ELIMINATING MEASLES AND RUBELLA AND PREVENTING CONGENITAL RUBELLA INFECTION

A situational analysis and recommendations

STRATEGY FOR IRELAND

Recommendations of the Measles and Rubella Elimination Committee of the Department of Health and Children

2007

Contents

I. PREFACE

Measles-Mumps-Rubella vaccine (MMR) was introduced into the routine childhood vaccination programme in Ireland in 1988. Despite its widespread usage, substantial numbers of indigenous measles cases continue to be reported in Ireland. The most recent large measles outbreak occurred in Ireland in 2000, with over 1600 cases reported and three associated deaths.

The World Health Organisation European Region has prepared a strategic plan (2005-2010) to eliminate measles and rubella and prevent congenital rubella. Elimination of these diseases will require the following objectives to be met:

- Achieving and sustaining very high coverage ($\geq$95%) with two doses of MMR vaccine through high quality immunisation services
- Provision of a second opportunity for MMR vaccination through supplemental immunisation activities to groups susceptible to measles
- Strengthening of the surveillance system by rigorous case investigation and laboratory confirmation of suspected cases
- Improving availability of high quality information for health professionals and the public on the benefits and risks associated with immunisation against measles and rubella

In 2004, the Department of Health and Children established the National Measles and Rubella Elimination Committee to advise the Department, and the HSE, on a recommended national action plan for the elimination of measles and congenital rubella infection in line with Ireland's commitments as a WHO member state. The membership was drawn from a broad range of professional groups and national stakeholders in immunisation activities.

This document presents the situational analysis of measles epidemiology and control in Ireland and presents options to eliminate this disease.

This document also discussed rubella and congenital rubella infection epidemiology which is also included in the WHO elimination strategy, because it is acknowledged elimination of measles through the use of MMR will also support the elimination of rubella.

II. MEASLES ELIMINATION COMMITTEE

Dr. Darina O'Flanagan, Director, HPSC (Chair)
Dr. Anna Clarke, Specialist in Public Health Medicine, HSE E
Ms. Teresa Cody, Principal Officer, Department of Health and Children (replaced by Mr. Peter Hanrahan 2006)
Dr. Jeff Connell, Principal Clinical Scientist, National Virus Reference Laboratory
Dr. Eibhlin Connolly, Deputy Chief Medical Officer, Department of Health and Children
Dr. Brenda Corcoran, Department of Health and Children, HSE National Immunisation Office
Dr. Suzanne Cotter, Specialist in Public Health Medicine, HPSC (Medical secretary)
Dr. Brendan Crowley, Consultant Microbiologist, St. James's Hospital
Mr. Pat Donnelly, CEO, South Western Area Health Board ERHA
Ms. Eleanor Dowling, Director of Public Health Nursing, MHB (deceased) replaced by Ms. Bridget Catterson in 2007
Dr. Joan Gilvarry, Medical Director, Irish Medicines Board
Dr. Johanna Joyce-Cooney, Senior Medical Officer, HSE Midlands
Dr. Alfred Nicholson, Consultant Paediatrician, Our Lady of Lourdes Hospital, Drogheda (representative of RCPI Faculty of Paediatrics)
Dr. Dermot Nolan, ICGP (representative of Irish College of General Practitioners), retired April 2005
Ms. Marian Wyer, HSE Professional Development Coordinator for Practice Nurses Nursing & Midwifery, Planning and Development Unit, Tullamore Representative for the Irish Practice Nurse Association

Acknowledgements:
Dr. Sarah Gee, HPSC - for collation of national measles data
Dr. Orla Healy, Specialist Registrar in Public Health Medicine (resigned 2006)

III. TERMS OF REFERENCE

The Committee was asked to develop a national action plan for the elimination of measles and rubella in line with the WHO strategic plan for 2010 to include:

- a situational analysis, including the epidemiology of measles and rubella and vaccination coverage
- review of disease surveillance capacity, including evaluation of laboratories and programmes
- rationale for recommended vaccination
- actions to implement the recommended strategies
- vaccine supply and cold chain logistics
- plans for staff supervision, training and development
- indicators for monitoring outcome and performance
- actions to ensure the safety of injection, including surveillance and management of adverse events following immunisation and
- timetable and costs, indicating sources of funding.

The Committee was asked to pay due regard to the National Immunisation Steering Committee Report (2002) and the work of the National Implementation Committee where relevant.

IV. EXECUTIVE SUMMARY

Measles and rubella remain important causes of vaccine-preventable disease, disability and death in Europe.

Measles-Mumps-Rubella vaccine (MMR) was introduced into the routine childhood vaccination programme in Ireland in 1988. Despite its widespread usage, indigenous measles cases have continued to occur in Ireland at high levels. The most recent large measles outbreak occurred in Ireland in 2000, with over 1600 cases reported and three associated deaths.

In 2002, WHO Regional Office for Europe developed and implemented a strategic plan for measles and congenital rubella infection in the WHO European Region. This plan targeted the elimination of measles, rubella and the prevention of congenital rubella infection for the year 2010.[1] In 2005, WHO EURO reported on progress of elimination in the European region and identified key strategies and actions required in the areas of national policy development, surveillance, vaccine quality and safety, communication and advocacy and the development of a certification process.[2]

In 2004, the Department of Health and Children established the National Measles and Rubella Elimination Committee to advise the Department, and the HSE, on a recommended national action plan for the elimination of measles and rubella in line with Ireland's commitments as a WHO member state.

The Committee undertook a situational analysis of measles and rubella in Ireland (epidemiology, surveillance and control) and reviewed MMR immunisation uptake. Based on this review the Committee have appraised options and made recommendations for an action plan for measles elimination. Although the focus of this report is primarily that of measles, it is widely acknowledged that control of measles through the use of MMR will contribute to the control of rubella.

Surveillance

Measles and rubella are still endemic in Ireland. In 2005 measles incidence was 93 cases (incidence rate 2.4/100,000): rubella incidence was 17 cases (incidence rate 0.4/100,000) and CRI incidence was 0 cases.

Successful measles elimination will require a sensitive surveillance system to detect every case of measles. A more sensitive case definition, recently recommended by ECDC will be used to ensure a very sensitive surveillance system. An increase in laboratory diagnosis is recommended to confirm diagnosis. Improving the timeliness of laboratory reporting will aid in rapid identification of cases and implementation of timely control activities. The National Virus Reference Laboratory (NVRL) will support clinical and epidemiological investigation through the testing of samples from suspected cases, confirmation of measles and rubella cases, and identification of genotypes of measles virus with the aim of enhancing investigations into sources of infection and epidemiologic chains of transmission.

As the responsibility for infectious disease surveillance and control activity lies within two HSE directorates (Population Health and Primary, Community and Continuing Care [PCCC]) response to a measles case and implementation of control activities will require close cooperation between these two directorates.

Public health surveillance systems already in place need to be strengthened by allocation of appropriate resources to ensure timely reporting, collection of data and sample collection on all suspect cases. Laboratory surveillance activities will need to be strengthened to provide genotype information. Enhanced surveillance on all cases, with laboratory confirmation, should be undertaken by Departments of Public Health in collaboration with primary care colleagues. Systems are already in place for surveillance of adverse events following immunisation. Additional efforts are needed to raise awareness of reporting responsibilities and reporting processes in this area.

Investigation and control of reported measles (and rubella) cases is currently under-resourced and most HSE areas experience difficulties in achieving timely investigation and response activities. This area needs to be resourced and strengthened to ensure rapid and complete investigation of measles (and rubella) cases.

Immunisation

MMR immunisation coverage has been inadequate for many years, but is improving. Most recent MMR coverage (2006) at 24 months was 86%; this fails to meet WHO recommended targets. National MMR_2 (two doses of MMR) coverage at 4-5 years is unknown and not routinely measured. Ireland needs to have systems in place to measure MMR_2 so that immunisation performance can be measured.

Immunisation activities needed for measles elimination should do the following:

1. Maintaining high routine immunisation coverage

Elimination of measles requires achieving and maintaining high immunisation coverage with two doses of MMR. To achieve this Ireland must ensure that:

- All regions should achieve and maintain high immunisation (>95%) coverage of all birth cohorts with two doses of MMR
- All areas should identify and follow-up MMR_1 and MMR_2 defaulters for immunisation
- Children presenting for MMR vaccination at 4-5 years without evidence of MMR_1 should routinely be scheduled for MMR_2 (at least one month later)
- Opportunistic MMR immunisation should be provided for children in other health care settings (GP, hospital settings)

2. Providing opportunity for 2nd dose of MMR – supplemental activity

In addition, because of the historic low coverage rates a catch-up campaign will be required.

For the supplemental activity the Committee considered a number of approaches (comprehensive and selective) and methods of delivery (GP versus school teams).

Population targeted - comprehensive versus selective approach

In the discussions on what population was most susceptible to measles and should be targeted for supplemental activities the Committee was informed by the situational analysis presented in the report, including the following:

- Epidemiology of measles (with consideration also given to epidemiology of mumps and rubella) in Ireland,
- Measles susceptibility age profile as demonstrated in the second European Sero-Epidemiology Network (ESEN2) study, the model and suggested strategy options developed by Dr. Nigel Gay, Modelling Unit, Centre for Infections, Health Protection Agency, UK
- Immunisation uptake data (MMR_1 at 24 months)
- Ability (and reported difficulties) to retrieve MMR_2 immunisation uptake data
- Costs of different strategies

The Committee discussed the advantages and disadvantages of a comprehensive versus selective approach, the summary of which is included here:

A. Comprehensive MMR approach

In this approach, all children 4-18 years of age regardless of immunisation status are targeted. This would mean targeting approximately 853,000 children (2002 census).

This approach will require more vaccine and staff than a selective approach (see below) but is considered logistically easier to do. Vaccine records do not need to be obtained (a recognised difficulty), the message to the public is clear (a booster campaign for all children), it is safe and effective to administer additional MMR doses to individuals already vaccinated with two doses. This approach was the preferred approach by the Specialists in Public Health Medicine when they were consulted.

B. Selective MMR approach

Targeting children 4-18 years of age who have no record (or it cannot be located) of ever receiving MMR_2 vaccine.

In the selective approach campaign it is assumed (expert opinion) that approximately 50% of children (426,000) aged 4-18 years will require MMR vaccine because they either never received MMR_2 or no vaccination records can be found.

As there are over 50 immunisation databases in the country the identification of this group will take a substantial amount of time and effort.

Because numbers are smaller, this selective approach will require less vaccine and less staff for vaccination teams, but will be logistically difficult as vaccine records will have to be retrieved from archives in most areas. This will require substantial resources within PCCC, additional time will be needed to obtain records and sort through them (PCCC administrative staff predominantly), the message to parents has the potential to be confusing (unless clearly stated that administration of additional

MMR is not a problem) and resulting public concern has the potential to negatively impact on the programme. The message associated with this campaign needs to very clear.

GP versus school-based vaccine delivery

GP delivery of such a programme would be more expensive than using school teams. Therefore school-based programmes are most cost effective and are the recommended mode for delivering this programme.

For both approaches additional resources will also need to be provided for mop-up clinics for children who miss the initial school-based clinics and for opportunistic MMR vaccination.

The Committee highlighted a number of issues that need to be considered in any national MMR catch-up campaign:

- Such a campaign will need additional funding
- A comprehensive planning process must take place involving consultation with, and cooperation of, all key stakeholders
- A National Steering Committee should be established to oversee the activity
- Close liaison with the Department of Health and Children and Department of Education will be required
- A project team should be established to include a project manager and vaccination teams and appropriate accommodation and facilities for these teams will be required
- Current school immunisation teams (where they exist) do not have the capacity to implement this campaign
- Project staff will be required to develop an education and training plan and materials, and also a robust national recording system as well as liaising with the HSE National Immunisation Office for vaccine procurement and distribution
- All areas have a system to monitor uptake of MMR_2, in place ahead of any national unified system
- A national communication plan will be required

3. Other groups for whom MMR is required during elimination phase

Recommendations already exist regarding groups at risk who should be appropriately vaccinated, these recommendations should be realised during the elimination phase;

1. *Women of childbearing age should be protected*
   Women who may not have been offered a rubella containing vaccine should be offered MMR if non-immune. All susceptible women identified during the antenatal period should be immunised after delivery.

2. *All health care workers should be appropriately immunised against measles and rubella*
   Those born after 1978 without evidence of measles infection or receipt of two doses of MMR should be given two doses of MMR at least one month apart.

3. *Immunisation during outbreaks*

   During outbreaks, consideration should be given to lowering the age of immunisation; infants may be vaccinated as young as 6 months of age but still require another dose of MMR at 12-15 months and another dose at 4-5 years. Active immunisation of susceptible contacts of measles cases should occur within 72 hours of contact.

   During outbreaks in day care centres/crèches, already immunised children and their siblings should receive their second dose of MMR.

   The Committee recommended that although there is no legislation requiring crèches, preschool facilities or schools to maintain immunisation records of children in their care this practice should be encouraged. In the event of measles cases occurring in the facility susceptible children need to be rapidly identified and immunised (or excluded for their own protection). Discussions with relevant government offices and HSE services are required to progress this issue.

Immunisation information systems need to be strengthened

Currently there are over 50 immunisation information systems used in Ireland and no single national immunisation information system. A proposal for such a system has been outlined but specifications and further development is required.

A national client-based system is urgently needed to comprehensively capture all relevant information on vaccines administered to children in Ireland. Current systems are unwieldy, inaccurate and user-unfriendly. With the current systems immunisation data is usually difficult to source for individuals, service providers from other areas and health professionals involved in client care. Monitoring national immunisation uptake of MMR1 and MMR2 at national, regional and LHO/CCA level is difficult when children move within and between different HSE areas and are not easily traced, records are difficult to find and parents often unsure of what vaccines have been administered.

The currently used immunisation information systems require the GP to manually complete the HSE immunisation form detailing the child's vaccination, forward this information to the immunisation office where the information is manually entered into the local immunisation database. The latter activity is done by HSE administrative staff. The work is labour intensive, prone to delays and potentially prone to data entry errors at all levels. Identification of defaulters triggers the generation of reminder letters which are sent to parents and encourages them to bring their children for vaccination. Lists of defaulters by GP practice are also generated from these systems and sent to the relevant GP practices.

Dedicated staff is required to ensure rapid entry of data so that the immunisation information systems accurately identify those children who are up to date and those who are defaulters. Currently most HSE areas have insufficient staff to input immunisation data in a timely manner.

Communications/advocacy
Increased communication and educational activities are needed to raise awareness among the many stakeholders in prevention, surveillance and control activities. Various and innovative media should be used for this purpose. Health promotion staff should play a key role in this activity.

Conclusions and summary of recommendations

The Committee recommended that the following areas need to be addressed and strengthened:

1. Immunisation activities

- Routine immunisation activities need to be strengthened to ensure that at least 95% of children receive two doses of MMR
- All children, aged 4-18 years, should be provided with an opportunity for a second dose of MMR through this approach
- A catch-up programme should be adopted using a school/education facility based programme using immunisation teams (similar to the MenC campaign)
- Secondary school children should be prioritised in the short term due to excessive levels of measles susceptibility in this population
- For hard to reach children, susceptible children alternative approaches should be identified at local level
- Children without evidence of two doses of MMR should receive MMR as part of catch-up campaign
- Either a comprehensive or selective approach can be undertaken. The approach taken will depend on availability of resources (retrieval of immunisation records and vaccination programme).

A comprehensive approach will be easier to implement (organisationally, logistically, communication messages and timeliness, less draining on human resources), but is more costly than a selective approach that targets only those for whom no record of MMR_2 can be located.

A selective approach will prove demanding for all HSE areas, particularly those that are unable to retrieve MMR_2 immunisation records from computer based systems. Whether these areas will have the staff to obtain vaccine records is unknown, and they may need to resort to a comprehensive approach as being most feasible.

2. Immunisation information systems strengthened

- Each HSE area needs to monitor MMR_1 and MMR_2 uptake
- Immunisation records need to be returned by GPs to HSE in a timely manner
- HSE immunisation administrative staff need to enter this data into local immunisation database in a timely manner
- A national immunisation register should be developed as a priority

3. Surveillance activities

- Surveillance needs to be strengthened (case reporting, investigation, laboratory diagnosis, adverse events). Timeliness and completeness of reporting and investigation is key.

4. Communication/advocacy

- Increased communication and information is needed to inform all stakeholders about measles, its preventability and MMR vaccination
- Specific communication strategies should be developed with input from various stakeholders
- Rapid access to information on the campaign should be available to parents. Telephone helplines should be available. Communication and information for specific groups such as non-nationals and those with reading difficulties must be addressed.

SECTION 1. INTRODUCTION

1. GENERAL EPIDEMIOLOGY AND INTERNATIONAL RECOMMENDATIONS

1.1 Measles

Measles is an acute viral illness caused by a virus in the family paramyxovirus, genus Morbillivirus. Measles is characterised by a prodrome (two to four days) of fever and malaise, cough, coryza, and conjunctivitis, followed by an erythematous maculopapular rash. The rash begins at the hairline, and then involves the face and upper neck. Over the next three days, the rash gradually proceeds downwards and outward reaching the hands and feet. Koplik's spots, an exanthema present on mucous membranes, is considered to be characteristic for measles. It occurs one to two days before the rash to one to two days after the rash, and appears as punctate blue-white spots on the bright red background of the buccal mucosa.[3]

The incubation period of measles from exposure to prodrome averages 10-12 days, and from exposure to rash averages 14 days (range 7-18 days, rarely as long as 21 days). Measles transmission is primarily person-to-person via large respiratory droplets. Measles is highly communicable, with >90% secondary attack rates among susceptible persons. Measles may be transmitted from four days prior to four days after rash onset. Maximum communicability occurs from onset of prodrome through the first three to four days of rash. Airborne transmission via aerosolised droplet nuclei has been documented in closed areas (e.g. examination room) for up to two hours after a person with measles occupied the area.[4]

Measles complications – general

Though usually a mild or moderately severe illness of childhood, measles can result in residual impairment. Encephalitis occurs in approximately 0.1% of reported cases. Deaths are reported in approximately 1-2 per 1000 cases. Complications such as otitis media, bronchopneumonia, laryngotracheobronchitis (croup), and diarrhoea occur more commonly in young children under the age of five years. Pneumonia (six percent of reported cases) may be directly attributable to measles or superimposed bacterial and is the most common cause of death. Complications such as pneumonia and acute encephalitis are increased in adults over the age of 20 years.[3]

Measles associated neurological complications

Acute encephalitis is reported in approximately 0.1% of reported cases. Onset generally occurs approximately six days after rash onset (range 1-15 days), and is usually characterised by fever, headache, vomiting, stiff neck, meningeal irritation, drowsiness, convulsions and coma. Case fatality can approximate 15%. Some form of residual neurological damage occurs in as many as 25% of cases. Seizures (with or without fever) are reported in only 0.6% to 0.7% of reported cases.[3]

The most common causes of death are pneumonia in children and acute encephalitis in adults. Subacute sclerosing panencephalitis (SSPE) is a rare degenerative central nervous system disease possibly due to persistent measles virus infection of the brain. The risk of developing SSPE following measles in the first year of life is much higher

than if measles is acquired later in life.[5] Average onset occurs seven years after measles (range 1 month – 27 years) and occurs in five to ten cases per million reported measles cases. The onset is insidious, with progressive deterioration of behaviour and intellect, followed by ataxia, myoclonic seizures, and eventually death.

Pregnancy complications associated with measles

Measles illness during pregnancy results in a higher risk of premature labour, spontaneous abortion, and low birth weight infants.[3]

1.2 Rubella

Rubella is a mild febrile viral disease characterised by a diffuse punctuate and maculopapular rash. In the absence of rubella immunisation programmes rubella occurs world-wide. Rubella infection in pregnancy is of major public health importance due to the teratogenic effects that can result from congenital rubella infection (CRI), which can lead to miscarriage, foetal death or birth of an infant with congenital rubella syndrome (CRS).[6]

Humans are the only know reservoirs for infection. Transmission is though contact with nasopharyngeal secretions of infected people. Infection is by droplet spread or direct contact with patients. Infants with congenital rubella syndrome (CRS) shed large quantifies of rubella virus in their pharyngeal secretions and urine and serve as a source of infection to their contacts.[4]

The incubation period ranges from 14-17 days (range 14-21 days). The disease is highly infectious with transmission occurring from about one week before to four days after onset of rash. Infants with CRS may shed virus for months after birth.[4] Immunity is usually permanent after natural infection and thought to be long term. Infants born to mothers are usually protected by maternal antibody for the first 6-9 months of life, the length of protection is dependent on the amount of maternal antibody acquired transplacentally.

Clinically it is often difficult to distinguish rubella from measles, parvovirus B19, dengue, Human herpes virus 6, Coxsackie virus, Echovirus, adenovirus or scarlet fever. Children usually present with few symptoms but adults may experience a 1-5 day prodrome with low grade fever, headache, malaise, mild coryza and conjunctivitis. Post auricular, occipital and cervical lymphadenopathy is a characteristic clinical finding and precedes the rash by 5-10 days.[4]

Rubella complications – general

Complications are more common in adults than children. Arthralgia or arthritis may occur in 70% of adult women but is rare in children and men. Joint symptoms occur about the same time or shortly after the rash and may last for up to a month. Encephalitis occurs in one in 6,000 cases and is more common in adults than children (especially females). Haemorrhagic manifestations occur in approximately 1 per 3,000 cases and are more common in children than adults.[3,4]

Pregnancy complications associated with rubella

Rubella control is needed primarily to prevent women acquiring infection during pregnancy and thus exposing their foetus to the virus (congenital rubella infection, CRI) and the development of congenital rubella syndrome (CRS). Maternal infection during pregnancy may cause death of the foetus, spontaneous abortion, or premature delivery. The gestational age of the foetus at the time of infection is crucial to the outcome.[3,4]

Congenital rubella syndrome (CRS)/Congenital rubella infection (CRI)

Infection early in pregnancy poses greatest risk to the developing foetus. The virus may affect all organs and cause a variety of congenital defects (CRS). Up to 85% of infants infected during the first trimester of pregnancy will be affected. The risk to the foetus decreases with gestational age. Defects are rare when infection occurs after the 20th week of gestation.[3,4,6] The most common defects are sensorineural deafness, eye defects, cardiac defects, neurologic abnormalities. Manifestations of CRS may be delayed for 2-4 years. Diabetes mellitus appearing later in childhood occurs frequently in children with CRS. Progressive encephalopathy (similar to SSP post measles) has also been observed in some children with CRS. Autism is a feature of some late onset neurologic disease in CRS patients.[6]

1.3 Prevention of measles and rubella

Measles and rubella can be prevented by vaccination. Prior to the introduction of measles and rubella vaccines both diseases were recognised to be common, predominantly childhood viral illnesses. Measles was a common cause of severe illness and occasionally death. Rubella was associated with foetal death, and congenital malformation in infants born to mothers who were infected with rubella during pregnancy.

Rubella vaccine was recommended for all adolescent girls since 1971 and measles vaccine for young children since 1985.

Despite widespread usage of MMR, indigenous measles and rubella cases have continued to occur in Ireland. Measles incidence has been particularly high. This is unacceptable for diseases that have the potential to be eliminated and potentially eradicated, as demonstrated in the Americas with measles. Ireland, in contrast has continued to have both sporadic measles cases reported as well as substantial community wide measles outbreaks. The most recent large measles outbreak occurred in Ireland in 2000, with over 1600 cases reported and three associated deaths.[7]

1.4 Eliminating measles, rubella and CRI - WHO strategy 2005–2010[1,2,8,9]

Strengthening national immunisation systems is an important goal in the WHO European Region. Immunisation programmes delivering quality vaccines in a safe manner, with age-appropriate vaccination coverage rates ≥95%, high-quality programme-monitoring capacity and laboratory-based disease surveillance, will enhance the cost-effectiveness of using existing vaccines.

