 40 infants in both institutions and stipulated that the mothers 'House Name' would be recorded as the only identifying factor on documentation relating to the trial.

34.184 GlaxoSmithKline archivists produced written notes and charts relating to Glaxo's infant milk trials to the Commission. Because of the passage of time, these records are difficult to read, and they did not assist the Commission's efforts to identify the children involved in the milk trials. It was possible, however, to discern that Drs Conlon and Foley selected 21 Bessborough infants for inclusion in the trial. These infants were fed Glaxo's new infant milk BY 0111. The extant records show that at least half of these infants experienced vomiting, excess wind and constipation.

34.185 It was also possible to extract from the records that Dr Coffey selected 89 infants resident in Pelletstown for inclusion in the trial. Dr Coffey noted that trial infants in Pelletstown experienced vomiting, regurgitation, irritability and green stools. In two instances, infants experienced 'violent vomiting' in reaction to the feed and these children were subsequently withdrawn from the trial.

34.186 Although the Commission has identified uncompleted Glaxo Infant Milk trial forms in the files of 32 former Bessborough residents, it is unlikely that these particular infants were involved in a clinical trial. All of these 32 infants were born after the

last known infant milk trial was undertaken in Bessborough in April 1969. There is no documentary evidence to show that infant milk trials occurred after that date. Fourteen of these 32 infants were born in a cluster of dates in December 1969 and January 1970. It may have been intended that they would be part of a further milk trial. The comprehensive feeding charts associated with this group of infants give no indication that they were part of a clinical trial but indicate that all infants concerned received commercially available infant milk. Most were fed on non-Glaxo products, generally SMA. The maternity records associated with these 32 infants include detailed daily feeding charts which appear to confirm that infants born in or admitted to Bessborough were subject to the same institutional feeding regime as all other infants resident in the institution at that time. In all cases, new-born infants were fed water and glucose for several days before being put on commercially available Ostermilk and SMA infant feeds.

34.187 The Commission is satisfied that the trial forms relating to infants who were involved in one of the infant milk trials were completed contemporaneously with the clinical trial and forwarded to Glaxo Laboratories.

Compliance with regulatory and ethical standards

34.188 It is not clear that the milk trials constituted clinical trials within the meaning of the *Therapeutic Substances Act 1932* so it is not clear if an import licence or a research licence was required. There is documentary evidence that Glaxo Laboratories considered the question of applying for an import licence to cover the importation of their experimental infant milk products into Ireland. The Commission has seen no evidence that it actually applied for or received such a licence. Likewise, the Commission has no evidence that any of the doctors involved held a research licence.

Consent

34.189 There is no documentation to suggest that Glaxo either applied for or received an import licence to import the L.20 and L.14 infant foods. The Commission has not seen any documentation to suggest that Glaxo or the clinicians involved in the Infant Food Trials either applied for or held Department of Health issued research licences to conduct these trials.

34.190 As it has not been possible to identify the children involved in the trials, it is not known if all or any were accompanied by their mothers. There is no evidence that any attempt was made to seek the consent of their mothers.

34.191 It would appear that the three doctors involved conducted the initial trials without consulting the authorities of either institution. While congregational nursing staff in both institutions took directions from the doctors it is unlikely that they were made aware of the experimental nature of the infant feed. It seems to the Commission that it was only when the congregational nursing staffs were tasked to take remedial action to counter the adverse reactions suffered by the children that the authorities at both institutions realised the true nature of the study.

34.192 The Mother Superior at Bessborough wrote to Glaxo Laboratories to voice her annoyance that she had not been consulted about the infant milk trials in the first instance. The documentary evidence, however, demonstrates that the administrators at both institutions did communicate with Glaxo about the April 1969 infant milk trial and assisted the company in its bid to produce a superior infant feed in what became known as the ‘Nun’s Trial’.