The WHO EURO office developed and implemented a strategic plan for measles and congenital rubella infection in the WHO European Region in 2002.[1] This plan targets the elimination of measles and the prevention of congenital rubella infection for the year 2010. Measles elimination has already been achieved in some European countries through routine immunisation programmes, which maintain high measles-vaccine coverage using a two-dose schedule.

All 52 Member States in the WHO European region now have routine two-dose measles immunisation schedules and 26 (50%) have achieved a measles incidence of <1 per million population, one indicator of measles elimination. Forty-eight (92%) member states are now using rubella vaccine; 47 use measles vaccine combined with rubella vaccine.[2]

In this measles elimination strategy rubella elimination is also proposed. Given that rubella is a less contagious illness compared with measles, and most Member States have elected to use combined measles/rubella vaccines, rubella elimination is feasible within a framework of measles elimination.

The most recent WHO EURO strategic plan for eliminating measles and rubella and preventing congenital rubella infection in the European region identified key strategies and actions required in the areas of national policy development, surveillance, vaccine quality and safety, communication and advocacy, and the development of a certification process.[2]

1.4.1 Measles, rubella and CRI elimination strategy objectives

The objectives for the 2010 WHO European region elimination strategy are:

- to eliminate endemic measles;
- to eliminate endemic rubella; and
- to prevent CRI (<1 case of CRS per 100,000 live births).

1.4.2 Key strategies

To achieve these objectives, the key strategies have been revised to take into account the rubella elimination target.

i) Achieve and sustain very high coverage (≥95%) with two doses of measles and at least one dose of rubella vaccine through high-quality routine immunization services.

Strategies need to be developed to improve vaccine coverage to ≥95%, especially among "hard-to-reach" populations.

ii) Provide a second opportunity for measles immunisation through supplementary immunisation activities to populations susceptible to measles.

These activities should consider trying to reach people that have inadequate levels of immunity for interrupting endemic transmission of measles and are likely to be exposed to measles virus should it be introduced into the community e.g. those attending schools or universities, those in the military and those working in health care settings.

iii) Provide rubella vaccination opportunities, including supplementary immunisation activities, to all rubella-susceptible children, adolescents and women of childbearing age.

Children and women of childbearing age may be susceptible to rubella due to lack of exposure to rubella virus or because they did not receive rubella vaccine; a small proportion of women (<10%) may not have responded to one dose of the vaccine or may have lost protective antibody levels. Even in countries that have used rubella vaccines for many years in childhood programmes, if they have been unable to sustain coverage at high levels, this may result in a larger proportion of unvaccinated girls becoming women of childbearing age without immunity to rubella than would have occurred before rubella vaccine was used. During a rubella outbreak, these women are at risk of infection during pregnancy, increasing the number of children with CRS compared with countries where rubella vaccine has never been used. Appropriate immunisation strategies need to be considered to reach these susceptible populations, both to interrupt endemic transmission and to ensure women of childbearing age are protected should rubella virus be introduced into their community.

iv) Strengthen surveillance systems by rigorous case investigation and laboratory confirmation of suspected cases.

Surveillance activities for measles, rubella and CRS need to be of sufficient quality to detect sporadic cases and provide adequate information on both the epidemiology and the virus genotype, so cases can be classified as being the result of endemic transmission or importation. This information needs to be collected, analysed and communicated effectively, in a timely manner, to enable appropriate public health action.

A surveillance system for the detection, investigation of and response to adverse events following immunisation (AEFIs) is also essential to monitor the quality and safety of immunisation and to guarantee transparency of the programme through providing information about possible AEFI cases.

Regular training in surveillance and the availability of adequate information systems are critical components of this key strategy.

v) Improve the availability of high-quality, valued information for health professionals and the public on the benefits and risks associated with immunization against measles and rubella.

The knowledge and perceptions of health professionals and the public about measles and rubella, including the benefits and risks associated with preventing these diseases, remain extremely important for public health officials seeking to increase and maintain the very high levels of immunisation coverage required to meet the objectives of measles and rubella elimination. Increasingly all people (general public and health professionals) get their health-related information from news media and the Internet. WHO recommend that more "Attention should be given to how the material is perceived and used by those with the right and desire to know – the parents of children about to be immunized or those who believe their child has been adversely affected".[10]

1.4.3 WHO recommended key areas for action:

1.4.3.1 National policy development

National immunisation plans for routine childhood immunisation

National immunisation plans should contain clearly defined objectives, immunisation strategies and activities, resource requirements and where appropriate, financial sustainability plans. National immunisation plans should identify mechanisms for strengthening immunisation programme management activities, including the ongoing evaluation of performance, and appropriate strategies to improve the collection, analysis and use of data on sub-national programme activities, including the identification of under-performing areas.

Measles/rubella/CRI plans

Disease-specific plans should be incorporated into national immunisation plans.

National measles and rubella elimination committees

Countries are encouraged to establish national measles and rubella elimination committees with national and subnational representation and involve partners. The committee can review progress towards the achievement of elimination and CRI prevention objectives.

1.4.3.2 Surveillance

Infrastructure capacity

European countries are recommended to assess the capacity of their surveillance for vaccine-preventable diseases to ensure it is of sufficient quality to monitor, measure and report on the regional elimination targets for measles and rubella and the prevention target for CRI. Countries are encouraged to report case-based information.

Ensuring quality surveillance and measuring performance

WHO has already provided (and will update) a detailed set of surveillance indicators for assessing surveillance quality and for monitoring progress toward the elimination targets.

Laboratory surveillance

The regional measles and rubella laboratory network needs further strengthening to ensure adequate laboratory investigation of >80% of suspected measles and rubella cases when the disease incidence approaches 1 per 100 000. The testing is done in WHO accredited laboratories or ones supervised by an accreditated national laboratory, and the measles and rubella virus genotype data are available on cases from all Member States.

1.4.3.3 Immunisation quality and safety

Vaccine management

All vaccines, which are procured and used, should be of assured-quality and that their national regulatory authorities are fully functional. High practice standards should be adhered to for vaccine management (vaccine storage, distribution and administration, including maintenance of cold chain), injection safety (availability of injection material and sharps containers) and proper disposal of injection material (safe, complete and environmentally friendly).

Adverse Events following Immunisation (AEFIs)

The strengthening detection and investigation of and response to adverse events following immunisation will be essential to monitor the quality and safety of immunisation and to guarantee the transparency of the programme through providing sufficient information about possible events.

1.4.3.4 Coordination and partnership

All European countries need to foster the appropriate partnerships, including plans for intersectoral cooperation, with governmental and intergovernmental agencies, nongovernmental organisations and other relevant partners, including the private health care sector and industry, to ensure the strengthening of routine immunisation services and the achievement of the elimination targets.

1.4.3.5 Communication/advocacy

Communication plans

All European countries, particularly those experiencing adverse publicity about immunisation, are recommended to have approved communication plans, by which they can respond to negative publicity and ensure health care providers and the public

have appropriately targeted, high-quality information on immunisation, addressing specific issues of concern.

Quality immunisation information

All countries should work with interested stakeholders to develop accessible information for their populations. European Immunisation Week is essential for the Region-wide promotion of immunisation using targeted national or subnational activities. This will also enable the sharing of experiences and information to promote evidence based advocacy and communication methods.

1.4.3.6 Certification process

The WHO Regional Office for Europe will collaborate with Member States, as well as stakeholders in other WHO regions, to refine the criteria used to assess the achievement of national and regional measles and rubella elimination and to develop a regional certification process.

Member States will need to establish national certification committees when appropriate and prepare documentation in line with that specified by the Regional Certification Commission for measles.

1.4.3.7 Indicators to measure progress

Outcome indicators

At the WHO European Regional level four outcome indicators will be used to measure regional progress towards meeting the objectives:

- the number of countries with measles incidence of <1 per 1 000 000 population
- the number of countries with rubella incidence of <1 per 1 000 000 population
- the number of countries with CRS incidence of <1 per 100 000 live births
- the number of countries with measles containing vaccine (MCV1) coverage of ≥95% at national level and ≥90% in all districts.

Ireland should strive to meet each of these outcome indicators.

Performance indicators

The following performance indicators (PIs) are linked to the key strategies and are presented here for particular relevance to Ireland. The comprehensive list is available from the WHO surveillance guidelines document.[8]

Performance indicator- Vaccination

Ireland should be administering two doses of MMR ≥95% of all children at the national level and/or ≥90% of children in all first administrative levels (i.e. LHO areas).

Performance indicator- Surveillance

By 2010 Ireland should meet at least 90% of primary surveillance indicators.

Performance indicator- Communication

Ireland should participate at either national or subnational level in the European Immunisation Week.

1.5 Ireland's progress to date

Ireland is already working towards meeting the objectives outlined by WHO and compares favourably with many of the proposed outcome indicators and performance indicators e.g. two doses of MMR are offered to all children, active and enhanced surveillance of measles cases takes place, cases are investigated and control measures implemented. However, with regard to measles in particular, additional efforts are needed if we are to meet the targets outlined by WHO. Improving quality and completeness of data collection within a rapid timeframe is required (notification of cases within 48 hours of rash onset, investigation within 48 hours of notification, laboratory results within 7 days of detection).

In 2002 the Measles Sub-Committee of the Scientific Advisory Committee of the NDSC published a document "*Guidelines for Control of Measles in Ireland*"[11] which outlined the actions required to control this disease. The document outlined the key strategies necessary to control measles:

Sustained high vaccination coverage with two doses of MMR immunisation (of at least 95% of susceptible targets)

Active and enhanced surveillance of all measles cases, rapid investigation of reported cases and immediate implementation of control activities to prevent ongoing transmission.

Additionally Ireland has participated in European Immunisation week since 2005.

Although the overall incidence of measles decreased in recent years, it has continued at unacceptably high levels.[12] Ireland will need to monitor its progress to eliminate measles, rubella and CRI by comparing its performance indicators against those proposed by WHO.

SECTION 2. DETAILED SITUATIONAL ANALYSIS

2. MEASLES AND RUBELLA EPIDEMIOLOGY IN IRELAND

2.1 Measles in Ireland

Since 1948, when measles first became a notifiable disease, the number of measles notifications in Ireland has decreased markedly. Much of the more recent sustained decline can be attributed to the introduction of measles vaccine to the early childhood vaccination programme in 1985.

In 1985, the year when measles vaccine was introduced, 9,903 cases were reported. The number of reported cases in the immediate subsequent years dropped significantly, so that by 1991 just 135 cases were reported. However, a number of major outbreaks subsequently occurred despite the routine immunisation programme.

Following introduction of the MMR vaccine in 1988 a further three major outbreaks have occurred; 1989 (1,248 cases), 1993 (4,328 cases) and 2000 (1,603 cases). During the 2000 outbreak, the highest incidence rate of measles was reported from the Dublin and Eastern region of the country.[13]

Measles vaccination and impact on incidence

The MMR vaccine was incorporated into the primary immunisation schedule in October 1988. In July 1992, a second MMR (MMR_2) for both boys and girls ages 10-14 years was introduced, replacing the previous selective rubella vaccine programme for prepubertal girls. A catch-up campaign was introduced in 1995 (aimed at children aged 5-12 years of age who were susceptible to measles). In 1999 it was decided to lower the age for routine administration of the MMR_2 dose from 10-14 years to children aged four to five years of age to improve immunisation coverage and decrease measles transmission (Table 2.1 and Figure 2.1).

Table 2.1. Dates of introduction of measles and rubella containing vaccines into Ireland and age groups targeted.

Year	Vaccine	Target population		Comment
		Age	Sex	
1971	Rubella only	12-14 years	Female only	
1985	Measles only	15 months-5 years	Both	
1988	MMR*	15 months-2 years	Both	
1988	MMR*	10-14 years	Female only	MMR to replace rubella only
1992	MMR*	15 months & 10-14 years	Both	2nd dose MMR introduced 1992
1995	Measles and Rubella (MR)	5-12 years	Both	Part of a measles/rubella campaign for 5-12 yr olds
1999	MMR*	15 months & 4-5 years	Both	Age 2nd dose MMR reduced from 10-14 to 4-5 yrs
2002	MMR*	12-15 months & 4-5 years	Both	Age at 1st dose reduced to 12-15 months

*MMR = Measles/Mumps/Rubella vaccine

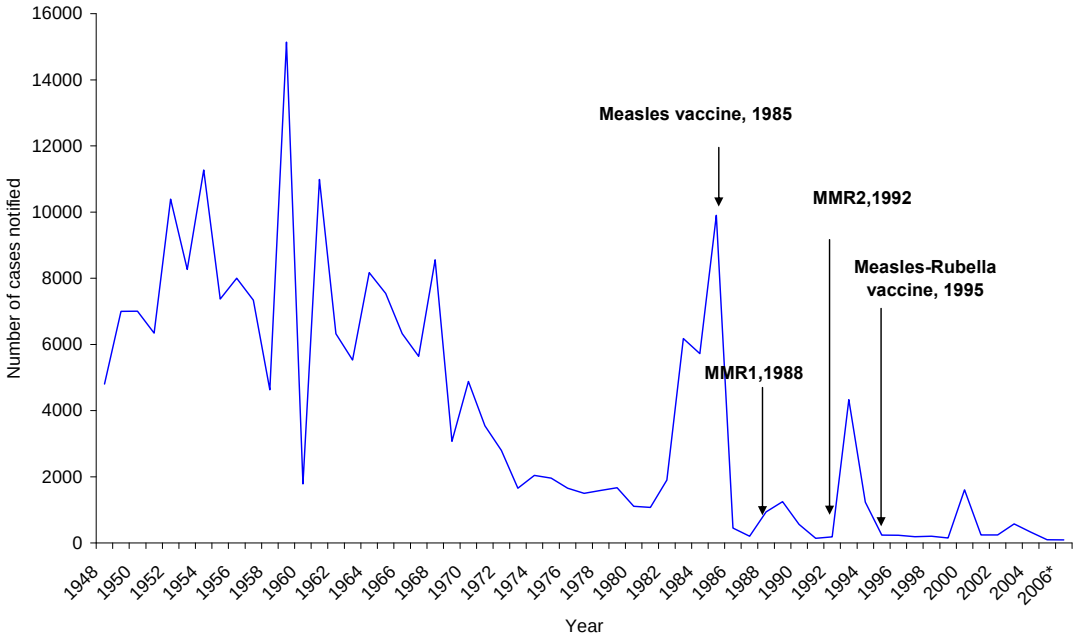


Figure 2.1. Notification of measles 1948-2006* and immunisation programme activities

*2006 data are provisional, data extracted from CIDR on 25/03/2007

Despite these changes to the immunisation schedule, aimed at decreasing measles incidence, outbreaks have continued to occur. Outbreaks occurred in 2003 and 2004. During 2004 three identifiable and epidemiologically linked outbreaks were reported. A total of 330 cases were reported that year (incidence rate 8.4/100,000). There was a decrease in notifications in 2005 (n=93), which continued into 2006 (n=87), (incidence rates of 2.4/100,000 and 2.0/100,000 respectively) (Figure 2.2).

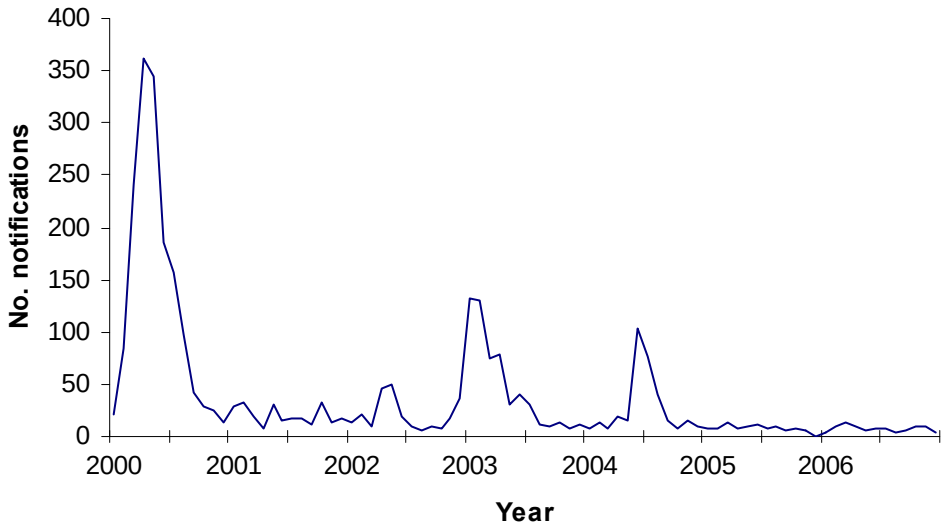


Figure 2.2. Measles cases by month of notification 2000- 2006*

*2006 data are provisional, data extracted from CIDR on 25/03/2007

Despite decreasing trends in incidence, measles virus continues to circulate. Confirming measles diagnosis by laboratory testing in all suspect cases is vital to

determine if reported clinical cases are truly measles. It is well recognised that as measles incidence decreases the number of suspect cases that are laboratory confirmed also decreases. A review of cases since 2004 has found that between 12%-47% of cases are classified as confirmed cases (i.e. either laboratory confirmed or linked to laboratory confirmed case). This clearly indicates that there is continued measles transmission in the community (Figure 2.3).

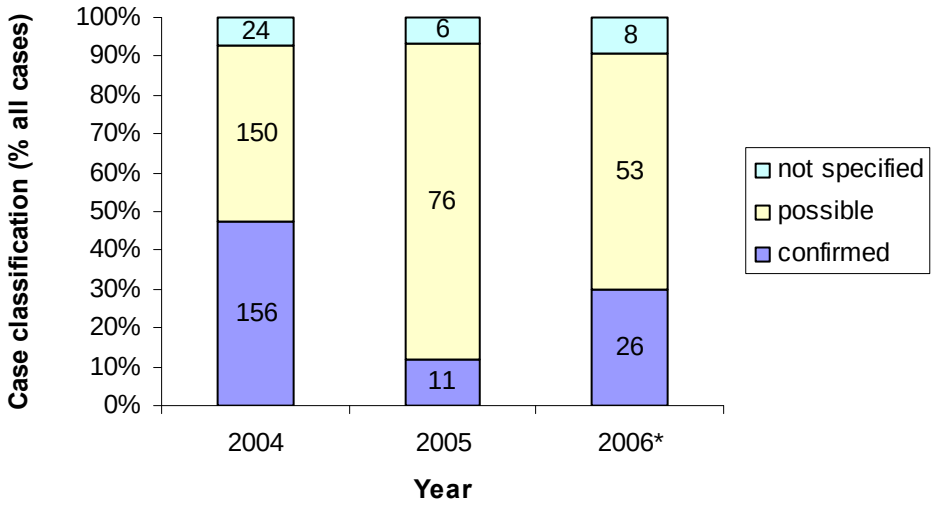


Figure 2.3. Case classification of measles cases, 2004-2006*
*2006 data are provisional, data extracted from CIDR on 25/03/2007

Over the years incidence rates have varied by HSE areas, with highest rates reported predominantly in HSE East (Figure 2.4).

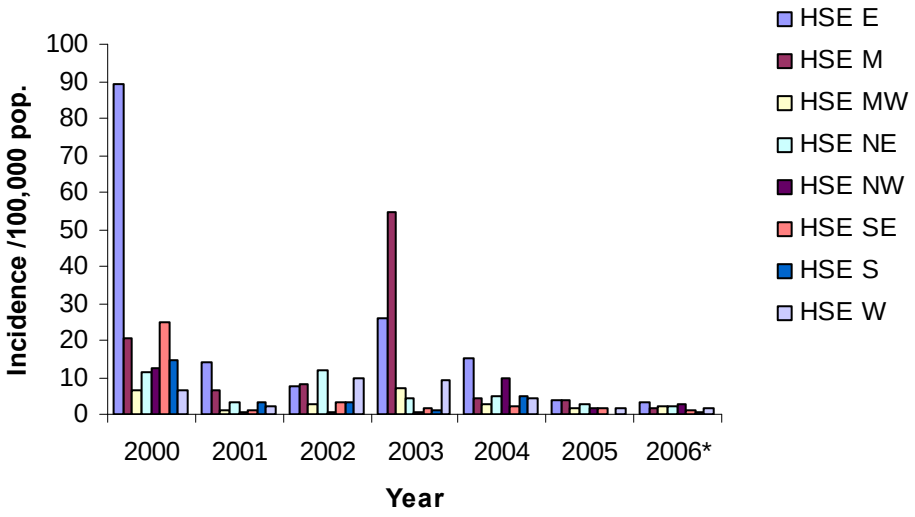


Figure 2.4. Measles incidence rate by HSE area 2000 – 2006*
*2006 data are provisional, data extracted from CIDR on 25/03/2007

Measles morbidity and mortality

Throughout the world measles infects 30-40 million children each year and kills over 750,000, often from complications related to pneumonia, diarrhoea and malnutrition. Many that survive are left with life-long disabilities such as blindness, deafness or brain damage.

The reduction of measles in Ireland was accompanied by a reduction in the number of deaths reported (Figure 2.5).

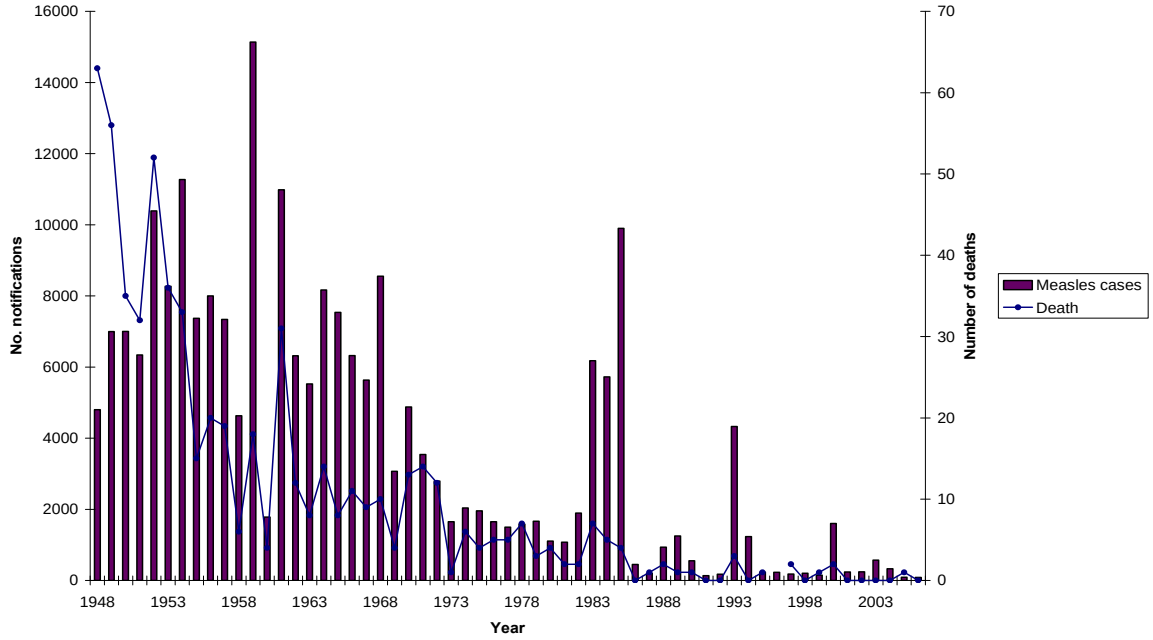


Figure 2.5. Measles notifications and reported deaths† in Ireland 1948-2006*
*2006 data are provisional, data extracted from CIDR on 25/03/2007
† source: Central Statistics Office

Despite the recent low numbers of measles associated deaths, measles remains an important preventable cause of morbidity and mortality in Ireland. During the measles outbreak in the ERHA (HSE East) in 2000 over 100 children were admitted to The Children's Hospital, Temple St., Dublin. Six of the children required treatment in intensive care and there were three measles related deaths.[13] Complication rates during that outbreak were in line with those seen elsewhere.

Description of measles cases in 2003-2006*

A total of 1,082 cases have been reported since 2003: 572 cases in 2003: 330 cases in 2004; 93 cases in 2005 and 87 in 2006*. Males and females were affected in similar proportions. During this time period, young children less than four years of age were most affected, with the highest age-specific incidence rates (ASIR) occurring among those less than one year of age. The highest ASIR in the < 1 year age group was in 2003 (200 cases/100,000 population) and the lowest in 2005 (50 cases/100,000 population) (Figure 2.6).

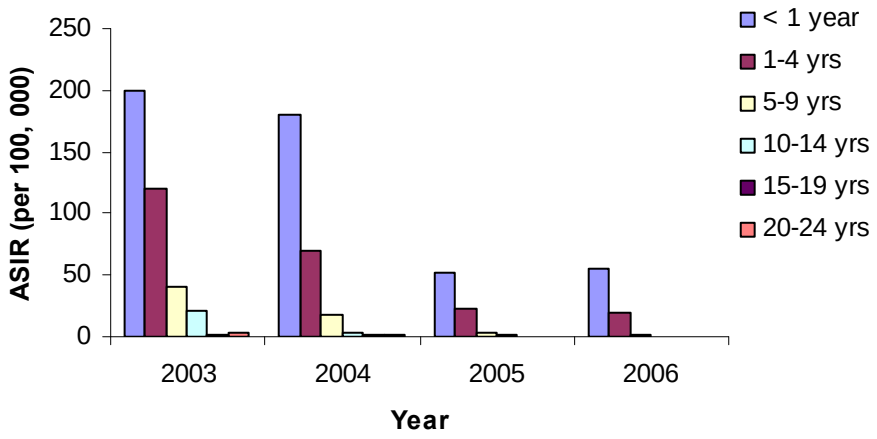


Figure 2.6. Age specific incidence rate (ASIR) measles cases by year 2003-2006*
*2006 data are provisional, data extracted from CIDR on 25/03/2007

Enhanced case data 2003-2005

Enhanced surveillance of all measles notifications has been in place in Ireland since 2002. In addition to the basic demographic information collected for all notifications, the enhanced surveillance system collects information on clinical details of the case, complications associated with illness (including hospitalisation), outcome, laboratory diagnostic information, epidemiological information related to likely source of infection, linkage with other cases and whether case was imported. Information on vaccination status is also requested. A final case classification is requested for each case notified (possible or confirmed). (From 2007 onwards revised ECDC case definitions will be used including possible, probable and confirmed -see Appendices).

Complete enhanced information is lacking on the majority of cases notified. Completeness of reporting for measles cases notified in 2003, 2004 and 2005 (selected variables) are shown in Table 2.2. Laboratory testing results were only available for 20%, 47% and 26% of all cases for the years 2003, 2004 and 2005 respectively. Vaccination status was only available for 52%, 55% and 63% respectively. Such incomplete data prevents meaningful interpretation of the surveillance data.

Table 2.2. Enhanced reporting, results 2003-2005

Data item	Data available	2003 (n=572)	2004 (n=330)	2005 (n=93)
Hospitalisation status	**Information provided**	120/572 (21%)	178/330 (54%)	38/93 (41%)
	Known hospitalised	12/120 (10%)	41/178 (23%)	5/38 (13%)
Laboratory result	**Information provided**	114/572 (20%)	156/330 (47%)	24/93 (26%)
	Lab confirmed	111/114 (97%)	145/156 (93%)*	11/24 (46%)
Vaccination status	**Information provided**	300/572 (52%)	180/330 (55%)	59/93 (63%)
	Unvaccinated	182/300 (61%)	141/180 (78%)**	36/59 (61%)†

*Among the children < 1 year of age, 28 of the 96 cases reported (29%) were lab confirmed
**51 (36%) of those unvaccinated were < 1 year of age, and would not normally have received MMR.
† 17% were aged >15 months and would have been eligible for MMR

Transmission patterns (cases linked to contact with other cases) were rarely identified and recognised outbreaks were only rarely reported; for instance in 2004 HSE South reported seven linked cases during June-August 2004; HSE North West reported 12 linked cases in July 2004; and HSE North East reported three linked cases in June 2004.

2.2 Rubella in Ireland

Rubella has been a notifiable disease in Ireland since 1948. To prevent congenital rubella infection a rubella-only vaccine was introduced in 1971 for female children 11-12 years of age. In 1988 MMR vaccine was introduced for all children (15 months – 2 years initially) and for females aged 10-14 years. In 1992 MMR was also recommended for boys 10-14 years of age. The measles rubella campaign in 1995 was directed at all children 5-12 years of age. The impact of this programme is evident with the low number of cases now reported (Figure 2.7).

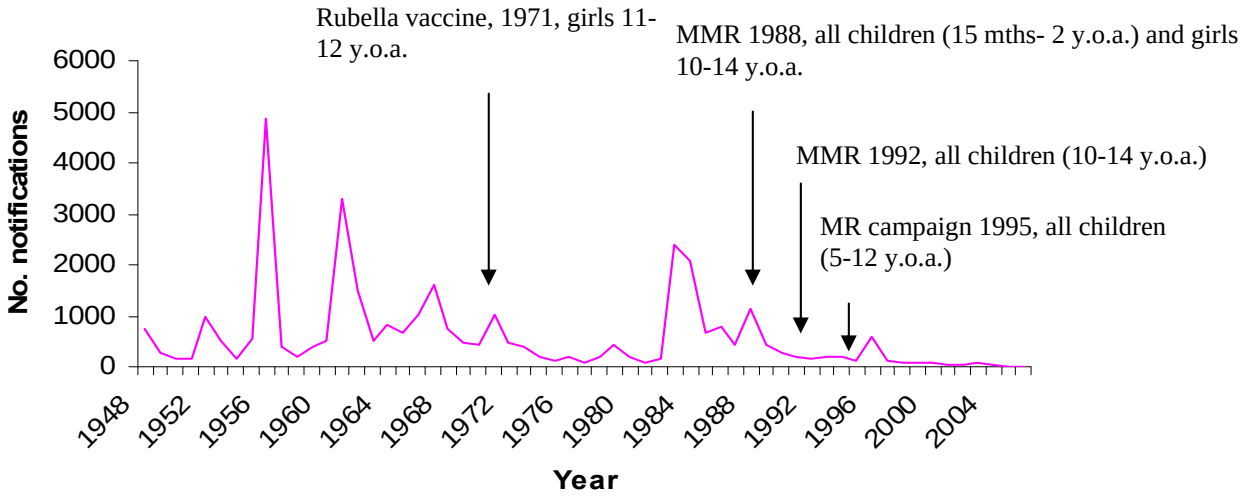


Figure 2.7. Rubella notifications Ireland 1948-2006* and rubella vaccine usage
**2006 data are provisional, data extracted from CIDR on 25/03/2007*

Rubella cases reported 1982-2006*

The decline in rubella notifications since the introduction of vaccine is dramatic although there have been a number of large outbreaks during this time period. The most recent outbreaks occurred in 1996 with 602 cases reported. Since then the number of notifications has fallen further, with only 17 and 14 cases reported in 2005 and 2006 respectively (2006 provisional data) (Figure 2.8).

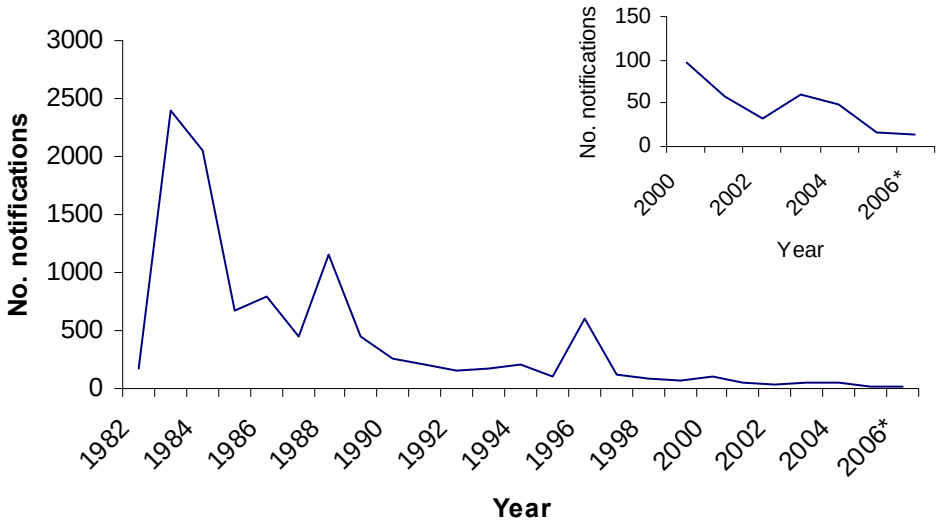


Figure 2.8. Rubella cases reported 1982-2006*
*2006 data are provisional, data extracted from CIDR on 25/03/2007

Rubella cases by age group 2000-2006*

Three hundred and twenty six cases of rubella were reported between 2000 and 2006. Most (65%) of cases reported have been in the 0-4 year age group (Figure 2.9).

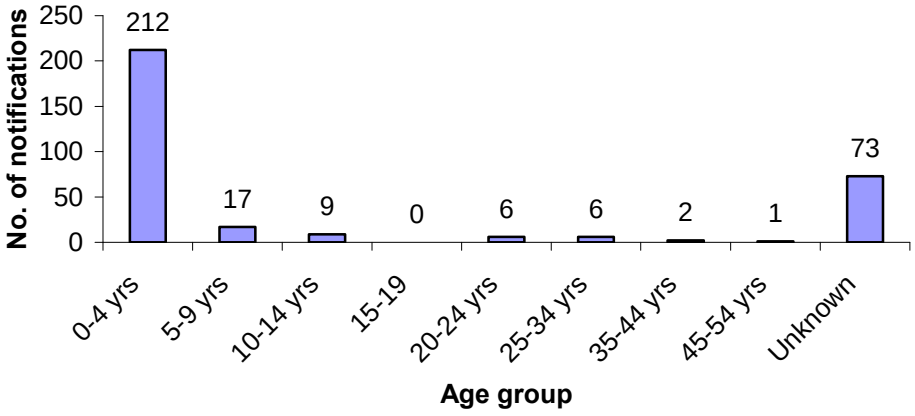


Figure 2.9. Rubella cases by age group 2000-2006* (n= 326).
**2006 data are provisional, data extracted from CIDR on 25/03/2007*

Twenty-two percent of all cases during the 2000-2006 time period were of unknown age group. However, reporting of age group has improved in recent years. Of the 73 cases with unknown age group, 68 cases (93%) were reported in 2000. In that year 70% of cases (68/97) were reported with no age information (Figure 2.10). It was only

after HPSC became responsible for notification data in July 2000, that age data became available at a national level. Prior to July 2000 only aggregate data was reported to the Department of Health and Children, and no age data was available for rubella notifications reported January-June 2000.

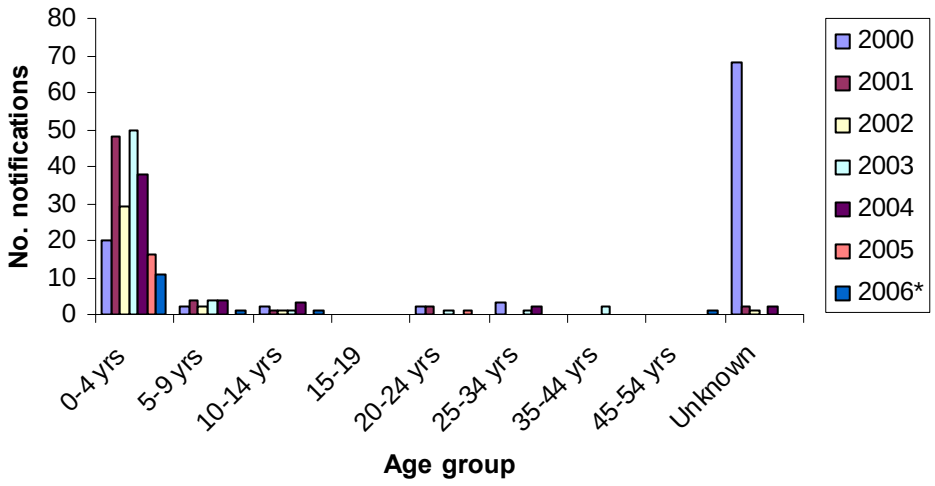


Figure 2.10. Rubella cases by age group and year (2000-2006*)
**2006 data are provisional, data extracted from CIDR on 25/03/2007*

2.2.1 Rubella cases laboratory confirmation

Laboratory confirmations are rare: in 2004 8% of cases were laboratory confirmed; none were laboratory confirmed in 2005; and one case in 2006 was laboratory confirmed. There was one case of congenital rubella syndrome in Ireland in 2004, born to a non-national mother with a history of rubella compatible illness during pregnancy (see following section – section 2.2.2).

Rubella sero-epidemiology

The European Sero-Epidemiology Network 2 study (ESEN2)[14,15] found relatively high levels of sero-immunity to rubella in most age groups except the very youngest (< 4 years). This coincides with timing of MMR_2 given at 4-5 years of age (Figure 2.11).

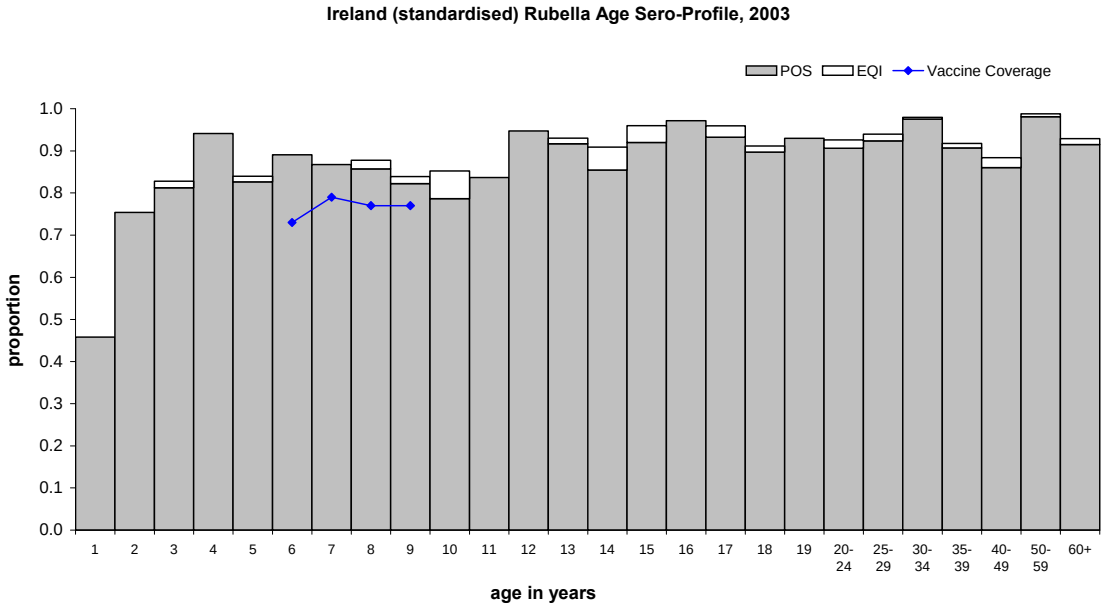


Figure 2.11. ESEN 2 study [14,15] –rubella seroimmunity among Irish population 2002

However, a small percentage of women of childbearing age were found to be non-immune at a cut-off of 4 IU/ml, with an even larger proportion non-immune at the higher cut-off of 10 IU/ml, putting them at risk of rubella infection during pregnancy and the risk of having a child with congenital rubella infection congenital rubella syndrome (Tables 2.3 and 2.4).

Table 2.3. Rubella seronegative samples (<4IU/ml) in children 2-14 years and young adults (15-39 years old) by gender 2002

	Age group 2-14 years				Age group 15-39 years		
	Overall	**2-4 years**	**5-9 years**	**10-14 years**	**Overall**	**Males**	**Females**
All	12.9%	15.5%	13.8%	10.2%	5.6%	9.2%	3.6%

Table 2.4. Percentage of women of childbearing age without protective immunity (defined as a titre of <10IU/ml) for rubella by age group

	Overall percentage	Percentage by age group		
	15-39 years	**15-19 years**	**20-29 years**	**30-39 years**
All	7.6%	10.7%	6.2%	7.4%

2.2.2 CRS incidence in Ireland

CRS reporting (as a distinct entity) only became notifiable on January 1st 2004. Prior to this, CRS cases were identified through other surveillance systems (British Paediatric Surveillance Unit (BPSU), or though European Surveillance of Congenital Anomalies (EUROCAT)). EUROCAT covers three regions in Ireland - HSE East, HSE South and HSE West (Galway).

Both BPSU and EUROCAT were contacted for information on historical CRS incidence in Ireland. Four cases were known to BPSU (since 1989) and two cases in EUROCAT (plus most recent case reported).

CRS cases reported through BPSU (1989-2005)

There were four confirmed cases reported, one born in 1989, and two in 1996 and one in 2004. An additional non-confirmed case was reported in 2001 (no further data available, but further information requested) (Table 2.5).

Table 2.5. Irish CRS cases reported to BPSU (1989-2005)

Year	Status	Mother - nationality	Immunisation status	Date infection	CRS manifestations
1989	Confirmed	Unknown	Unknown	Unknown	Unknown
1996*	Confirmed	Non-national – in Ireland 1-2 years at time of delivery	Unknown	In 2nd month	Hearing, opthalmic, neurological problems identified in 1st month of life
1996	Confirmed	Unknown	Unknown	Unknown	Unknown
2001	status unknown	Unknown	Unknown	Unknown	? stillborn
2004	Confirmed	Non-national	Not vaccinated	4th-5th month	Microcephaly Deafness Cranial calcifications

Most recent CRS case Ireland (2004)

The most recent case was a child born to non-national mother in 2004. The mother reported a history of fever illness and arthralgia in the 4-5th month of pregnancy. She had never received rubella vaccine. The child was born with bilateral congenital deafness, microcephaly and cranial calcifications. (source: HPSC)

3. REVIEW IRISH MMR IMMUNISATION PROGRAMME

Immunisation is the most effective way to prevent and control measles outbreaks. For successful measles control, immunisation of at least 95% of susceptible individuals with a two-dose schedule is required. In the current schedule, the first dose should be given at 12-15 months and the second dose at four to five years of age.

The age of administering and the target groups for receiving rubella and measles vaccine has varied since these vaccines were first introduced in Ireland (Table 2.1).

Measuring MMR uptake

Each HSE area maintains a childhood immunisation register. Each HSE area provides HPSC with immunisation uptake data on a quarterly basis. These uptake data related to all children on the HSE area databases who reached their first or second birthday (uptake at 12 and 24 months, respectively) in that quarter. MMR uptake (MMR_1) is measured at 24 months only. Data on the number of children eligible for immunisation in each cohort, the number immunised and the percentage immunised are provided. However there is no unique identifier and no linkage between the different databases to ensure there is no duplication between areas. There is no national data available to calculate national MMR_2 uptake.

HPSC collates and analyses these data and produces quarterly reports which are available on the HPSC website and distributed electronically to HSE area immunisation staff. Annual immunisation uptake rates presented in this report are calculated by collating the quarterly data provided by the HSE areas.[16]

Since mid 2006, each HSE area has sent immunisation uptake data by CCA/LHO area. This data is currently being routinely analysed to assess comparability with HSE area aggregate reports. Clarification is being sought on identified discrepancies. It is anticipated that from Q1 2007 CCA/LHO data for all regions will be available on the HPSC website. This data is already available to the HSE areas and is sent out via email.

MMR_1 immunisation process

Once a child reaches 12 months of age parents receive an invitation from their LHO to bring their child to their general practitioner for the first dose of MMR. The GP completes a vaccine return form that is used for the compilation of uptake statistics and payment.

Immunisation uptake – 1999- Q4 2006

Since the national collection of uptake data commenced in 1999 Ireland has never reported a 95% national uptake of a measles containing vaccine. MMR_1 uptake has varied from 69% in Q4 2001 to 88% Q4 2005 (the latter probably an overestimate, in this quarter HSE East did not submit data on MMR uptake).[16]

The most recent report on immunisation uptake in Ireland during the fourth quarter of 2006 estimated national uptake of the first dose of MMR at 24 months to be 86%, ranging from 82-94% between HSE areas. This is an improvement from the MMR uptake reported in Q4 2001 (69%) but still lags behind the uptake necessary to prevent outbreaks. The difference in uptake of the MMR in contrast to other childhood vaccinations is apparent throughout this time frame, but was particularly marked during 2001. The marked fall off in MMR uptake evident in that year (Figure 3.1) can be directly attributed to unsubstantiated media scares about an alleged association between MMR and inflammatory bowel disease and autism following publication of an article in the Lancet in 1998.[17] This report generated substantial media coverage and a loss of confidence in MMR in particular, but also in the general immunisation programme. This paper was found to be flawed and the lead author was subsequently found to have an undeclared conflict of interest. The other authors of the paper subsequently retracted their interpretation in this paper stating that "no causal link was established between MMR vaccine and autism as the data were insufficient".[18]

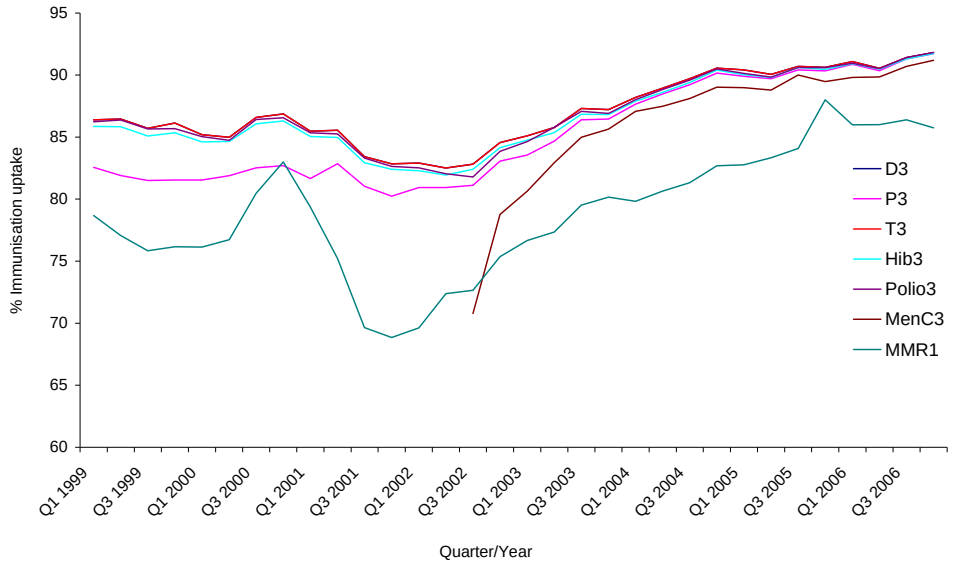


Figure 3.1. National quarterly immunisation uptake rates for primary vaccines at 24 months (Q1, 1999 – Q4 2006)

*The Q4 2005 MMR_1 figure is based on data from 7 of the 8 HSE areas as HSE East were unable to provide MMR_1 uptake data in Q4-2005

**The Q1 2006 MMR_1 includes HSE East MMR_1 Q1-2006 uptake figure, which is an estimate only (due to technical problems with extracting MMR_1 data from HSE East database)

Vaccination uptake rates vary between HSE areas. The impact of the low uptake in HSE East (former ERHA) has been reflected in the high incidence rates reported in this region (Figure 3.2).

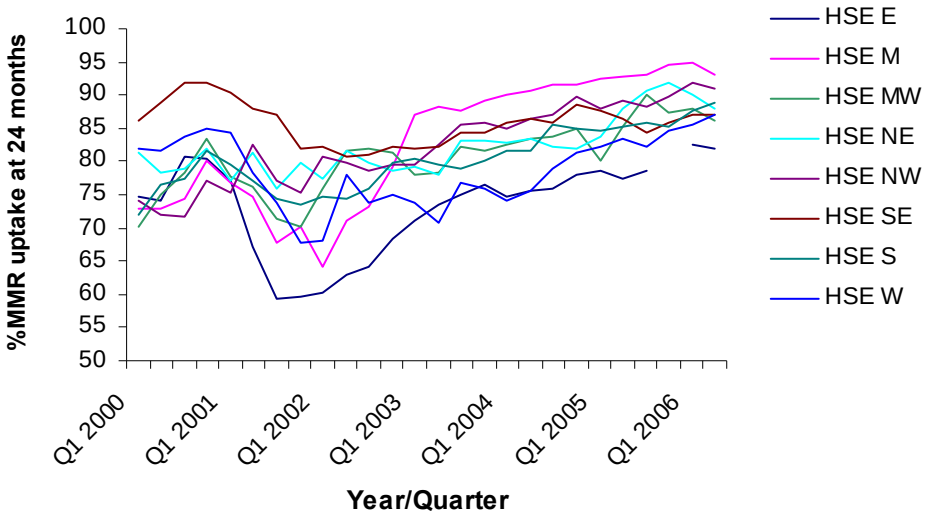


Figure 3.2. Quarterly MMR vaccination uptake at 24 months, by quarter, year and HSE area, Q1 2000-Q4 2006

Overall, the average MMR uptake rate for 24-month-old children from 1999-2006 was 79% nationally (range 73%-86%). MMR uptake was consistently lowest in HSE East (with an average of 74% for the seven years) and overall highest was in HSE South East, (average 86%). In no area did the average annual MMR uptake reach the 95% level recommended (Table 3.1).

Table 3.1. MMR uptake among children at 24 months of age by year and HSE Area (% eligible population) by year, 1999-2006

	HSE area/Health Board								
Year	**HSE E**	**HSE M**	**HSE MW**	**HSE NE**	**HSE NW**	**HSE SE**	**HSE S**	**HSE W**	**ROI**
1999	77	70	73	79	75	87	73	83	**77**
2000	78	75	77	80	74	90	77	83	**79**
2001	66	72	74	79	77	87	76	76	**73**
2002	64	72	76	79	80	82	76	74	**73**
2003	74	88	80	81	83	83	80	74	**78**
2004	76	91	84	83	87	87	83	78	**81**
2005	78	93	86	89	89	86	85	83	**84**
2006	82	94	88	89	91	87	88	86	**86**
Average	74	82	80	82	82	86	80	80	**79**

These uptake rates are insufficient to prevent measles virus transmission. Ireland needs to reach a minimum and consistent 95% uptake rate of two doses of MMR to meet WHO targets.

MMR_2 uptake data lacking nationally

As previously mentioned, there is no national data available with regard to MMR_2 uptake among school children at 4-5 years of age. The immunisation systems in place were not designed to accommodate the 2nd dose of MMR in most areas. Therefore, immunisation records have usually been stored in hard copy (notebooks, registers, or other paper records) at the CCA office or archived. These records are frequently not easily accessible to CCA/LHO staff. Searching for children's records is time consuming and manpower intensive. To facilitate record retrieval some HSE areas have scanned this data into computerised databases using software designed for this purpose. What proportions of records in these areas have been scanned is unknown.

Immunisation records should be accessible for health services so that timely identification and follow-up of non-immune, or incompletely vaccinated, children can be achieved.

Without national data on MMR_2 uptake it is not possible to assess Ireland's performance in relation to achieving WHO targets of 95% uptake of two doses of MMR.

Parent-held record of child's immunisations

There is no nationally agreed or implemented system whereby all parents are expected or encouraged to hold a parent-held immunisation record for their child. Some GPs/HSE areas routinely provide parents with a record of their child's immunisations, others do not. Many parents have no personal record of what immunisations their child has received.

Parents should have a record of vaccines administered to their child provided in a standardised format by the vaccinator.

Monitoring immunisation uptake in childcare facilities/schools

There is no requirement for schools or childcare services to monitor or record whether the children in their care have been appropriately immunised. This could be achieved if parents had easy access to their children's immunisation records and were asked to provide this information to the schools. In the absence of a national agreement for day care facilities/schools to do this it is difficult for HSE areas to rapidly identify susceptible children for immunisation or exclusion when measles cases occur in that facility. Informal discussions have taken place between National Immunisation Office staff with Department of Education staff on the feasibility of schools maintaining a record of enrolled children's vaccination status but there is no agreement that this will be implemented. Schools do routinely provide the lists of enrolled children in specific classes upon request from HSE (for the purpose of vaccination programmes).

Ideally all children in day care centres, nurseries and schools should have age appropriate proof of immunisation recorded/obtained at the beginning of each school year so that children who are susceptible can be rapidly identified. The authority responsible for obtaining this information has not been agreed. The Committee

recommended that this should be discussed between Department of Education and Department of Health and Children.

Implementing school-based programmes (usually MMR_2) and measuring immunisation uptake

MMR at 4-5 years is administered as a school-based programme in most Local Health Offices (LHOs) although in some areas it may be implemented solely (HSE NW) or partly (HSE NE, HSE E) by the GPs.

The school-based programmes are managed by the Community Medical Services under the direction of the Principal Medical Officer (PMO). However due to staff recruitment issues these programmes have not been continuous in these areas. There are currently no school-based MMR programmes in Donegal, Leitrim, Sligo, Cavan, Monaghan, Louth, Meath and parts of North Dublin (National Immunisation Office 2007) and GPs provide school boosters in these areas.

As stated, there is no national data available with regard to MMR uptake among children at 4-5 year age group. A few HSE areas have systems in place for collating this data.

Obtaining high immunisation coverage through school-based programmes – experience of HSE Midlands

School-based immunisation programmes can achieve excellent results if resourced. A report from HSE Midlands has clearly identified that school-based clinics, and active follow-up of children can achieve 95% coverage of vaccine uptake.[19] This was achieved through the allocation of dedicated resources to the school immunisation programme (including two Public Health Nurses (PHN), one Senior Medical Officer (SMO) and one WTE Clerical Officer).

The activities included:

- Obtaining names and addresses of all children in targeted classes with the name of the class teacher.
    - Information and letters of invitation were distributed and included the following;
        - A letter of invitation for vaccination with a specific appointment.
        - A copy of the relevant information leaflet(s), as revised in summer 2001.
        - Consent Form(s) for relevant vaccination(s).
- Scheduling of dates and confirming dates with schools
- Attending school on pre-agreed date and informing parents about vaccination process
- Clinics held

During the clinics the SMO assessed the child's well being, suitability for immunisation, responded to any queries from parents, and signed the vaccine record section of the consent form if the child was considered fit for vaccination. This, in

effect, acted as a prescription, authorising subsequent administration of the vaccine by one of the PHNs. The PHNs administered the MMR and DTaP/IPV vaccines.

The teams undertook active follow-up of children who did not avail of the school-based clinics. Children were offered vaccination at mop-up clinics. Siblings of the children identified to be due vaccines were also accommodated and offered vaccines.

Table 3.2 presents the uptake of vaccines in the 2001-2002 programme.

Table 3.2. School immunisation programme Longford/Westmeath Community Care Area 2001-2002

Number of schools = 115					
	Junior Infants DTaP/IPV	**Junior Infants MMR**	**Senior Infants DTaP/IPV**	**5th Class BCG**	**6th Class MMR**
% Uptake	95.3%	95.6%	95.2%	99.5%	94.04%

HSE Midlands undertook additional detailed reviews of MMR uptake for subsequent years, 2003-2004 and 2005-2006. In both time periods >95% MMR uptake was achieved among most cohorts (Tables 3.3 and 3.4).

Table 3.3. Vaccine specific coverage by school class, 2003-2004 HSE Midlands

CCA /LHO area	**Vaccine**	**Jnr. Infant**	**Snr. infant**	**3rd class**	**4th Class**	**5th Class**	**6th Class**
Co. Longford							
	MMR	97.5%	93.2%	96.4%	97.0%	96.2%	92.3%
Co. Westmeath							
Mullingar Sector	MMR	97.6%					
Athlone Sector	MMR	94.5%					

Table 3.4. Vaccine specific coverage by school class, 2005-2006 HSE Midlands

CCA/LHO area	**Vaccine**	**Junior Infants**
Co. Longford		
	MMR	97.7%
Co. Westmeath		
Mullingar Sector	MMR	95.4%
Athlone Sector	MMR	97.0 %

These reported uptake rates are very good and demonstrate the acceptability to parents of school-based vaccination programmes and the feasibility of delivering such a service through the schools and obtaining high uptake. It is important to mention that this required dedicated resources.

What is needed to monitor and achieve high coverage;

At PCCC level:

Priority should be given to resourcing the development of a national immunisation information system. A proposal for this has already been prepared and submitted to HSE by the NIO.

GP practice staff should send in their immunisation returns to the local immunisation office so that the data can be entered into the Child Health immunisation registers and areas/practices with low uptake identified rapidly.

Administrative staff should enter immunisation returns into Child Health immunisation registers as soon as possible (rapidly) so that data on the system accurately reflects uptake in their area.

2nd dose of MMR and booster DTaP/Td should also be routinely returned and entered into the Child Health Immunisation registers.

Defaulters for MMR should be identified and followed up by CCA/LHO and GPs.

School-based programmes can achieve excellent MMR uptake and should be appropriately resourced.

At Departments of Public Health (HSE Area) level:

Departments already review quarterly MMR_1 uptake for children at 24 months of age. This data is sent to HPSC (by HSE area and CCA/LHO). MMR_2 uptake for children at 4-5 years is not routinely available for Departments of Public Health but is required for local information and action.

Capacity to systematically collate and review MMR_2 uptake is required at HSE area level. Information systems to support this are needed locally and should be developed. This data should then be extracted and forwarded to HPSC at regular intervals.

At HPSC:

Quarterly analysis of MMR_1 uptake for children at 24 months of age is already done by HSE area and CCA/LHO area.

Analysis of MMR_1 uptake by CCA/LHO area has identified areas with particularly low immunisation coverage. These areas should be targeted with specific appropriate local interventions to improve immunisation uptake.

MMR_2 uptake analysis by HSE area and CCA/LHO is required nationally. This data is currently not provided to HPSC. Monitoring this data nationally is crucial to the measles elimination strategy.

Improving communications – all levels:

Rapid response to media scares is required and should be coordinated in close cooperation between NIO/HSE/HPSC.

Appropriate methods of communicating with health professionals and general public are already in development by NIO. On going work will be needed in this area.

Training – all levels

Health professionals will require additional training to improve their own knowledge of immunisation and immunisation activities, and their ability to communicate effectively with parents and the general public.

Administrators in HSE working in immunisation will also require training to optimise their skills in their area of work.

4. REVIEW OF SURVEILLANCE CAPACITY

This section provides information on current surveillance, investigation and response activity since 2002 when guidelines were developed for control of measles and recommendations were made on improving surveillance.

Effective surveillance is required in order to:
- Detect cases and the source of infection rapidly so that timely control measures can be implemented
- Detect resurgence of indigenous transmission
- Detect importations of measles
- Monitor serious complications of measles infection (death, encephalitis, seizures, and pneumonia).

Requirements for an effective surveillance system are:
- Clinicians promptly notify the Medical Officer of Health of each suspect measles case
- Standard sensitive case definitions are applied (Section – Expert guidance)
- Appropriate control measures are rapidly implemented for each case (as required)
- Rapid reporting of all cases to HPSC
- Public Health should investigate each suspect case and confirm the diagnosis
- Rapid laboratory diagnosis
- Prompt investigation of contacts
- Complete and timely collection of enhanced data is obtained and reported on each case
- Efforts should be made to find additional cases and identify their contacts.

The following sections identify what is recommended as best practice, the current situation and specifies deficits in the current system.

4.1 Public Health surveillance

4.1.1 Responsibility for measles case(s) surveillance, investigation and control

The responsibility for infectious disease surveillance and control activity lies within the HSE services, Directorate of Population Health. In the new HSE structures vaccination programmes lie within the responsibility of PCCC. Therefore, surveillance and control activities straddle two HSE directorates and will require close collaboration between staff going into the future. Additionally, clinical care is provided both through the private and public sector.

4.1.1.1 National surveillance

Measles is a notifiable disease since 1948. Measles is one of the priority diseases selected by the European Network Committee for European Surveillance, (Decision 2119/98/EC and Decision 2000/96/EC). The WHO has also targeted this disease for elimination in Europe by the year 2010. Case definitions for measles were detailed in

the Infectious Diseases (Amendment) (No. 3) Regulations 2003, (S.I. No. 707 of 2003).[20, 21]

4.1.1.2 International surveillance

Ireland is required to report measles to WHO and ECDC. This is done by HPSC at monthly intervals.

To standardise reporting of measles cases ECDC have recommended that one standard case definition be adopted and used for reporting to ECDC. Following consultation with member states during 2006, the ECDC Advisory Forum has proposed a measles case definition. The proposed case definition is more sensitive than that used in Ireland since 2004. It is presented here as a working case definition until it is endorsed by the EU Commission in 2007.

ECDC measles case definition

Clinical criteria:

Any person with:

Fever, **and**

Maculo-papular rash, **and** at least one of the following three:

Cough, coryza or conjunctivitis

Laboratory criteria:

At least one of the following four:

- Isolation of measles virus from a clinical specimen
- Detection of measles virus nucleic acid in a clinical specimen
- Measles virus specific antibody response in serum or saliva
- Detection of measles virus antigen by DFA in a clinical specimen using measles specific monoclonal antibodies

Laboratory results need to be interpreted according to the vaccination status

Epidemiological criteria:

An epidemiological link by human-to-human transmission

Case classification:

A. Possible case

Any person meeting the clinical criteria

B. Probable case

Any person meeting the clinical criteria and with an epidemiological link

C. Confirmed case

Any person not recently vaccinated and meeting the clinical and the laboratory criteria

For Ireland to meet its international reporting commitment HPSC will report both probable and confirmed cases to ECDC. Comparisons between EU countries will then be more meaningful.

4.2 Case and outbreak investigation – recommendations and situation

4.2.1 Case investigation

Investigation and control measures should be initiated with the identification of a single case clinically compatible with measles. Investigation and management of cases, and their contacts, should be completed within 48 hours of rash onset, as per WHO recommendations.

Comment: this is dependent on timely reporting of any suspect case, Departments of Public Health report that this is highly variable. Capacity of local Departments to investigate is dependent on local resources and demands.

Although it is reasonable to delay major control activities, such as vaccinating an entire school, pending the return of laboratory results, the results should be obtained as quickly as possible (ideally within one working day on receipt at the laboratory).

Accurate and complete immunisation history should be obtained on all confirmed cases or highly suspect cases if there is a delay in laboratory diagnosis. Written records or immunisation registry/database information is required as acceptable evidence of immunisation status.

Comment: Due to lack of national immunisation database and parent/patient-held records obtaining validated immunisation history is difficult and rarely achieved among older children/adults.

Surveillance information collected

The following data are epidemiologically important and should be collected in the course of case investigation, using an enhanced surveillance form (see Appendix for details and enhanced form):

- Demographic information
- Clinical details
- Laboratory information
- Case classification
- Vaccination status
- Risk factors for disease including contact with a case or an outbreak
- Travel history (in 8-17 days before rash onset to determine if imported case)
- Setting (i.e. sporadic case or outbreak related)
- Relevant dates of notification, investigation etc.
- Details on vulnerable contacts and contact details for local use

Comment: Complete data is rarely obtained. Increased efforts are required during elimination phase (Table 4.1).

Table 4.1. Completeness of reporting for 2005 measles notifications (n=93)

Data item reported	Completeness of reporting
Case classification	94%
Age	100%
Gender	100%
Laboratory data results provided	26%
Proportion of lab results confirming measles	46%
Vaccination data	63%
Hospitalisation data	41%
Length of hospitalisation stay (among hospitalised)	40%
Measles complications reported	11%

4.2.2 Outbreak investigation and control – recommendations and situation

Outbreak investigation involves rapid investigation of suspect cases, confirming diagnosis of cases, investigation of contacts, ascertaining vaccination status and vaccinating susceptible individuals as required.

Activities for each case reported include:

History taking from case:
Full demographic and clinical details on all suspect cases, determination of vaccination status, identification of all contacts
Follow-up of all contacts
Organisation (and delivery if required) of vaccination activities
Follow-up of laboratory results
Reporting requirements locally, nationally and internationally

Sporadic cases require the above activities to be completed rapidly to out rule the possibility of outbreaks occurring.

Each measles notification requires immediate investigation by Public Health to confirm the diagnosis, implement control activities and prevent ongoing transmission.

Comment: In small outbreaks GPs frequently administer the vaccine. In large school-based or crèche facilities SMOs in the community have in the past usually organised vaccine clinics. In the new HSE structures, this working arrangement will need to be agreed between PCCC and Population Health prior to any outbreaks occurring. Lack of agreement may cause unnecessary delays in response and control measures being implemented.

Responding to and investigating measles notifications is time consuming and draws staff away from other ID and public health activities. When measles outbreaks occur (defined as any number of measles cases including one or more locally acquired cases) there is an immediate impact on Public Health departments. Investigating an outbreak requires many person-days of work as all the above activities are multiplied, and depend on the number of cases, contacts to be followed up etc.

During outbreak situations personnel are often transferred to the activity from other responsibilities in the HSE Departments of Public Health or LHO areas so adequate surge capacity is required. Therefore, they may only be involved in outbreak investigation for a few days before someone else replaces them. This turnover in personnel during the investigation may cause problems unless activities are organised so that the status of the investigation is documented at all times.

As the responsibility for infectious disease surveillance and control activity lies within two directorates response to a measles case and implementation of control activities will require close cooperation between these two directorates.

Analysis of resources required in recent measles outbreaks

As part of the situational analysis Departments of Public Health in each of the HSE areas were asked to try to estimate the costs (manpower and time) associated with the investigation and management associated with each measles case notification.

The time required to investigate, verify and follow-up information, communicate advice and recommendations ranged from between 3-10 hours per case (sporadic case) to 39 full-time hours (during outbreak situation). Additional time for communications to the GPs, clinicians, community and media is often required but was difficult to quantify.

Table 4.2. Time involved in each measles case notified.

Staff grades involved	Initial notification*	Patient contact†	Contact tracing‡	Outbreak investigation and management
SPHM, SMO, Nurse, SpR, SS, Admin/clerical support	15-60 min	30 min-5 hours	2-5 hours	~ 2 days per case†† in large complex outbreaks may involve most staff for 1-2 weeks

* *verification, additional information*
† *enhanced data, follow-up of data*
‡ *depends on number of contacts, verbal plus written communication to contacts, GPs, schools, hospitals*
†† *during outbreak involving 7 cases associated with an institution during 2004, 4 full days were spent by 3 staff (total 12 days), plus 0.5-1 day for the surveillance scientist (SS), to manage the outbreak*

One HSE area (HSE South East) estimated costs associated with an outbreak that occurred during 2000 (105 measles cases reported). They estimated that the investigation, management and health care costs amounted to approximately £143,430 (€182,118) (minimum) with an average cost per measles case reported of £1,366 (€1,734).[22]

Status of surveillance performance in Ireland

1. Rapid investigation of all suspect sporadic cases

Recommendation: All reports of suspected measles cases should be investigated immediately by the public health department/local health office area.

Status: The timeliness of reporting suspect cases varies and response by Departments of Public Health also varies and is dependent on local clinical awareness and resources respectively. Increased emphasis on this activity will be required as elimination activities progress.

2. Collection of enhanced data (see Appendix- Measles enhanced questionnaire)

Recommendation: The measles enhanced surveillance form is recommended for use to collect demographic and epidemiological data during case investigation. Essential components of case investigation include establishing a diagnosis of measles and adequate history taking to identify contacts and identify possible sources of infection.

Comment: The completeness of data collected and the timeliness of reporting is dependent on availability of local resources

3. Confirming measles diagnosis

Necessary clinical information must be obtained to establish whether or not a reported case meets the clinical case definition. If the case was diagnosed within three days of onset of rash, there should be appropriate follow-up to establish duration of rash (measles rashes typically last three days) and obtain samples for laboratory confirmation.

Comment: This activity is time intensive and requires contact with patient, carer and clinician(s).

4. Diagnostic testing (See Algorithms in Expert guidance section)

Measles specific IgM antibody is present in about 80% of cases at the time of the rash onset and can still be detected up to 60 days later. Although its presence confirms measles, a negative result does not out rule the diagnosis. If measles is still suspected and the sample was collected within 72 hours of rash development, the IgM testing should be repeated.

Oral fluid samples, collected using a foam swab, provide a non-invasive method for the confirmation of measles infection. Specimens should be obtained from rash onset to eight weeks following the appearance of the rash. Samples early on in illness may result in false negative results and should be repeated if clinical suspicion is high.

Occasionally, false positives can occur and as with any laboratory test, it is important to consider the epidemiological and clinical information together with the laboratory report.

Alternatively, measles infection can be confirmed serologically by demonstrating seroconversion to measles IgG or a significant rise in antibody titre (IgG), with the

first (acute) sample taken within seven days of rash onset and the second (convalescent) sample taken two to three months later.

The oral fluid samples described above can be used for molecular diagnosis or epidemiological investigation (described below).

Alternatively, specimens (nasopharyngeal aspirates, throat swabs using viral transport media maintained at a temperature of 4^{o}C) should be collected in the first five days (preferably within three days of rash onset) and sent to the National Virus Reference Laboratory (NVRL), within 24 hours of collection. These samples can be used to culture the measles virus and for molecular investigation.

If SSPE is suspected the NVRL requests that they are contacted to discuss which samples ought to be collected.

Comment: Oral fluid sampling is non-invasive and more acceptable to patients and clinicians. Adequate supplies of oral fluid sample kits are required to ensure diagnostic testing is done. A minority of cases were laboratory confirmed during 2003-2005.

4.3 Laboratory surveillance

The NVRL is the main laboratory for all surveillance and diagnostic measles testing in Ireland. Some regional laboratories may undertake their own testing.

As reported earlier, a minority of cases have had laboratory data (whether sample sent to laboratory and outcome) provided to HPSC. A minority of cases reported in the last few years have been laboratory confirmed. This aspect of surveillance needs to be improved.

Laboratory confirmation is essential for all outbreaks and all sporadic cases of measles. In an area of low incidence, most cases that meet the clinical case definition will not turn out to be measles. Even in outbreaks, laboratory confirmation should be obtained on as many cases as possible. Once community awareness is increased, many cases of febrile rash illness may be reported as suspected measles, and the magnitude of the outbreak may be exaggerated, if these cases are included in the absence of laboratory confirmation. This is particularly important as the outbreak is ending; at that point, laboratory confirmation should be sought on all suspected cases.

The occurrence of measles-like illness in recently vaccinated persons can pose particular difficulties in the outbreak setting. Ten percent of recipients of measles-containing vaccine may develop fever and a rash approximately one week after vaccination and results in production of IgM antibody that cannot be distinguished from natural infection. A positive measles IgM test cannot be used to confirm the diagnosis of measles in persons with measles-like illness who received measles vaccine 6-45 days before onset of rash. A negative test would exclude the diagnosis.

Persons with measles-like illness who received the vaccine 6-45 days before onset of rash should be classified as confirmed cases of measles only if:

they meet the clinical case definition and there is identification of wild virus.

For persons receiving vaccine 6-14 days prior to rash onset, specimens for viral isolation should be obtained in addition to serological testing (see “Laboratory testing”); isolation of wild measles virus would allow confirmation of the case.

It is recommended that case investigation and vaccination of susceptible household contacts should not be delayed pending the return of laboratory results.

The NVRL is the only laboratory in the country able to undertake molecular testing of measles samples as part of surveillance activities. Molecular epidemiological surveillance is important to determine:

the origin of the virus, which viral strains are circulating and distinguish between vaccine virus and wild strains.

Comment: The experience of the NVRL has been that they are rarely sent additional (non serum or oral fluid) samples for measles diagnosis.

Comment: Prior to 2007 NVRL was unable to do molecular epidemiological surveillance on the samples received. From 2007 onwards they will be routinely undertaking this testing.

4.4 Performance indicators

WHO has identified a number of performance indicators that are used to assess quality of measles elimination programmes. Ireland's status is compared with WHO targets in Table 4.3.

Table 4.3. Measles programme Performance Indicators compared with WHO recommended target

Performance indicators	***WHO Target***	***Ireland's status w.r.t. target***
Percentage of measles cases notified ≤ 48 hours after onset of rash	≥ 80%	Measles form captures dates of rash onset and notification - data incomplete but will be analysed
Percentage of measles cases investigated ≤ 48 hours after notification	≥ 80%	Measles form captures dates of rash onset, notification, and investigation - data incomplete but will be analysed
Percentage of cases with adequate specimen and laboratory results	≥ 80%	Measles form captures data – but only 26% cases had lab results provided *
Percentage of cases with laboratory results within 7 days of detection	≥ 80%	This data is not currently measured but data can be extracted using CIDR
Percentage of cases with specimens sent for virus isolation	≥ 80%	Measles form captures data – but only 26% cases had lab results provided *
Percentage of confirmed cases with sources of infection identified	≥ 80%	Measles form seeks epidemiological link data, this data is usually incomplete but will be analysed
Percentage of febrile rash clusters investigated	100 %	Not known – CIDR could be used to catch information on 'rash outbreaks' in future
Validated national coverage for 1st and 2nd dose measles vaccine	> 95 %	1st dose validated 86% (Q4 2006)
Coverage of 1st and 2nd dose of measles vaccine in all areas	> 90%	Coverage data currently only available for 1st dose - was 86% in Q4 2006

*2005 reporting

4.5 Outcome indicators

Outcome indicators are additional measures that are used and recommended by WHO for countries involved in measles and rubella elimination. The recommended outcomes indicators are detailed in Table 4.4 and Table 4.5.

Table 4.4. WHO Measles outcome indicators[8]

Approaching measles elimination and prevention of CRI (Stage IIIb)	***Target***	***Ireland's status w.r.t. target***
Incidence of measles	< 1 per 1 000 000 population	2.4 per 100 000 (2005)
Susceptibility of profile needed for interruption of indigenous measles transmission	Reproductive rate (R) <1	Susceptibility estimated to exceed WHO targets in children* (based on ESEN2 study)
Size of measles outbreaks and number of generations	Reflection of effective reproductive number (R) and size of outbreaks and generations of spread	Systems in place to collect information (CIDR) but data incomplete
Measles virus genotype distribution	Should reflect identified source of (imported) cases and chain of transmission	Not currently available but will be in future (NVRL)

* WHO age specific targets[23]

Age group	WHO target susceptibility
2±4 years	<15%
5±9 years	< 10%
10±19 years	< 5%
20±39 years	< 5%
40 years	< 5%

Table 4.5. Rubella outcome indicators[8]

Approaching measles elimination and prevention of CRI (Stage IIIb)	***Target***	***Ireland's status w.r.t. target***
Annual reported incidence of laboratory confirmed rubella in countries with a comprehensive rubella immunisation programme	< 1 per 1 000 000 pop.	0.43 per 100 000 (2005*)*
Rubella susceptibility level among women of childbearing age	< 5%	7.6%†
Annual reported incidence of laboratory confirmed CRS	< 1 per 100 000 live births	< 1 per 100 000 live births

† ESEN2 study (Nardone A et al.)[15]

5. MEASLES VACCINE SUPPLY AND COLD CHAIN

5.1 MMR Supplies

As part of the national schedule, immunisation against measles is available in the MMR (measles, mumps and rubella) vaccine. Manufacturing companies are awarded tenders to supply MMR vaccine on an annual basis. Since January 1 2005 all MMR vaccines are stored under temperature-controlled conditions by the pharmaceutical distribution company contracted to provide the HSE National Cold Chain Delivery Service. This is managed by the HSE National Immunisation Office.

Orders for MMR vaccine are phoned, faxed or emailed on a monthly basis to the HSE National Cold Chain Delivery Service. Vaccines are then delivered directly to GP surgeries and LHOs. In an emergency additional MMR supplies can be delivered.

5.2 Recommended practices

5.2.1 Guidelines for the Management, Storage, Stock Control, Distribution and Disposal of MMR vaccine at Local Health Offices

There should be a designated person (ideally a community pharmacist) in each Local Health Office with overall responsibility to ensure the monitoring of the cold chain and the use of all vaccines including MMR in schools and clinics. This designated person should have responsibility with regard to the day-to-day receipt, storage and issue of vaccines and there should be a designated deputy to cover in times of absence. All significant difficulties should be brought to the attention of the designated person.

5.2.2 Receipt of Vaccines

On receipt of vaccines at LHOs, the order must be checked to verify that the vaccine received is that which was ordered. The person receiving the vaccines should make a physical count of the vaccines before signing the delivery docket. The special temperature print out which is included with each delivery of vaccines, should be read and recorded by the person receiving the order. If the temperature print out indicates that the vaccine was exposed to temperatures outside the range 2^{o}C to 8^{o}C during transport, the order should be refused and returned by the National Cold Chain Delivery Service. The number of doses and date received, the manufacturing company, batch numbers, expiry dates and invoice/delivery docket number should be recorded on a stock control system (manual or computer).

5.2.3 Managing Vaccine Stocks

Care should be taken to avoid over-ordering or stockpiling of vaccines. When vaccine stocks deplete to about 20% of the normal amount, supplies should be ordered from the National Cold Chain Delivery Service. A stock control system should be in place and rotation of stock should be monitored. Checks on stock levels and expiry dates of vaccines and time of removal of expired vaccines, should be made weekly or fortnightly depending on local usage. Vaccines nearing their expiry date should be

identified e.g. by tagging with a red sticker. Expired vaccines should be returned to the National Cold Chain Delivery Service at the next delivery.

5.2.4 Storage

- Vaccine refrigerators are recommended for storage of vaccines. Manufacturer's recommendations on storage should be observed. Vaccines must be kept at temperatures between 2-8^{o}C.
- Vaccines should be stored in their original packaging in the pharmaceutical refrigerator which should not be overfilled to allow air to circulate around the packages. They should not be stored on the shelves or storage compartments of the door of non-pharmaceutical refrigerators.
- The vaccine packs should not touch the sides or back of the refrigerator.
- Door opening should be kept to a minimum.
- A maximum/minimum thermometer should be used in refrigerators where vaccines are stored, irrespective of whether the refrigerator incorporates a temperature indicator dial. The maximum and minimum temperatures reached should be monitored and recorded daily. Temperature record logs are best kept close to the refrigerator for ease of reference. If temperatures are recorded outside the permitted range or if there is a breakdown in supply or equipment, the local community pharmacist or SMO should be contacted for further advice.
- The vaccine refrigerator should be cleaned every two months with a 1:10 solution of sodium hypochlorite.
- Care should be taken to ensure that the electricity supply to the vaccine refrigerator cannot be accidentally interrupted. This can be achieved by using a switchless socket or by placing cautionary notices on plugs and sockets.
- Food and drink must not be stored in refrigerators used for vaccines.

The MMR vaccine should be stored at temperatures of 2^{o}C to 8^{o}C at all times. If the temperature deviates outside this range the Chief Pharmacist in the National Immunisation Office should be contacted for further advice.

5.2.5 Transport of vaccines to GP Surgeries

As from January 1 2005 vaccines are transported directly to GP surgeries by the HSE National Cold Chain Delivery Service.

5.2.6 Transport of vaccines for use in clinics or schools

Vaccines should generally be collected from Local Health Office refrigerators on the day of use in clinics or schools. In exceptional circumstances, e.g. travelling distances involved, vaccines may be kept overnight by an SMO for use the following day. In these circumstances, the recommended procedure below should be strictly adhered to.

Recommended procedure when vaccines are returned to vaccine fridge within 6 hours of removal.

When vaccines are being transported to schools or clinics, cool-boxes with two freezer packs (ice-packs) should be used. Frozen ice-packs, should be left at room temperature for 15 to 20 minutes, should be wrapped with foil bubble wrap before placing in the cool-box in order to prevent vaccines adjacent to these packs from freezing. This procedure will keep vaccines at the required temperature of between 2^oC and 8^oC for six hours. A maximum/minimum thermometer or disposable "cold chain monitor" should be placed in the cool-box to monitor the temperature during transport of vaccines. If vaccines are unused and have been maintained between 2^oC and 8^oC they can be returned to the vaccine refrigerator on return to the Local Health Office.

Where spare freezer capacity is not available, a small freezer chest should be acquired in each Local Health Office to allow ice-packs which are not frozen to be replaced with pre-frozen ones when vaccines are being collected.

Recommended procedure when vaccines are kept overnight by SMO for use at a Clinic or School on the following day.

To keep vaccines overnight and maintain the integrity of the cold chain, two frozen ice-packs, which have been left at room temperature for 15 to 20 minutes, should be wrapped in foil bubble wrap and placed in the cool-box, together with a maximum/minimum thermometer. After 20 minutes the temperature should be checked and if the temperature has reached the required range of between 2^oC and 8^oC, the vaccines should be placed in the cool-box. The ice-packs should be replaced with pre-frozen ones approximately 6 hours later and the temperature should be checked again. The following morning, the ice-packs should again be replaced with the original ice-packs which have been frozen overnight in a domestic freezer. The vaccines may then be transported to the school and the temperature checked in the usual way at the beginning and end of the immunisation session.

5.2.6 Recording the Distribution of Vaccines

Senior Medical Officers should complete the *Senior Medical Officer Vaccine Request/Issue Form* when collecting vaccines for use in schools/clinics. Expiry dates should be checked before distribution of vaccines.

Disposal of Vaccines

Reconstituted vaccine must be used within the recommended period, varying from one to four hours, according to the manufacturer's instructions. Single dose containers are preferable as once opened, multi-dose vials must not be kept after the end of the session. Unused vaccine, spent or partly spent vials should be disposed of safely by incineration. Contaminated waste and spillage should be dealt with by heat sterilisation, incineration or chemical disinfection as appropriate.

Needles and Syringes

Needles and syringes must be securely stored and delivery and distribution recorded. Needles and syringes should be disposed of in sharps bins. Sharps bins must not be

left unattended in schools. Sharps bins should be collected regularly and be disposed of safely.

Audit

The procedures being followed should be audited regularly to ensure that they comply with written guidelines.

6. VACCINE SAFETY

The Irish Medicines Board (IMB) has a well established system in place to monitor vaccine safety. The following section explains the actions which are undertaken at a national level to ensure the safety of vaccines. These actions include surveillance and management of Adverse Events Following Immunisation (AEFI).

6.1 National legislation

Vaccines can be licenced for sale in Ireland by one of two different procedures. The first is a national procedure and applies to vaccines that can only be sold in Ireland following assessment of the product by the IMB. The second, a more commonly used procedure for the licencing of vaccines, is through the European Union (EU system). These systems of regulation apply not just to vaccines but also to all medicinal products.

The national medicines legislation can be divided into the following categories:

6.1.1 Licencing of medicinal products

Nationally authorised medicinal products including vaccines are licenced in accordance with the following legislation:

Medicinal Products (Prescription and Control of Supply) Regulations 1996-2002
Medicinal Products (Licencing and Sale) Regulations 1998
Medical Preparations (Labeling and Package Leaflet) Regulations 1993-1999
Medical Preparations (Advertising) Regulations 1993-1996

Such products can be identified as they carry a Product Authorisation (PA) number on their labels.

6.1.2 Licencing to Manufacture

Each Irish based manufacturer of medicinal products for human use is required to hold a Manufacturing Licence (ML) granted by the IMB in accordance with the Medical Preparations (Licencing of Manufacture) Regulations 1993-1996. There are no manufacturers of vaccines for human use in Ireland at this time.

6.2 European Legislation

At a European level the following legislation governs the licencing of vaccines for human use:

EU Council Regulation (EEC) No. 2309/93 of the 22nd July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the evaluation of medicinal products.
EU Council Directive 2001/83/EC of the European parliament and the Council of the 6th November 2001, on the Community Code relating to medicinal products for

human use. This Directive brings together, in one piece of legislation, all the directives relating to human medicinal products 1965 to 2001.

In accordance with the above legislation medicinal products can be authorised by one of two procedures.

6.2.1 Mutual Recognition Procedure

This is applicable to the majority of conventional products. An application is made to the EU member state competent authority selected by the applicant. That competent authority assesses the product in respect of its quality, safety, and efficacy and if deemed acceptable then a product authorisation is issued. The mutual recognition procedure is then invoked and other member states where the applicant has submitted an application and wishes to have the product authorised "mutually recognise" the original authorisation and issue national authorisations. A member state may object to the licencing of the product in their jurisdiction on "public health" grounds. As with nationally authorised products, products authorised through the mutual recognition procedure carry an authorisation number on the label.

6.2.2 Centralised Procedure

In accordance with EU Council Directive 2309/93 a product authorisation application is made directly to the European Agency for the Evaluation of Medicinal Products (EMEA). Products licenced in this way may then be marketed in all EU Member States and are granted an EU marketing authorisation number by the European Commission, which is carried on the product label. Use of this procedure is compulsory for the products derived from biotechnology and optional for other innovative medicinal products.

6.2.3 Official Control Authority Batch Release

The major difference in the legislation governing vaccines and the legislation covering the majority of non-vaccine medicinal products is that, in accordance with Article 114 of directive 2001/83/EC a member state may apply Official Control Authority Batch Release (OCABR) to a vaccine.

At the time of authorisation all vaccines are required by the IMB to be subjected to OCABR. This procedure involves an approved official state laboratory carrying out an independent evaluation of the production records of each batch of vaccine produced by a given manufacturer and testing samples of each batch against a standard protocol where this is considered necessary. The activity is controlled under the umbrella of the Official Medicines Control Laboratories (OMCL) network run from the European Directorate for the Quality of Medicines Council of Europe. The OMCL network controls the consistency of the individual laboratories nominated in this process. It is also possible to require OCABR at the time of renewal of the product authorisation.

For each authorised vaccine the company is normally asked to indicate which control authority is responsible for carrying out the OCABR. OCABR is another level of

assurance of ongoing quality and safety of marketed products, however ongoing good manufacturing compliance by the manufacturers is also essential to this process, as are regular updates to the assessment file e.g. to reflect the latest additions, or revised or new monographs of the European Pharmacopoeia.

It should be noted that OCABR is not considered a safety net for the product authorisation holder but rather is a quality assurance step for the competent authority such as the IMB, where as the OMCL laboratory also reviews the company's documentation supporting the production and release of a given batch of vaccine and retesting as required is carried out where the laboratory considers that it is necessary.

6.3 Pharmacovigilance

Once the product is authorised and is released by the independent laboratory the vaccine can be made available in the market place. The IMB is responsible for post marketing surveillance for all medicinal products in Ireland including vaccines. In accordance with the conditions of the product authorisation the PA holder is legally obliged to report all suspected adverse drug reactions (ADRs) to the IMB within defined time periods depending on the seriousness of the ADR. In addition there is a voluntary ADR reporting system for health care professionals including doctors, dentists, pharmacists and nurses who are actively encouraged to report suspected ADRs to the IMB in order to facilitate ongoing monitoring of safety of medicinal products. In particular, the IMB requests that all suspected ADRs to vaccines are reported. The IMB Pharmacovigilance Unit also liaises with regulatory authorities from other European member states and third countries (i.e. those included in the WHO Collaborating Programme for International Drug Monitoring) in relation to issues in those countries that may affect products available in Ireland. All ADR reports are assessed by the IMB and appropriate action is taken as necessary.

The Department of Health and Children (DoHC) is notified annually of the breakdown of ADRs received by the IMB and is informed immediately of any safety issues that are considered to have the potential to pose a serious risk to public health. The DoHC and the IMB then decide on necessary action based on the seriousness of the issue and take into consideration advice from HPSC or other appropriate sources. Any recall is coordinated by the IMB in conjunction with the company.

Healthcare professionals are informed of updated information regarding medicinal products and vaccines via the IMB Drug Safety Newsletter, monthly articles in MIMS (Ireland), "Dear Healthcare Professional letters" and statements issued on the IMB website.

A quality defect is defined by the IMB as an "unplanned attribute" of a product which may affect the quality, safety and/or efficacy of the product and which is not in line with the approved registration file of the product. Quality defect reports may include notification of suspected ADRs. The IMB coordinates any action necessary following a quality defect report, analysis, e.g. recall etc. Healthcare professionals, members of public, PA holders themselves or inspectorates of other competent authorities may report quality defects. Any action taken (i.e. Caution in Use letter, newsletter to

healthcare professionals, through a full recall of the product from the market place) depends on the seriousness of the defect.

7. SERO-IMMUNITY TO MEASLES

Sero-immunity studies to monitor susceptibility

Elimination requires the achievement and maintenance of low levels of susceptibility in a population. Age-specific targets for the WHO European Region have been established[23] so that sustained transmission does not occur following the introduction of a measles case.

The proportion of measles susceptible individuals in each age group must not exceed 15% in children aged 1–4 years, 10% in 5–9 years old children, 5% in 10–14 year old children, and 5% in each cohort of adults above this age. These levels are those felt to be sufficient to interrupt measles transmission.[23-25]

In addition to the routine monitoring of vaccine coverage, coverage surveys and well standardised and representative serological surveys have been used to assess population susceptibility to measles and/or rubella and to identify susceptibility gaps, particularly in those countries with poor-quality historical coverage data.

To predict the potential for future outbreaks, the likely achievement of elimination and to inform the correct vaccination strategy requires an estimate to be made of the age-specific proportion of the population who are susceptible to measles. This can be obtained by performing serological surveys or can be estimated by mathematical modelling using accurate surveillance data.

As it is recognised that ongoing serological surveillance is not feasible in all countries, countries may be able to predict the age-specific proportion of susceptible individuals in the population by mathematical modelling based on vaccination coverage data and/or age-specific disease incidence. Such modelling may also be used to inform future strategy by predicting the effects of alternative programmes.

7.1 European Sero-Epidemiology Network 2 (ESEN2)[14,15]

The European Sero-Epidemiology Network (ESEN2), based on the original ESEN project, was established in 2001 with funding from the Research Directorate of the European Commission. The aim of ESEN2 was to standardise the serological surveillance of eight vaccine preventable diseases (measles, mumps, rubella, diphtheria, pertussis, varicella zoster virus, hepatitis A and B virus). By standardising both laboratory and epidemiological methodology, international comparisons can be made to allow the effectiveness of different immunisation programmes to be evaluated and to coordinate vaccine policy to ensure that adequate levels of immunity exist throughout Europe. A total of 22 European countries, including Ireland, participated in ESEN2.[14]

During 2003, in collaboration with HPSC and the NVRL, laboratories from six HSE areas participated in the collection of 3,300 samples, stratified by age and sex. Testing of these sera for immunity to measles, mumps, rubella, pertussis, diphtheria, varicella zoster, hepatitis A and hepatitis B was done. The sero-profiles (sero-positivity rates) for these diseases were compared to vaccination uptake rates.

Methodology ESEN2

A total of 2,590 samples were analysed for the presence of measles IgG as part of the study. Additional samples were taken in the younger age groups; between 47 and 84 samples were tested for each year age group between 1-19 years; 194-250 samples were tested for each five-year age group between 20-39 years of age and 140-170 samples were collected for the age group 40-59 years of age. Information on national vaccination uptake for a measles containing vaccine was correlated to the sero-immunity profiles for appropriate age groups.

7.2 Measles susceptibility – results ESEN2

Overall, 90% of samples tested indicated immunity to measles. However sero-immunity differed by age group. Lowest levels of immunity were reported in children less than three years of age (58% for one year olds and 75% for two year olds), (Figure 7.1).

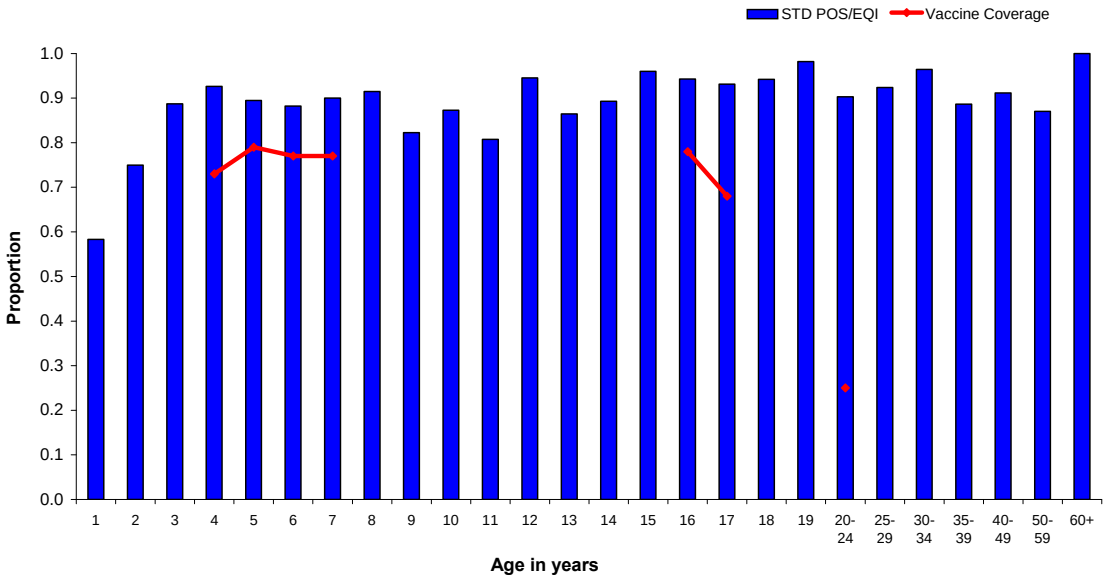


Figure 7.1. Proportion of population with measles immunity (sero-profile) by age group (ESEN2 2003 data)

At the age of four years there is an increase in sero-immunity reported. This may reflect vaccination induced immunity (school vaccination programme at four to five years of age) or immunity induced by exposure to wild virus (this particular cohort are also more likely to have been exposed to the measles outbreak in 2000).

The proportion of samples that were sero-immune in the four to seven year age groups exceeded the reported measles vaccination rates reported for this age group (Figure 7.1). The higher than expected sero-immunity in this population may reflect both natural immunity among these children, obtained from exposure to wild virus, or

vaccine induced immunity, which may be under-reported in national immunisation coverage data.

Among older age groups, most adults 20 years of age or older were not vaccinated. Most young adults less than 20 years of age would have been offered MMR vaccine as part of the school-based MMR vaccination programme initiated in 1992 (10-14 year olds) or during the MR catch-up programme in 1995 for five to twelve year olds. The relatively high levels of reported measles immunity among those in the older age groups reflect immunity following exposure to wild measles virus circulation. Most of this population would undoubtedly have been exposed to measles in early childhood. Even among the older age groups, a greater than expected proportion (87-90%), were reported as immune (Figure 7.1).

7.3 Rubella susceptibility - results ESEN2

In ESEN2 the following cut-offs were applied to standardised antibody titres: <4IU/ml were sero-negative samples, 4-7IU/ml were equivocal and >7IU/ml were sero-positive. Equivocal samples were included with sero-positives only if stated. Amongst women of child-bearing ages 15-39 years of age (WCBA), protective immunity was defined as a rubella antibody titre >10IU/ml. ESEN2 have taken an antibody titre of 10IU/ml as being indicative of protective immunity in WCBA as risks of foetal transmission are greatly reduced, although other investigators have employed a higher threshold of 15IU/ml.[15]

In previous WHO strategies, targets of <5% rubella susceptibility amongst WCBA have been set.

Rubella sero-negativity (<4IU/ml) in Ireland in 2003 exceeded 10% among children 2-14 years of age. At this level modeling studies have estimated that smaller epidemics could occur.[25] Among the 15-39 year age groups overall >5% of both males and females were sero-negative (with higher seronegativity seen among males than females) (Table 7.1).

Table 7.1. Percentage sero-negative samples (<4IU/ml) in children (2-14 years old) and young adults (15-39 years old) by gender in Ireland (ESEN2 2003)

	Age group 2-14 years			Age group 15-39 years		
Overall % (n)	**2-4yrs**	**5-9 yrs**	**10-14yrs**	**Overall % (n)**	**Males**	**Females**
12.9% (805)	15.5%	13.8%	10.2%	5.6% (1212)	9.2%	3.6%

Looking at the seronegativity cut-off point of >10IU/ml to ensure prevention of CRI, among WCBA sero-negativity exceeded 5% in all age groups. Seronegativity was highest among the youngest age groups (15-19 years) and lowest among the 30-39 year olds (Table 7.2).

Table 7.2. Percentage of women of childbearing age (WCBA) without protective immunity (defined as a titre <10IU/ml) for rubella by age group, Ireland 2003

Overall percentage	Percentage by age group		
15-39 years % (n)	**15-19 years % (n)**	**20-29 years % (n)**	**30-39 years % (n)**
7.6% (778)	10.7% (159)	6.2% (307)	7.4%(312)

7. 4 Using ESEN2 data for modelling a vaccination –Cfi HPA

The Centre for Infections (Cfi), Health Protection Agency (HPA) undertook a modelling exercise using the ESEN2 data, vaccination coverage, and incidence data and looked at various options for measles catch-up campaign (Dr. Nigel Gay, Modelling & Economics Unit, Cfi, London, UK). Their first step in assessing potential for measles transmission was to estimate the measles susceptibility profile using the ESEN2 data (Figure 7.2).

The baseline estimate of susceptibility drew heavily on the sero-prevalence survey, and also on the information specifying which cohorts have been targeted by which vaccination programmes. A single national profile was used, with no attempt to investigate regional differences in susceptibility. The model found that among cohorts that have completed the national schedule (i.e. aged 5 years or more), susceptibility is highest among 11-14 year olds. It appears that this age group have only been targeted to receive a single dose of MMR at 15 months.

Susceptibility is lower than can be explained solely by vaccine derived immunity at the reported coverage (even in young children), suggesting that naturally acquired immunity and/or higher than reported coverage (including late doses) may contribute significantly to sero-immunity.

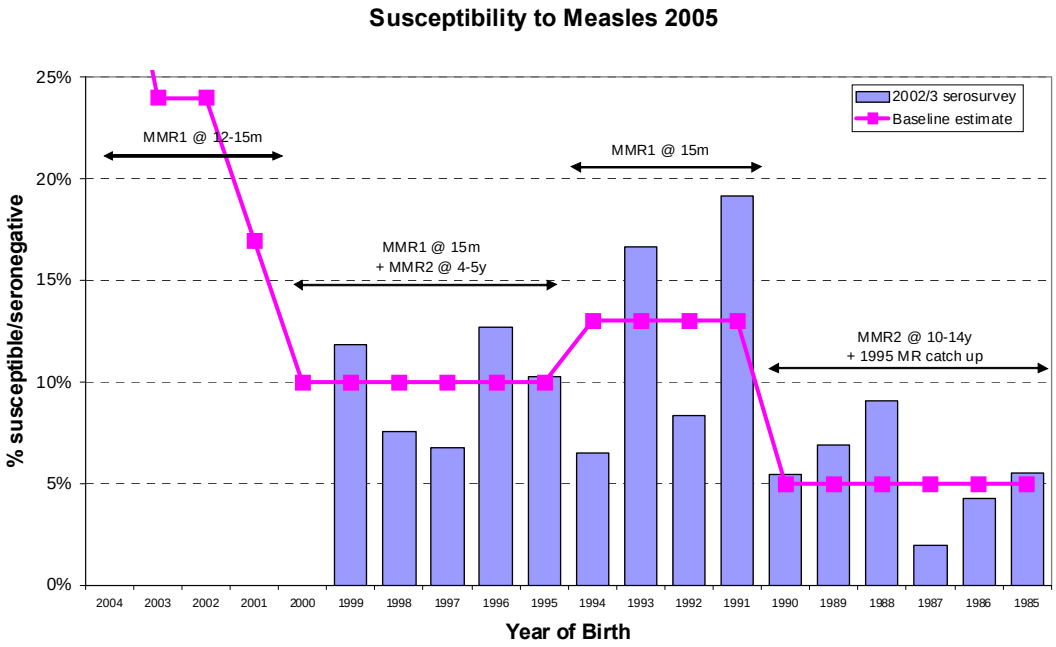


Figure 7.2. Susceptibility to measles 2005

Susceptibility exceeds the WHO target in 11-14 year olds and in pre-school children. Secondary school children have a high potential to transmit measles infection, and it is this age group that should be given the highest priority in the short term. The cohorts aged 5-10 years, who do not currently exceed the 10% target for this age group, will also require further vaccination initiatives to reduce the proportion susceptible to less than five percent before they reach secondary school age (Figure 7.3).

Figure 7.3. Comparison of Measles susceptibility with WHO target

Although continued improvements to first dose coverage would contribute to reducing susceptibility among pre-school children in the medium term, the lower contact rates within the pre-school age group allow this group to be given lower priority for catch-up vaccination.

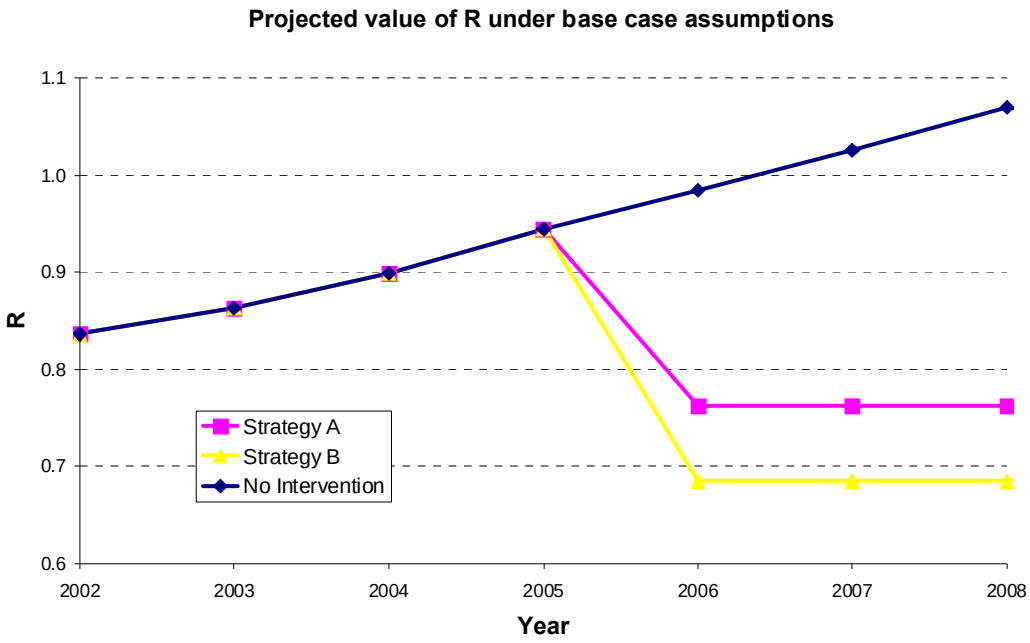


Figure 7.4. Projected value of Reproductive rate (R) under base case assumptions

R = Reproductive rate. The average number of persons infected by a single disease source. This rate is affected by the duration of infectivity, the infectiousness of the organism, the number of susceptible people with whom the infected patient comes in contact. In general, if Ro is greater than one, the disease will continue to spread within a population. If Ro is less than one, the disease will eventually disappear from a population.

The effective reproduction number for measles in each year can be calculated from the susceptibility profile and (previously estimated) age-specific measles transmission rates (based on data for the UK). Predicting the exact timing of a potential epidemic is fraught with difficulty because of uncertainty in the levels of susceptibility, the contact rates, regional differences etc and because of the stochastic nature of the early stages of an epidemic. Nevertheless, under the current vaccination programme and coverage, the continual accumulation of susceptible children, and particularly the increasing susceptibility of secondary school children (as the most susceptible cohorts reach this age), are expected to provide the potential for widespread transmission of measles within the next few years as the effective reproduction number exceeds unity (R>1) (Figure 7.4).

Two alternative strategies to avert the epidemic and set the path for measles elimination were investigated by Cfi (Figure 7.4).

Cfi Strategy option A: Catch-up campaign for 11-14 year olds + ongoing checking and completion of vaccination status at entry to secondary school.

Cfi Strategy option B: Catch-up campaign for 5-14 year olds + ongoing checking and completion of vaccination status at entry to primary school.

In either campaign it would only be necessary to vaccinate those without two previous doses. In either strategy the aim of the ongoing school entry programme would be to reduce susceptibility to five percent or less.

While either strategy, if implemented effectively, should lead to sustainable measles elimination, strategy B was the recommended strategy by the Cfi, as it would lead to a lower level of susceptibility in primary schools, and therefore a lower R and less potential for outbreaks.

7.5 Recommended vaccine strategy for measles elimination in Ireland

The results reported in the ESEN2 study and used in the model by Cfi, HPA clearly indicate that susceptibility exceeds the WHO target in 11-14 year olds and in pre-school children.

The Committee reviewed the two Cfi recommended strategies (A or B) against the backdrop of the national mumps outbreak 2004-2005 in third level colleges, ongoing mumps transmission and the recommendation that all new entrants to third level colleges since 2005 should have MMR if not already in receipt of two doses of MMR vaccine. An additional strategy was considered.

Strategy option C: Catch-up campaign for school children aged 4-18 years of age, to include students in other training facilities as well plus ongoing checking and completion of vaccination status at 4-5 years of age.

The Committee recommended including 4 year old children in the target group due to age composition of children in junior/senior infants and the potential difficulty to vaccinate part of the class rather than the whole class.

The sero-epidemiology study found high levels of susceptibility among 11-14 year olds. As secondary school children have a high potential to transmit measles infection, secondary students should be given the highest priority in the measles campaign in the short term.

8. MAXIMISING IMMUNISATION UPTAKE

Achieving and sustaining high coverage with two doses of MMR through high quality routine immunisation services is key to the success of elimination of measles, rubella and CRI. As outlined already this has not been achieved for children at 24 months of age and there is no national system in place to be able to assess uptake of the second dose of MMR. Each HSE area needs to have a system for estimating and monitoring MMR_2 uptake. Standards are required to allow comparability across areas and to monitor national uptake of MMR_2.[26]

Age appropriate immunisation

By the age of 6 years, all children should have received two doses of MMR (unless contraindications) and have documentation of same. Identifying older children who are inadequately vaccinated is important so that they can be offered a second dose of MMR. In Ireland there is currently no systematic system to identify school children in older age groups who may have missed the second dose of MMR. Other countries have implemented routine review of immunisation records at the beginning of each school year to identify students in need of vaccines. This requires close cooperation between health and educational services but has been instrumental in reaching targets.[25,27]

Immunisation Registers

HSE areas currently have a variety of electronic or paper based systems in place for the recording of childhood immunisations. These individual client immunisation records include date of birth and age at receipt of vaccine, batch number, expiry date and date of administration of all vaccines and all antigen combinations. There are currently 50 independent databases in use which are not interlinked and in the majority of areas primary and school records are maintained separately

The National Immunisation Office (NIO) is currently working on a national immunisation registry project whereby all immunisation records will be linked to a unique identifying number. This system will be able to capture all immunisations from birth to adulthood. Such a system will allow the development of standardised timing and methods for assessment of vaccine coverage and provide comparable national data for analysis. However, it will be at least three years before such a system is in place. In the meantime, all HSE areas should give high priority to improving the quality on their current systems (in terms of completeness, accuracy and availability of data in a timely manner) in order to improve immunisation information necessary for programme monitoring and targeted activities.

In addition to the recording of vaccinations administered to children in the first two years of life, the current information systems should be used to record all childhood immunisations (administered either through the school-based programmes or GPs).

Record-keeping for the individual

Immunisation providers routinely record immunisations on patient records held at the GP practice or at the CCA office (school-based clinics). It is important that whatever vaccines are given are also provided on a record given to the individual.[28] This allows individuals to be fully aware of vaccines received and provides documentary evidence of vaccination when required.

Retrieval of archived paper based immunisation records at CCA/HSE level

In the past school-based immunisation records were kept in paper format and archived. Review of this immunisation information required obtaining the records from the archive and hand-searching records or files to obtain the immunisation information on individuals. In recent years some HSE areas have scanned these immunisation records into databases and are now able to rapidly retrieve immunisation records on children as required. This activity has proved cost saving to these areas (less man hours required to search for data) avoids unnecessary vaccine administration in children already fully vaccinated and provides information to parents seeking their children's immunisation records. HSE areas that have not yet put in place similar systems are recommended to do so.

Addressing public concerns about vaccines

As seen in the past, widespread public concern about vaccines, even when unfounded, can severely impact on immunisation coverage for years. HSE needs to ensure that mechanisms are in place to rapidly respond to expressed parental or public concerns about vaccines. Close collaboration is needed between and within various HSE directorates to ensure accurate and clear messages are provided to the public. Health Promotion communications need to be rapidly disseminated to avert unnecessary negative impact on immunisation programmes.

Summary and recommendations

1. Immunisation uptake of at least 95% is required with a two-dose MMR schedule. Information systems are required to monitor that this is achieved (both MMR_1 and MMR_2).
2. All vaccinated children should be provided with a vaccine record of immunisations provided.
3. All HSE areas should give high priority to improving the quality of their current systems.
4. HSE areas should routinely input all child immunisation records into the local childhood immunisation system, including those administered after 24 months of age.
5. Where historic paper-based immunisation records of children are available HSE areas are encouraged to scan this information into databases to allow rapid retrieval of immunisation records of children immunised in their area.
6. Ideally, all children in care and educational settings should have proof of age appropriate immunisation monitored routinely. Systems should be put in place to

allocate responsibility for this activity and support this activity in a standardised manner across all areas.

7. Health Promotion communications need to be rapidly disseminated to avert unnecessary negative impact on immunisation programmes.

9. RESOURCES REQUIRED FOR MEASLES CONTROL

The resources that will be needed of the Measles and Congenital Rubella Elimination programme can be identified as those necessary to

- Ensure sustained high levels of vaccination coverage through the routine childhood immunisation programme and
- Facilitate an opportunity for catch-up for those that have missed vaccination with 2nd dose of MMR
- Rapid identification and investigation and follow-up of all suspect or confirmed measles cases, and appropriate action taken immediately.

Inadequate programme activities in any of the above will impede progress in this area and prevent successful elimination.

9.1 Identifying resource requirements in Ireland

Following consultation and agreement on methods of measles elimination (including controlling outbreaks), the implications for resource provision at local, regional and national levels were discussed. Since 2002 HSE areas have been following national recommendations (NDSC Measles Sub-Committee).[11] Valuable experience on the requirements for controlling measles has been obtained since these guidelines were implemented. The following points were raised by the Committee and are based on HSE areas experience in the past.

9.1.1 Resources for measles control - investigation and control activities

Elimination activities will be more resource intensive than routine measles control activities that have been implemented in recent years. To eliminate these diseases will require adequate allocation of resources (manpower, time, vaccine supply, communication material and supportive IT system).

9.1.2 Routine investigation and control - sporadic cases

Based on experience of measles control in recent years the Committee outlined the lessons learned from recent experience in measles control:

Time is needed for investigation and control
Actual time taken to complete infection control tasks takes longer than theoretical time

Experienced staff is required
Staff who are trained and experienced in investigation and control activities provide a more efficient and cost effective service. There are already experienced and trained public health clinicians who are ideally placed to lead the community part of the programme (e.g. SMOs in Public Health). Public health nurses are integral to the measles elimination programme activities.

Home visitation either by Primary Care, or Public Health is important

Home visitation is considered a useful part of measles control and should be undertaken and resourced whenever possible. Home visits can prevent transmission occurring in the health care setting and enable additional clinical assessment opportunities, collection of enhanced data, and diagnostic testing and provision of advice and education on control measures. Where home visits are not possible and patients are referred to GP health care settings, rapid triage and isolation is essential to prevent transmission to others.

9.1.3 Routine investigation and control during outbreaks

In the investigation and control of outbreaks (as detailed above) it is vital to have time, experienced staff and opportunities for home visitation to prevent on-going transmission.

Need for surge capacity to enable rapid response
Additional surge capacity is required to respond during outbreak situations. Rapid investigation of suspect cases is required to ensure that necessary control measures can be implemented. To avoid unnecessary delays in identifying staff (from different HSE areas or directorates) for outbreak response it is important that relevant service managers and staff have pre-agreed plans.

9.1.4 Additional costs associated with elimination activities

To date the experience of public health in Ireland has been the control of measles, which is different from measles elimination. The capacity of public health to do enhanced surveillance and to control measles varies across the country. Despite strong efforts in many areas to control measles it is clear that current control strategies have failed. Continued circulation of measles virus occurs because of inadequate herd immunity (secondary to inadequate MMR uptake), and inadequate control measures.

Inadequate control can occur when:

- Cases are not recognised as possible cases
- Suspect cases are not reported to Public Health or are reported too late
- Failure to identify all case contacts
- Inadequate acceptance of MMR by those recommended vaccine

Intensive, comprehensive contact tracing is required in any elimination programme. Current contact tracing follow-up tends to focus on those people with the most contact - a conservative approach. During the elimination phase a more aggressive approach will be required with a more liberal interpretation of who is at risk. This will usually involve a much wider spread of contact tracing and control measures (such as vaccination). The Committee recommended that during the early part of the elimination programme that the majority of efforts should be focussed on increasing routine and mop-up immunisation of children. Towards the latter stages of the programme an increased emphasis on rapidity and completeness of investigation will be most important.

9.1.4 Allocating adequate resources for elimination activities

The goal of elimination is a priority, every effort to eliminate measles should be put in place. Inadequate resources for measles elimination will lead to failure.

9.1.5 Prioritising measles elimination work

Elimination efforts will require immediate and extensive response, that cannot always be anticipated. To be successful, PMOs, SMOs will need to be in a position to prioritise this work when required to do so. Additional support from ICNs/CNM2s and other staff will also be required.

Having adequate surge capacity (i.e. the possibility to call on additional staff to assist in emergencies) is essential. This might include extra administrative support; extra nursing support for vaccination programmes etc. Prior agreement on stepping up response to meet measles elimination activities is required with service managers. Prior consultation with all stakeholders is integral to the planning process, ensuring that there is both corporate and individual recognition on roles and responsibilities. Processes should be predefined and agreed in advance as part of planning process.

Recommendations: HSE needs to put in place a corporate response to measles outbreaks (surge capacity) across HSE directorates and HSE areas so that this work can be prioritised.

9.1.6 Allocating time for surveillance and control activities

Allocating time to surveillance and control activities is a critical factor in measles elimination. This time is required for communications with index case/family, public, medical community, media and within the HSE local, regional and national service. Experienced staff can complete tasks and communications much more quickly than inexperienced staff.

9.1.7 Preventing opportunities for measles transmission- home visitation

Although home visiting is not currently always done due to lack of manpower and time, it is perceived as being vital to the investigation of measles cases during an elimination programme. Home visitation, although resource intensive, facilitates preliminary assessment and investigation, and procurement of diagnostic samples (oral fluid or serum). (In some areas GPs currently undertake this activity). A home visit also offers the opportunity to educate the family members *in situ*, to bring information leaflets, to organise “isolation” for the case and to answer any queries that may occur. It is important for all suspect, probable or confirmed measles cases to be isolated immediately, to prevent ongoing transmission.

9.2 Specifying resources at various levels in HSE

Regardless of the strategy agreed (school-based or GP provided), the following resources will be required at various levels of the health service:

9.2.1 National (HSE, HPSC, NIO, IMB, NVRL) services need

Adequate vaccine supply and distribution (NIO)
Education and training plan, materials (HSE)
National communication plan (HSE)
Publication and dissemination of guidelines and information (HSE/NIO/HPSC/IMB)
AEFI monitoring and reporting (IMB)
Monitoring of immunisation uptake MMR_1 and MMR_2 by HSE area and LHO level (HPSC)
Priority and resources given to development of national immunisation registry (NIO)
Strengthened laboratory surveillance (NVRL)

9.2.2 Public Health will require

Trained and experienced human resources (SPHMs, SMOs, PHNs, Surveillance Scientists, clerical/administrative/management staff) for
Additional staff training and capacity building
Resources for investigation, control and follow-up (Public Health)
Capacity for routine diagnostic testing (if not done by GP – LHO)
Resources to improve enhanced surveillance (Public Health)
Rapid case investigation and contact tracing (Public Health)

Comment: Communication between general practice, PCCC and public health departments will be required. Additional training and capacity building may be required.

9.2.3 Primary Care will require

Trained and experienced human resources GPs, Practice nurses, support staff for
Rapid reporting of all suspect cases to Departments of Public Health
Appropriate laboratory diagnostic testing
Oral fluid sample diagnostic testing (if not done by local PH)
Serum sample diagnostic testing if required
Identification of new entrants to area not already registered on immunisation information system – facilitate contact with local LHO office
Support for enhanced surveillance activities (if required)
Resources for routine and emergency (outbreak situation) vaccination of susceptible individuals (opportunistic and on request)

Comment: Additional training and capacity building may be required for staff in primary care. Accessible and rapid supply of diagnostic equipment (if needed).

9.2.4 PCCC (LHO) will require

Trained and experienced human resources SMOs, PHNs, GPs, practice nurses, administrative staff, IT experts for
Routine vaccination activities (SMOs, PHNs)
Involvement in mop-up vaccination activities to prevent and control outbreaks

Timely input of immunisation data into immunisation register (clerical)
Establishing systems to monitor uptake of MMR_2, in place ahead of any national unified system
Special arrangements for remunerating GPs who immunise school age children during outbreaks

Comment: Additional training and capacity building may be required.

9.2.5 Laboratory

Trained and experienced human resources. Scientists for
Diagnostic testing (local or national, NVRL)
Genotype investigation and surveillance activities
Reporting of results

9.3 Achieving high and sustained immunisation coverage – resource needs

Vaccine procurement
Budgets already exist to ensure that there is sufficient MMR vaccine supply for the population cohorts due MMR (at 12-15 months and 4-5 years). There is also adequate budget for payment to GPs to administer the vaccine.

Immunisation information systems
In February 2001 the Health Board Chief Executive (HEBE) Officers undertook a Review of Immunisation/Vaccination Programmes. The National Steering Committee convened for this purpose completed their report in January 2002.[26] A number of recommendations were made, including the recommendation for "*The establishment of the recommended Project Structure for the procurement and implementation of a National Immunisation Information System"*. This project group is currently working within the National Immunisation Office to scope what is required. The development of a national immunisation information system will be crucial to developing a modern, high quality system that will provide information required for individuals, health professionals and programme management and monitor performance in meeting performance indicators.

A national immunisation information system is vital to ensure that there is a high quality national system that will capture and exchange client-based vaccination information across all HSE areas and will meet the information needs of the client, GP and HSE. Such a system should have functionality to link with other IT systems used in the HSE and facilitate key activities such as payment, stock management and procurement, evaluation and real time monitoring of immunisation uptake rates at local, regional and national levels. Such system will also have the possibility to rapidly identify vaccination histories on individuals who are notified with vaccine preventable diseases and assist in identifying vaccination status of case contacts who may require either active or passive immunisation.

9.4 MMR Catch-up Programme – target population

The estimated population eligible for the MMR catch-up programme is approximately 853,691 students (Census 2002 data**)** in the 4-18 years age group. This target

population includes all children in the age group who are eligible for participation in the campaign, regardless of immunisation status (Table 9.1).

Table 9.1. Total population potentially eligible for participation in MMR catch-up campaign (4 – 18 Year olds)

Age group	4 years	5 – 9	10 – 14	15 – 17	Total
Population*	55,526	264,090	285,708	248,612	**853,691**

** Population based on Census 2002 figures*

Generally children who have documented evidence of receiving two doses of MMR at the appropriate age (1st dose after 12 months of age) do not require additional doses of MMR. If immunisation information systems exist to easily identify those that require a second dose of MMR then a targeted approach of vaccinating just those in need of MMR_2 is usually adopted (cost saving). This approach assumes that resources (vaccine and administration costs) are saved because of the smaller numbers vaccinated.

However, in areas where immunisation information systems are lacking and service providers cannot readily identify children requiring MMR then adopting a comprehensive catch-up is also safe and effective. In this approach all children in the cohort are offer MMR, regardless of immunisation history. Such an approach is feasible and has been implemented in other countries.[24] However, this approach (which requires more vaccine and staff to administer vaccine) is usually more costly than vaccinating a sub-group of the population requiring the second dose of MMR.

In Ireland, it is widely recognised by those in the field of immunisation, that obtaining readily accessible and accurate vaccination records is difficult, if not impossible, for many children. It is likely to be particularly difficult for those in the older age groups (see section on situational analysis). Without documentary evidence of having received two doses of MMR all children should be administered MMR as part of the catch-up campaign.

Therefore, the Committee considered a number of approaches

Population for MMR campaign - A: Immunisation of sub-group of cohort-children without documented evidence of two doses of MMR

Population for MMR campaign - B: Immunisation of full cohort all children (comprehensive catch-up campaign) regardless of immunisation history

The importance of a National Immunisation Information System is highlighted by this strategy.

Costs associated with MMR catch-up campaign

The following section details the resources that are required to implement the recommended strategy. These resources are necessary to fully implement the measles

and rubella elimination strategy. As part of the process of identifying resource needs, a needs assessment was undertaken to identify current resources available for immunisation programme including the primary care setting and what resources would be needed for a supplemental school-based catch-up campaign to be carried out as a once off activity.

Additional resources are required for

- School-based teams (detailed below)
- GP payments for outstanding children as mop-up activities
- Communication activities (detailed below)
- Surveillance activities
- Surveillance, monitoring and investigation
- Resources to support management of information systems and inputting of immunisation records
- Outbreak control response

At a national level the following resources will be required

- Adequate vaccine supply and delivery to meet both routine and catch-up needs
- Adequate school-based vaccination teams with appropriate supervision, training
- National communication plan
- Training activities
- Dissemination of guidelines
- Enhanced surveillance on all cases with laboratory confirmation
- Development of national immunisation registry or failing that, capturing all information currently on file in a readily retrievable format (electronically)

Comparison of different options for vaccination programme

GP versus school-based vaccination teams

A comparison was made of estimated costs associated with administering MMR vaccine to children at the GP practice or in schools (using a school team approach). Vaccine costs were provided by NIO, staffing costs estimates were provided by HSE NW and also from the NIO.

The vaccine can be procured at €8.40 (incl. VAT) per dose (2007 costs). The cost of MMR vaccine administration is more costly through GPs than if using a school team approach (€44.10 versus €24.82 respectively) (Table 9.2).

Table 9.2. Costs of vaccine and administration by site (GP practice or school)*

Cost item	Unit cost
Vaccine (one dose)	€8.40 (incl. VAT)
Estimated cost of one GP visit *	€44.10 per visit
Estimated cost per person using School Team approach**	€24.82 per person

based on HSE North West costings 2003:based on HSE North West costings 2003 – vaccination team only*

Estimated costs of a catch-up campaign by approach (GP versus School team approach) and proportion of target population administered vaccine are shown in Tables 9.3 and 9.4 respectively.

Using a school team approach is more cost effective (and more efficient) for the funders than using a GP based approach for the population. However, this will require the recruitment of additional school vaccination teams. It should be noted that these costs do not include clerical or administrative costs associated with implementing such a programme and these substantial costs are an integral part of the programme.

Table 9.3. GP vaccination programme. Estimate of associated costs by proportion of target population vaccinated (national)*

% Target (Population)	GP Providing Vaccination	Vaccine Costs	Total Costs for GP Vaccinating
10% (85,369)	€3,764,777	€717,100	€4,481,873
25% (213,423)	€9,411,943	€1,792,753	€11,204,708
50% (426,846)	€18,823,887	€3,585,506	€22,409,415
75% (640,268)	€28,235,830	€5,378,251	€33,614,070
100% (853,691)	€37,647,773	€7,171,004	€44,818,778

NB These figures do not include clerical/admin costs from each Health Area.
**estimates based on cost estimates provided by HSE NW*

Table 9.4. Schools Based Vaccination Programme. Estimate of associated costs by proportion of target population vaccinated (national)*

% Target (Population)	School Teams Vaccinating	Vaccine Costs	Total Costs for School Teams
10% (85,369)	€2,118,861	€717,100	€2,835,958
25% (213,423)	€5,297,153	€1,792,753	€7,089,912
50% (426,846)	€10,594,305	€3,585,506	€14,179,824
75% (640,268)	€15,891,458	€5,378,251	€21,269,703
100% (853,691)	€21,188,611	€7,171,004	€28,359,615

**estimates based on cost estimates provided by HSE NW*

National Immunisation Office estimation of costs for school-based programme (Men C campaign approach)

The estimated costs associated with a measles campaign in school (pay and non pay) using a model similar to the MenC campaign in 2000 are detailed in Table 9.6 (50% target population) and Table 9.7 (100% population). Minimum estimated costs for such a programme, assuming vaccination of 50% of children would be approximately €11.7 million. Total estimated cost of the campaign could cost an overall budget of €14-20 million depending on numbers of children requiring vaccination and possible increased vaccine cost.

The alternate strategy which is the vaccination of all children in the cohort would at a minimum cost €20.5 million. Total estimated cost of the campaign could cost an

overall budget of €20-25 million. These figures do not take into account increased vaccine costs, the requirement for mop-up clinics and assumes that 0.5 WTE Grade III clerical support per LHO region will be sufficient at LHO level.

Public Information campaign for catch-up programme

An additional budget will be required for a media campaign to announce and promote the programme. Total costs for a full TV, newspaper and radio media campaign are estimated at €850,000 (Media campaign B). Exclusion of TV is less expensive but also seen as less effective (Media campaign A) (Table 9.5).

Table 9.5. Budget for media campaign as part of MMR booster catch-up campaign

Media Campaign type	Total
Media Campaign A Two-week media awareness campaign (national & regional newspapers and national & regional radio) together with printing of leaflets	€600,000
Media Campaign B Two-week media awareness campaign (TV, national & regional newspapers and national & regional radio) together with printing of leaflets	€850,000

Source: National Immunisation Office

9.5 Summary and recommendations

1. A school-based booster programme will be more cost efficient than GP based programme and is the preferred option.
2. Minimum estimated costs for a school team approach, assuming vaccination of 50% of children would be approximately €11.7 million (NIO estimate). Such an approach is dependent on the ability of HSE areas to identify vaccination status of children within resources available to them.
3. If a comprehensive approach is taken (100% offered vaccine) the programme could cost in the range of €20-25 million (excluding administrative costs).
4. A two-week media campaign (Media campaign B) to cover national and regional media is recommended and will cost approximately €850,000.

TABLE 9.6 MEASLES ELIMINATION CAMPAIGN – 50% POPULATION						
	2007		2008		2009	
	PAY	NON PAY	PAY	NON PAY	PAY	NON PAY
Vaccine Purchase Total cohort 853,000 2 year campaign Assume 50% have had MMRx2 – cohort 426,000 **Total**		To start Oct 2007 Require vaccine purchase in 2007 for 25% cohort 106,000@ €10/dose **€1,065,000**		Require vaccine purchase for 50% cohort 213,000@ €10/dose **€2,130,000**		Require vaccine purchase for 25% cohort 106,000@ €10/dose **€1,065,000**
Communications Promotional materials Media campaign IT changes to existing systems **Total**		€100,000 €300,000 €100,000 **€500,000**		€100,000 €250,000 €100,000 **€450,000**		
Staffing Requirements **Measles elimination campaign (Staff in post 3-6 months prior to start in Sept 07)** 1 Grade VIII (Project Manager) 16 Grade III clerical support staff 8 MMR vaccination teams with 1 medical officer & 4 RGNs Pay increases (10% pa) Total	€37,500 €17,500 x16 = €280,000 €20,000 +4x€ 10,000= €60,000 x8 = €480,000 €79,750 **€761,750**	(12% PAY COSTS) **€105,270**	€75,000 €35,000 x16 =€560,000 €(80,000 + 4x40,000) x8 =€1,920,000 €255,550 **€2,810,500**	(12% PAY COSTS) **€337,260**	€56,250 €26,250x16 = €420,000 (€60,000 +4x€30,000)x8 =€1,440,000 €191,635 **€2,107,875**	(12% PAY COSTS) **€252,945**
TOTAL	**€877,250**	**€1,670,270**	**€2,810,500**	**€2,917,260**	**€2,107 875**	**€1,317945**
ANNUAL TOTAL	**€2,547,520 SAY €2,540,000**		**€5,727,760 SAY € 5,728,000**		**€3,425,820 SAY €3,426,000**	

- FIGURES DO NOT INCLUDE ANY INCREASE IN VACCINE COSTS
- ASSUMES 0.5 WTE GRADE III PER LHO SUFFICIENT TO IDENTIFY COHORT, PREPARE LISTS AND IMPUT RETURN DATA
- DOES NOT INCLUDE PROVISION FOR REPORTS ETC POST END OF CAMPAIGN
- ASSUMES ALL VACCINATIONS CARRIED OUT AT SCHOOL – NO PROVISION FOR MOP UP CLINICS

TABLE 9.7 MEASLES ELIMINATION CAMPAIGN – TOTAL POPULATION TARGET						
	2007		2008		2009	
	PAY	NON PAY	PAY	NON PAY	PAY	NON PAY
Vaccine Purchase Total cohort 853,000 2 year campaign **Total**		To start Oct 2007 Require vaccine purchase in 2007 for 25% cohort 213,000@ €10/dose **€2,130,000**		Require vaccine purchase for 50% cohort 416,000@ €10/dose **€4,160,000**		Require vaccine purchase for 25% cohort 25% cohort 213,000@ €10/dose **€2,130,000**
Communications **Promotional materials** **Media campaign** IT changes to existing systems **Total**		€100,000 €300,000 €100,000 **€500,000**		€100,000 €250,000 €100,000 **€450,000**		
Staffing Requirements **Measles elimination campaign (Staff in post 3-6 months prior to start in Sept 07)** 1 Grade VIII (Project Manager) 16 Grade III clerical support staff 16 MMR vaccination teams with 1 medical officer & 4 RGNs **Pay increases (10%pa)** **Total**	 €37,500 €17,500 x16 = €280,000 €20,000 +4x€ 10,000= €60,000 x16 = €960,000 €124,000 **€1,364,000**	 (12% PAY COSTS) **€163,800**	 €75,000 €35,000 x16 =€560,000 €(80,000 + 4x40,000) x16 =€3,840,000 €44,750 **€4.922,500**	 (12% PAY COSTS) **€590,700**	 €56,250 €26,250x16= €420,000 (€60,000 +4x€30,000)x16 =€2,880,000 €327,625 **€432,465**	 (12% PAY COSTS)
TOTAL	**€1,364,000**	**€2,793,800**	**€4,922,500**	**€5,200,700**	**€3,603,875**	**€2,562,465**
ANNUAL TOTAL	**€4,157,800 SAY €4,158,000**		**€10,123,200**		**€6,166,340 SAY €6,167,000**	

- FIGURES DO NOT INCLUDE ANY INCREASE IN VACCINE COSTS
- ASSUMES 0.5 WTE GRADE III PER LHO SUFFICIENT TO IDENTIFY COHORT, PREPARE LISTS AND IMPUT RETURN DATA
- DOES NOT INCLUDE PROVISION FOR REPORTS ETC POST END OF CAMPAIGN
- ASSUMES ALL VACCINATIONS CARRIED OUT AT SCHOOL – NO PROVOISION FOR MOP UP CLINICS

SECTION 3. RECOMMENDED STRATEGY AND ACTION PLAN

10. SUMMARY OF RECOMMENDED STRATEGY AND ACTION REQUIRED

10.1 Achieve and sustain very high coverage (≥95%) with two doses of measles and at least one rubella vaccine through high quality immunisation services

Specifically this means that Ireland needs to

Ensure high coverage (≥95%) of MMR_1 at 12-15 months of age

Ensure high coverage (≥95%) of MMR_2 at 4-5 years of age

Necessary action points

Achieving high coverage requires strengthening routine services:

- Identification and registration of all children due MMR_1 and MMR_2
- Identification and active follow-up of defaulters (MMR_1 and MMR_2)
- Children presenting for MMR vaccination at 4-5 years without evidence of previous MMR dose should be routinely scheduled for another dose (with at least one month interval between doses)
- Provide opportunistic MMR vaccination (GP, hospital settings with enhanced reporting system)

10.2 Provide a second opportunity for measles immunisation through supplemental immunisation activities to populations susceptible to measles

Supplemental activities will include a national booster campaign, any mop-up campaigns required to augment vaccination activities undertaken for contacts of suspect cases

Necessary action points

- Implement national MMR vaccination campaign for all children 4-18 years of age without documented evidence of two doses of MMR. Achieving high coverage requires strengthening routine services:
- Organise mop-up clinics for children due MMR (if missed in schools)
- Provide opportunistic MMR vaccination
- Secondary school children should be prioritised in the short term due to excessive levels of measles susceptibility in this population

10.3 Provide rubella vaccination opportunities, including supplementary immunisation activities to all rubella susceptible children, adolescents and women of child bearing age

The planned measles elimination strategy, using the MMR vaccine will provide protection against rubella for susceptible children. Women are routinely screened at antenatal clinics for rubella immunity and offered MMR vaccine post-natally.

Necessary action points

- Implementation of proposed MMR vaccination programme as above

- Identify women who may not have been offered a rubella vaccine (e.g. particularly non-national) and offer MMR to non-immune (if from country without rubella programme may be more cost efficient to vaccinate without serological screening)

10.4 Strengthen surveillance system by rigorous case investigation and laboratory confirmation of suspected measles cases

- System needs to be able to detect sporadic measles cases and provide adequate information on both epidemiology (public health) and the virus genotype (laboratory) so cases can be classified as being the result of indigenous transmission or importation.

- Congenital rubella surveillance systems are already in place. Their quality should be monitored routinely during the elimination phase (cross-validating with BPSU/local surveillance systems).

- Timely collection, analysis and communication of data to enable appropriate public health action (including rapid identification of contacts and vaccination as necessary).

- Surveillance of adverse events following immunisation (AEFIs) to detect, monitor and respond to suspect cases in timely manner.

Necessary action points

- Public health surveillance system already in place needs to be strengthened by allocation of appropriate resources to ensure timely reporting, collection of data, and sample collection of all suspect cases
- Laboratory surveillance will need to be strengthened to provide genotype information
- AEFI reporting system already in place. Increase awareness/train clinicians of reporting responsibilities, reporting processes.
- Strengthen communication links in area of AEFI reporting to appropriate stakeholders (NIAC, HPSC, NIO)
- Training of primary care, hospital and public health clinicians on clinical, public health and laboratory aspects of measles and rubella through professional groups, journals, relevant media

10.5. Improve availability of high quality, valued information for health professionals and the public on the benefits and risks associated with immunisation against measles and rubella

Necessary action points

- Develop appropriate and targeted educational materials for strategy and campaign to inform health professionals and public about campaign
- Increase accessibility of accurate and up to date information at all levels
- Provide rapid, accurate and up to date information, responsive to expressed concerns. Lessons learned from the media scares alleging links between MMR

and autism/inflammatory bowel disease are that information needs to be rapidly disseminated to key health professionals who are directly involved in patient care or responding to public concerns.
- Telephone helplines provide useful and rapid access for parents seeking information and should be provided during campaign activities

WHO targets for sero-immunity to measles

To prevent measles outbreaks, the World Health Organisation (WHO) has set a target for the proportion of measles non-immune by age group.

WHO recommendations for proportion of population non-immune to measles
- < 15% of children (2-4 years of age)
- < 10% of children (5-9 years of age)
- < 5% in the older age groups.

The results reported in the ESEN2 study and used in the model by Cfi, HPA clearly indicate that susceptibility in 11-14 year olds and in pre-school children exceeds the WHO targets set. To achieve satisfactory sero-immunity levels in these age groups will require a catch-up campaign in Ireland.

10.6 Recommendations of the Committee

Having reviewing the two recommended strategies (A or B) and taking into account the ongoing mumps outbreak in third level colleges since 2004 the Committee recommends that a comprehensive vaccination strategy be adopted aimed at all students aged 4-18 years of age. Such a campaign will increase the proportion of children in the 4-18 year age group who are measles sero-immune.

10.7 Maintaining a High Vaccine Uptake

For successful measles control, immunisation of at least 95% of susceptible targets is required with a two-dose MMR schedule. Vaccine records should be accessible and allow timely identification and follow-up of non-immune children. Children who have successfully attained age appropriate vaccines by two years of age should be provided with a vaccine certificate/parent-held child health record. All children in day care centres, nurseries and schools should have age appropriate proof of immunisation monitored annually.

10.8 Immunisation Registers

HSE areas currently have a variety of electronic or paper based systems in place for the recording of childhood immunisations. These individual client immunisation records include date of birth and age at receipt of vaccine, batch number, expiry date and date of administration of all vaccines and all antigen combinations. There are currently 50 independent databases in use which are not interlinked and in the majority of areas primary and school records are maintained separately.

The National Immunisation Office is currently working on a national immunisation registry project whereby all immunisation records will be linked to a unique

identifying number. This system will be able to capture all immunisations from birth to adulthood. Such a system will allow the development of standardised timing and methods for assessment of vaccine coverage and provide comparable national data for analysis. However, it will be at least two-three years before such a system is in place. In the meantime, all HSE areas should give high priority to improving the quality on their current systems (in terms of completeness, accuracy and availability of data in a timely manner) in order to improve immunisation information necessary for programme monitoring and targeted activities.

Key recommendations

1. Immunisation uptake of at least 95% is required with a two-dose MMR schedule

2. All vaccinated children should be provided with a vaccine certificate/parent-held child health record.

3. All HSE areas should give high priority to improving the quality on their current systems

4. All children in care and educational settings should have age appropriate proof of immunisation monitored annually.

11. RECOMMENDED INVESTIGATION AND CONTROL MEASURES

As already outlined, each HSE Area already has in place systems and protocols for investigating and implementing measles control activities.

The following is a summary of required activities.

11.1 Improving surveillance

Surveillance depends on health care providers reporting all cases of measles to local health authorities. As the incidence of measles declines, aggressive surveillance becomes increasingly important.

It is essential that every case be reported so that trends and risk factors can be documented to guide the development of control policy. Effective surveillance can detect inadequate levels of protection, define groups needing special attention and is important in evaluating the effectiveness of control activities.

All cases and outbreaks should be reported in the first instance to the local Medical Officer of Health (Departments of Public Health) that in turn report to HPSC.

Rapid investigation is required

- History taking
- Full demographic and clinical details on all suspect case
- Determination of vaccination status
- Laboratory confirmation (see appendix for guidelines)

Enhanced Measles surveillance information should be collected on all cases (see form appendix).

Isolate the case while infectious

Additional activities in investigation include

- Follow-up of all contacts, identify non-immune and immunise as necessary
- Organisation (and delivery if required) of vaccination activities in wider setting (e.g. school)
- Active surveillance for other cases in community
- Follow-up of laboratory results
- Reporting requirements locally, nationally and internationally

11.2 Outbreak investigation

A measles outbreak is defined as the occurrence of any number of measles cases including one or more locally acquired cases. Because investigating an outbreak requires many person-days of work personnel are often transferred to the activity from other responsibilities in the HSE Departments of Public Health or Local Health Office areas. Therefore, they may only be involved in outbreak investigation for a few days before someone else replaces them. This turnover in personnel during the investigation may cause problems unless activities are organised so that the status of the investigation is documented at all times.

The case investigation described in the previous section should be followed.

Some additional practical suggestions for organising the information that results from outbreak investigations are outlined as follows.

Recordkeeping

1. Departments of Public Health should use the Computerised Information System (CIDR) for inputting all their data (for CIDR using sites). Non-CIDR using sites should enter the case into their notification database.

2. A logbook (or spreadsheet) to record all suspected cases as they are received is also recommended (particularly for non-CIDR using sites). The person who receives the initial call should attempt to obtain the information needed to fill in the line listing.

3. Create a column in the logbook for actions required for each suspected case ("get specimens", "phone GP for vaccination history", "check contacts" etc.).

4. Identify a team leader for case investigators so that at least one person knows about all the new cases called in that day and what still needs to be done. Daily briefings are a good way of keeping the whole staff informed of the status of the investigation.

5. Keep the logbook, in one well-defined location, preferably with folders with the case investigations of all the cases that have been reported. It is useful to have one group/stack of all the confirmed cases, one group of suspected or probable cases awaiting further investigation or laboratory results, and a separate group of discarded cases. The latter are very useful for reassuring people who call the health department concerned that they have been exposed to measles. Track the information on a line listing on a computer database or hand written form (see Linelisting in Appendix).

Establish Local Protocols

1. Establish protocols for control measures for all likely situations (e.g. exposure in a day care centre, school, surgery, workplace, etc.) and clearly define who will make the decision that might require major investment of resources (such as vaccinating a whole school).

2. Local GPs should have a protocol for dealing with suspect cases and contacts; HSE areas should consider providing a helpline for concerned parents. Active surveillance should be maintained until at least one month after the last confirmed case is reported.

Identify the population affected by the outbreak.

Case investigation

Every suspected case should be investigated thoroughly. Although in very large outbreaks this may not be possible. In such situations a sample of cases should be thoroughly investigated to describe the epidemic. The population affected should be described in terms of:

Person (who is contracting measles and how many have had zero, one or two doses of measles containing vaccine?)
Place (where are the cases?)
Duration (when did it start and is it still going on?).

These are the essential elements that allow public health specialists to determine the population at risk (unvaccinated pre-school children, secondary school children who received one dose MMR etc), and to determine where transmission is occurring (day care centres, schools, health care settings).

Finally, resources that are available for outbreak control are always limited and are most effectively targeted when based on epidemiological data. In large outbreaks investigations should be most thorough at the start and end of the outbreak (to guide initiation and cessation of control measures).

Outbreak control in high risk settings /population groups

High risk settings are considered to be those which have population groups considered to be at particular risk of measles-associated complications (e.g. young children, adults 20 years of age, older pregnant women, immunocompromised individuals). Such settings include schools, day care centres, hospitals and other institutions.

The primary strategy for preventing measles outbreaks is achieving a high level of immunity in the population in which the outbreak is occurring; this is achieved with high coverage with two doses of measles containing vaccine. Only vaccine histories with written evidence of the date of receipt of vaccine should be accepted as valid. Persons who have not been immunised should be offered immunisation. Persons who cannot be immunised for medical or other reasons should be advised that they are at risk in affected institutions (e.g. schools, day care centres etc) until 21 days after the onset of rash in the last case of measles and they should consider staying away for this period.

If many confirmed cases are occurring in infants under 12 months, measles vaccination of infants as young as six months may be undertaken as an outbreak

control measure. Children vaccinated before the first birthday should be revaccinated when they are 12-15 months old and again when they are four to five years of age.

Control of outbreaks in schools

Recent experience in the United States has shown that measles outbreaks do not occur in schools whose pupils have received two doses of vaccine as a pre-requisite for school entry.[27] In 2002 the National Immunisation Advisory Committee of the Royal College of Physicians of Ireland (RCPI) recommended a reduction of age of second MMR dose to four to five years. A catch-up programme was implemented in most areas. The vaccination status of all children in the affected school or institution should be assessed, and all born after 1978 should complete the two-dose schedule of MMR (the second dose given at least a month after MMR_1). Adults born before 1978 have a high probability of measles immunity due to exposure to wild type virus. The findings in the ESEN2 study support this. A study by Johnson et al in Dublin in 1991/1992 demonstrated 95% seroprevalence of measles antibodies in 11-14 year old children (born 1977-1980).

Control of outbreaks in day care centres

During an outbreak in a day care centre/crèche, vaccination with MMR is recommended for all those attending and their siblings who have not received two doses of measles containing vaccine on or after the first birthday and who do not have other evidence of measles immunity. MMR vaccine may be given to children as young as six months of age. However, the presence of maternal antibodies may compromise the response to the vaccine. Therefore children vaccinated before their first birthday should have a repeat vaccination at 12-15 months of age, at least one month after the first vaccine with a further dose at 3-5 years of age.

Staff born after 1978 who cannot provide acceptable evidence of immunity (positive serology or documented evidence of MMR vaccination with two doses measles containing vaccine) also should be vaccinated with MMR. Vaccination should also be considered for unaffected childcare facilities in the community that may be at risk for measles exposure and transmission.

During outbreaks in schools and other educational facilities, vaccination with MMR is recommended in the involved schools. Vaccination of students and staff in unaffected schools in the same geographic area who may be at risk for measles transmission may also be considered. For persons born after 1978 adequate vaccination consists of two doses of measles containing vaccine separated by at least 28 days with the first dose administered no earlier than the first birthday.

Control of outbreaks in health care settings

All health care workers born after 1978 should have proof of immunity or evidence of MMR vaccination with two doses of vaccine. If an outbreak occurs in an institution or in an area served by the institution all personnel should receive a dose of MMR if they cannot satisfy the above criteria. Serological testing of staff during an outbreak is not generally recommended. Serological testing of staff may be considered for those staff that are unable to receive the vaccine due to pregnancy or other contraindications. Susceptible staff should be excluded from contact with suspect cases. All elective admissions to an institution associated with a current measles outbreak should be immunised prior to admission – preferably with two doses of MMR. Unimmunised

children who require urgent admission should be immunised if there are no contra-indications. All long-term patients born after 1978 attending the health care facility associated with an outbreak should have their immunisation status checked and vaccinated if necessary.

Susceptible personnel (i.e. those born after 1978 who do not have evidence of two doses of MMR vaccine or who have no serological evidence for immunity to measles) who have been exposed to measles should be removed from patient contact and excluded from the 5th to the 21st day after exposure, regardless of whether they received vaccine or immunoglobulin (see below) after the exposure. Personnel who become ill should be removed from all patient contact and excluded from work for seven days after they develop the rash.

Post-exposure vaccination and use of immunoglobulin to prevent measles in susceptible exposed persons

If given within 72 hours of exposure to measles, measles vaccine may provide some protection. In most settings, post-exposure vaccination is preferable to the use of human normal immunoglobulin (HNIG).

The following children and adults who come into contact with measles should be considered for treatment with human normal immunoglobulin (HNIG) as soon as possible after exposure (at least within 5 days):

1. those with compromised immunity (including non-immune pregnant women)
2. infants aged 5-11 months (those aged <5 months will usually have maternal antibodies)
3. infants of mothers who develop measles, as such infants will not have maternally derived antibodies.

Although administration should not wait for laboratory confirmation of measles in the index case, a complete risk assessment should be undertaken prior to administration of the HNIG.

Human Normal Immunoglobulin (HNIG) for intramuscular use

HNIG is available in two, five and 10ml vials. It is given by deep intramuscular injection. It should be stored at 0-4°C and the expiry date on the package observed. Unused portions of an ampoule must be discarded. As recipients of intramuscular immunoglobulin can experience local pain and discomfort at the injection site, it should be administered deep into a large muscle mass, such as the gluteal region. Ordinarily, no more than 5ml should be administered at any one site. Intramuscular HNIG should not be administered to any patient with severe thrombocytopenia or with a coagulation disorder. Caution should be exercised with any patient who has a history of adverse experience following HNIG administration.

The usual recommended dose of HNIG is 0.25mL/Kg of body weight (maximum dose = 15mls). However, the recommended dose of IG for immunocompromised persons is 0.5mL/kg of body weight (maximum dose=15mls).

If HNIG is not available, in certain high-risk situations IVIG can be given, as it usually contains similar measles antibody levels to HNIG.

Those contacts on maintenance IVIG do not need either HNIG or IVIG if they have been given IVIG within 3 weeks prior to exposure.

Any person exposed to measles that lacks evidence of measles immunity and to whom HNIG is administered should subsequently receive MMR vaccine, which should be administered no earlier than three months (ideally five to six months) after HNIG administration, provided the person is then aged greater than or equal to 12 months and the vaccine is not otherwise contraindicated.

SECTION 4. EXPERT GUIDANCE

ECDC case definitions

From 2007 onwards the following case definition will be used at the EU level pending endorsement from the EU commission. It is proposed that this definition replaces the measles case definition outlined in *Case Definitions for Notifiable Diseases* (*2004).*

MEASLES CASE DEFINITION (ECDC 2007)

Clinical criteria:
Any person with:
- Fever, **and**
- Maculo-papular rash, **and** at least one of the following three:
- Cough, coryza or conjunctivitis

Laboratory criteria:
At least one of the following four:
- Isolation of measles virus from a clinical specimen
- Detection of measles virus nucleic acid in a clinical specimen
- Measles virus specific antibody response in serum or saliva
- Detection of measles virus antigen by DFA in a clinical specimen using measles specific monoclonal antibodies

Laboratory results need to be interpreted according to the vaccination status

Epidemiological criteria:
An epidemiological link by human-to-human transmission

Additional information
Incubation period 7-18 days, most often 10 days

Case classification:
A. Possible case
Any person meeting the clinical criteria
B. Probable case
Any person meeting the clinical criteria and with an epidemiological link
C. Confirmed case
Any person not recently vaccinated and meeting the clinical and the laboratory criteria

In case of recent vaccination:
Any person with identification of wild-type measles virus strain

Measles outbreaks

In case of an outbreak, many cases may not be tested. However the notification of these cases is still needed for the surveillance of the disease. Therefore HPSC asks for reporting of all cases (possible, probable, confirmed).

ICD-10:
B05.0 Measles complicated by encephalitis
B05.1 Measles complicated by meningitis
B05.2 Measles complicated by pneumonia
B05.3 Measles complicated by otitis media
B05.4 Measles with intestinal complications
B05.8 Measles with other complications
B05.9 Measles without complication

RUBELLA (RUBELLA VIRUS) CASE DEFINITION (ECDC 2007)

Clinical criteria:

Any person with sudden onset of generalised maculo-papular rash
and at least one of the following five:

- Cervical adenopathy
- Sub-occipital adenopathy
- Post-auricular adenopathy
- Arthralgia
- Arthritis

Laboratory criteria:

Laboratory criteria for <u>case confirmation</u>

At least one of the following three:

- Isolation of rubella virus from a clinical specimen
- Detection of rubella virus nucleic acid in a clinical specimen
- Rubella virus specific antibody response (IgG) in serum or saliva

Laboratory criteria for <u>probable case</u>

- Rubella virus specific antibody response (IgM*)

Laboratory results need to be interpreted according to the vaccination status

**Important Note:*
When rubella in pregnancy is suspected, further confirmation of a positive rubella IgM results is required (e.g. a rubella specific IgG avidity test showing a low avidity). In certain situations, such as confirmed rubella outbreaks detection of rubella virus IgM can be considered confirmatory in non-pregnant cases

Epidemiological criteria:

An epidemiological link by human-to-human transmission

Additional information

Incubation period 14 - 21 days

Case classification:

A. Possible case

Any person meeting the clinical criteria

B. Probable case

Any person meeting the clinical criteria and with at least one of the following two:
- An epidemiological link
- Meeting the laboratory criteria for a probable case

C. Confirmed case

Any person not recently vaccinated and meeting the laboratory criteria for case confirmation. In case of recent vaccination, a person with detection of wild-type rubella virus strain

Disease specific: Rubella

Biologists consider rubella IgM detection as non specific enough to confirm a rubella infection because of frequent cross reactions with rheumatoid factor and Parvovirus B19. When the diagnosis is crucial for the patient (such as in case of pregnancy), that test alone cannot confirm the disease. However notification of positive rubella IgM clinical cases is necessary for the epidemiological surveillance of the disease.

ICD-10:
B06 Rubella [German measles]
B06.0 Rubella with neurological complications
B06.8 Rubella with other complications
B06.9 Rubella without complication
M01.4A Rubella arthritis

CONGENITAL RUBELLA INFECTION (INCLUDING CONGENITAL RUBELLA SYNDROME) CASE DEFINITION (ECDC 2007)

Clinical criteria:
Congenital rubella infection (CRI)
No clinical criteria can be defined for CRI

Congenital rubella syndrome (CRS)
Any infant < 1 year of age or any stillborn with:
- At least two of the conditions listed in (A)

OR

- One in category (A) and one in category (B)

(A)
- Cataract(s)
- Congenital glaucoma
- Congenital heart disease
- Loss of hearing
- Pigmentary retinopathy

(B)
- Purpura
- Splenomegaly
- Microcephaly
- Developmental delay
- Meningo-encephalitis
- Radiolucent bone disease
- Jaundice that begins within 24 hours after birth

Laboratory criteria:
At least one of the following four:
- Isolation of rubella virus from a clinical specimen
- Detection of rubella virus nucleic acid
- Rubella virus specific antibody response (IgM)
- Persistence of rubella IgG between 6 and 12 months of age (at least two samples with similar concentration of rubella IgG)

Laboratory results need to be interpreted according to the vaccination status

Epidemiological criteria:
Any infant or any stillborn born to a woman with a laboratory confirmed rubella infection during pregnancy by human-to-human transmission (vertical transmission)

Case classification (CRI/CRS):
A. Possible case
NA
B. CRI Probable case

Any stillborn or infant either not tested OR with negative laboratory results with at least one of the following two:

- An epidemiological link AND at least one category “A” CRS clinical criteria
- Meeting the clinical criteria for CRS

C. CRI Confirmed case

Any stillborn meeting the laboratory criteria

OR

any infant meeting the laboratory criteria AND at least one of the following two:

- An epidemiological link
- At least one category “A” CRS clinical criteria

An infant with positive laboratory criteria only without a history of rubella in the mother during the pregnancy and without “A” clinical criteria will therefore be reported as rubella case.

ICD-10:

No specific code for congenital infection.
Included in Rubella infection: B06.0 – B06.9, M01.4A
P35.0 Congenital rubella syndrome

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Measles Enhanced Surveillance Form

hpsc

HSE Area Use Only

Patient Name _____ Address _____ Phone _____

(This section is for HSE Area use only and should not be sent to HPSC)

PATIENT DETAILS

ID No. | Initials | HSE Area | CCA | County

Sex: M ☐ F ☐ NK ☐ DOB | Age (Please state whether Years or Months) | Not Known = NK | Nationality

Reporting GP/Consultant/Lab/Hospital _____ Date of Notification

CLINICAL DETAILS

	Yes	No	Not Known
Morbilliform Rash	☐	☐	☐
Fever at Time of Rash Onset	☐	☐	☐
Cough	☐	☐	☐
Coryza	☐	☐	☐
Conjunctivitis	☐	☐	☐
Koplik's Spots	☐	☐	☐
Underlying Illness	☐	☐	☐

Date of Onset of Symptoms

Date of Rash Onset

Rash Duration **(days)** Not Known = NK

If **Yes** please specify

COMPLICATIONS

	Yes	No	Not Known
Hospitalised	☐	☐	☐
Pneumonia	☐	☐	☐
Encephalitis	☐	☐	☐
Seizures	☐	☐	☐

If **Yes**, Name of Hospital

No. of Days Hospitalised Not Known = NK

Other complication, please specify

Outcome: Recovered ☐ Died ☐ Not Known ☐

Date of Death Cause of Death

LABORATORY

Was laboratory testing for measles done?	Yes	No	Not Known	Date Specimen Taken	Result
Salivary Testing	☐	☐	☐		
Blood for serology	☐	☐	☐		
Culture	☐	☐	☐		

If laboratory confirmed, date of 1st positive test

EPIDEMIOLOGICAL

Date Investigation Started

Where did they most likely acquire measles?

	Yes	No	Not Known
Is this case epidemiologically linked?	☐	☐	☐
Was it linked to an imported case?	☐	☐	☐
Is this case related to an outbreak?	☐	☐	☐
Did case arrive from overseas 8 - 17 days before rash onset?	☐	☐	☐

Outbreak Name/Number

If yes, country arriving from

VACCINATION

	None	One	Two	Not Known	Manufacturer	Batch Number
Number of Doses of MMR	☐	☐	☐	☐		
Date of 1st MMR						
Date of 2nd MMR						

FINAL CASE CLASSIFICATION

Laboratory Confirmed ☐ Epi-linked to Laboratory Confirmed Case ☐ Possible ☐

	Yes	No	Not Known
Preventable	☐	☐	☐
Denotified	☐	☐	☐

Rationale for De-notification

ALTERNATIVE DIAGNOSIS

Rubella ☐ Parvovirus ☐ Not Known ☐ Other

Form Completed by: **Date of Completion**

LABORATORY DIAGNOSIS OF MEASLES INFECTION

Laboratory diagnosis of measles is based on one of the following:

Antibody investigations

- *Positive IgM antibody*
- *Significant increase in IgG antibody between acute and convalescent specimens or seroconversion to IgG*
- *Detection of measles RNA*
- *Isolation of measles virus from clinical specimen*

Table 1. Measles laboratory testing, specimen required and optimal timing of sample

Virus	Investigation*	Specimen required (optimal timing of sample, days after onset)
Measles	IgM detection	Serum >200µl (>4d to 2-3 months), Oral fluid ('Oracol'*) (>7d to 2 months)
	PCR / genotyping	Throat swab (<7 days); Oral fluid ('Oracol'*) (up to 5 days)
	Virus isolation	Throat swab, (up to 5 days) Urine; (up to 2 weeks)

Antibody testing is the most frequently used test to confirm acute measles infection. In specific situations PCR/genotyping or cell culture is performed following consultation with the NVRL.

If SSPE is suspected, contact the NVRL to discuss the appropriate samples to collect.

Antibody investigations on either serum or oral fluid samples

Antibody investigation on either serum or oral fluid samples is the most common method used to diagnose measles infection. IgM antibodies usually become detectable in serum after four days post illness and can be detected for 2-3 months. Diagnosis based upon IgG testing requires the identification of seroconversion to measles IgG or the detection of a significant increase in antibody between an acute and convalescent sample separated by 2 weeks. IgM can be detected in oral fluid samples between 7 days (in 80% cases at time of rash onset) and 2 months post disease manifestations. Enzyme immunoassays (EIAs) are used for diagnosing acute measles, by the detection of IgM or a rise in IgG titre, or immunity to measles by the detection of IgG.

Molecular investigation
Measles RNA can be detected in oral fluid and throat swabs up to 5 days post disease manifestation

Isolation of measles virus
Measles virus can be isolated from clinical specimens, including
Throat swab: collected up to 5 days post rash development
Urine: Up to 2 weeks post rash

Specimen collection

Obtaining specimens for virus isolation

Efforts should be made to obtain clinical specimens (throat swabs, oral fluid and urine) for viral isolation for at least some cases in each outbreak at the time of the initial investigation.

Clotted Blood

For serological investigations serum samples (>1ml) or 1 x 5 to 10ml container of clotted blood should be sent to the NVRL.

Oral fluid (Saliva) specimens

Oral fluid (Saliva) specimens should be collected using a foam swab (Oracol) supplied by the NVRL or using commercially available collection devices. The kit consists of an absorbent foam swab (designed to collect up to 1 ml of saliva), centrifuge tube and cap. Please contact the Serology laboratory with queries (Tel: 01 716 1626).

Urine

10 to 20ml of urine should be sent in a sterile container. Specimens should be transported without delay, ideally at $4^{o}C$.

Collection and transport of specimens

Specimens must be collected in appropriate plastic leak proof containers with a screw top lid. The containers should be clearly labelled with patient details (name/DOB) and dated. They should then be placed inside another plastic leak proof container of suitable strength. Glass containers must not used. Specimens suspected of containing a blood borne virus e.g. HIV or Hepatitis B should be labelled with a biohazard-warning sticker.

All pathological material should be packaged and transported according to the requirements of current legislation. Advice on packaging and transport is available from the NVRL

Please avoid use of staples for closure of packages, as these present a safety hazard to the laboratory staff.

Specimens accompanied by their appropriate request forms should reach the NVRL with minimum delay.

Useful contact numbers:

NVRL Serology laboratory Telephone: 01 716 1626

Laboratory Diagnosis of Rubella Infection

Laboratory diagnosis of Rubella is based upon:

Antibody investigations
Positive IgM antibody
Significant increase in IgG antibody between acute and convalescent specimens or seroconversion to IgG
Detection of Rubella RNA

Table 1. Rubella laboratory testing, specimen required and optimal timing of sample

Virus	Investigation*	Specimen required (optimal timing of sample, days after onset)
Rubella	IgM detection	Serum >200µl (>4d to 2-3 months), Oral fluid ('Oracol') (> 7 days to 2 months)
	PCR/ genotyping	Thoat swab (<7 days); Oral fluid ('Oracol') up to 5 days If congenital infection suspected contact NVRL for appropriate serological and molecular investigations

Antibody investigations on serum

Serological investigation using serum is the method used to diagnose rubella infection at the NVRL. IgM antibodies usually become detectable in serum after four days post illness and can be detected for 2-3 months. Diagnosis based upon IgG testing requires the identification of seroconversion to rubella IgG or the detection of a significant increase in antibody between an acute and convalescent sample separated by 2 weeks. IgM can be detected in oral fluid samples between 7 days and 2 months of disease onset.

Molecular investigation
Rubella RNA can be detected in oral fluid and throat swabs up to 5 days post disease manifestation

If congenital rubella infection is suspected please contact the NVRL so that the appropriate investigations can be performed on both the baby and the mother.

Specimen collection

Clotted Blood

For serological investigations serum samples (>1ml) or 1 x 5 to 10ml container of clotted blood should be sent to the NVRL. Contact the NVRL if it is not possible to collect this volume of blood.

Collection and transport of specimens

Specimens must be collected in appropriate plastic leak proof containers with a screw top lid. The containers should be clearly labelled with patient details (name/DOB) and dated. They

should then be placed inside another plastic leak proof container of suitable strength. Glass containers must not used. Specimens suspected of containing a blood borne virus e.g. HIV or Hepatitis B should be labelled with a biohazard-warning sticker.

All pathological material should be packaged and transported according to the requirements of current legislation. Advice on packaging and transport is available from the NVRL.

Please avoid use of staples for closure of packages, as these present a safety hazard to the laboratory staff.

Specimens accompanied by their appropriate request forms should reach the NVRL with minimum delay.

Useful contacts numbers:

NVRL Serology laboratory Telephone: 01 716 1626

LINE LISTINGS FOR CASE MANAGEMENT DURING OUTBREAKS

Example of line listing for outbreak investigation										
Case ID	**Name**	**Age**	**DOB**	**Rash onset**	**Source of exposure**	**Specimen taken date**	**IgM results**	**MMR_1 date**	**MMR_2 date**	**Case status**

Note: for CIDR using sites, this data, entered into CIDR for each notification can be viewed as a report as frequently as required

Contraindications to MMR vaccine (NIAC guidelines 2007)

1. Immunocompromised persons, such as those with untreated malignant disease and immunodeficiency states other than HIV infection, and those receiving immunosuppressive therapy, high-dose x-ray therapy and current high-dose systemic corticosteroids. (See Chapter 2).
2. Anaphylaxis following a previous dose of MMR or one of its constituents (e.g. neomycin, gelatin).
3. Pregnancy. Furthermore, pregnancy should be avoided for two months after MMR

There is no evidence to recommend or support the use of single vaccines against measles, mumps and rubella in the place of the combination MMR vaccine.

The following are NOT contraindications to MMR vaccine:

1. Allergy to egg, even anaphylaxis. If there is a genuine concern regarding serious allergy, a paediatrician may be consulted and the vaccine given in hospital although this is not medically necessary. Currently used measles and mumps vaccines do not contain significant amounts of egg cross-reacting proteins and recent data suggests that anaphylactic reactions to MMR are not associated with hypersensitivity to egg antigens but to other vaccine components (Gelatin or Neomycin).
2. Breast-feeding
3. HIV positive patients who are not severely immunocompromised.
4. Personal or family history of convulsions. Advice regarding the possibility and treatment of pyrexia should be given.
5. Immunodeficiency in a family member or household contact.

Precautions

1. Moderate/severe illness; defer until recovery.
2. Injection with another live vaccine within the previous four weeks.
3. Recent administration of blood or blood products- see above.
4. Evolving neurological condition; defer until stable.
5. Patients who developed thrombocytopenia within 6 weeks of their first dose of MMR should undergo serological testing to decide whether a second dose is necessary. The second dose is recommended if the patient is not fully immune to the 3 component viruses.

The above information is taken from “Immunisation Guidelines for Ireland” 2007 edition (in press at time of writing).

ADVERSE REACTION REPORT FORM [29]

IN CONFIDENCE

(FOR COMPLETION BY HEALTHCARE PROFESSIONALS)

PLEASE SEND TO:-
FREEPOST
PHARMACOVIGILANCE UNIT
IRISH MEDICINES BOARD
EARLSFORT CENTRE
EARLSFORT TERRACE
DUBLIN 2
Telephone: 353-1-6764971
Fax: 353-**1-6762517**
E-mail: imbpharmacovigilance@imb.ie

REPORTER'S NAME & ADDRESS:

_____

_____

_____

_____

AREA OF SPECIALITY:_____

Patient Initials/Record No:		**Sex: M F**		
Age:		**Weight (if known):**		**Ethnic Origin:**
Indication for Use:				
Suspect Drug/Vaccine: **..1.1.1** *Please use brand names where possible*	**Daily dose**	**Route**	**Batch No.**	**Dates of Treatment**
Suspected Reaction: (Brief description of the toxic effects or side effects)				
Onset of Reaction: (Date)	**Duration of Reaction:**			
Any other drugs used over this period? (Please state below)				
Drug	**Daily Dose**	**Indication for Use:**		
Recovery from Side Effects: **Complete** **Symptoms Continuing** **Fatal** ***(Please circle)*** **If treatment was required please specify*:***				
Drug Discontinued: **Y** **N** **Drug Rechallenge:** **Y** **N** **Improvement on discontinuation** **Y** **N**				
Supply of Report Cards Required: **Y** **N**		**Manufacturer Notified:** **Y** **N**		

Signature: _____ _ __ Date: _____

Thank you for taking the time to complete this form

Further information on ADR reporting is available from the Pharmacovigilance Unit at the IMB at http://www.imb.ie. The IMB Adverse Reporting Form from IMB is shown in the Appendices.

Healthcare professionals may download the ADR report form on the IMB website and forward by Freepost to the following address –

'Freepost', Pharmacovigilance Unit,
Irish Medicines Board,
Earlsfort Terrace,
Dublin 2.
Telephone + 353 1 6764971, Fax + 353 1 6762517

Email enquiries to the Pharmacovigilance unit at imbpharmacovigilance@imb.ie.

PERFORMANCE INDICATORS

1. Outcome indicators

Four outcome indicators will be used to measure progress towards meeting the objectives

Measles incidence < 1 per 1 000 000 population
Rubella incidence < 1 per 1 000 000 population
CRS incidence with CRS < 1 per 100 000 live births
MMR_1 coverage of ≥95% at national level and ≥90% in all areas
MMR_2 coverage of ≥95% at national level and ≥90% in all areas

Reporting requirements

WHO recommends the following data analyses, presentations, reports to review progress on elimination of measles

Mortality reduction phase

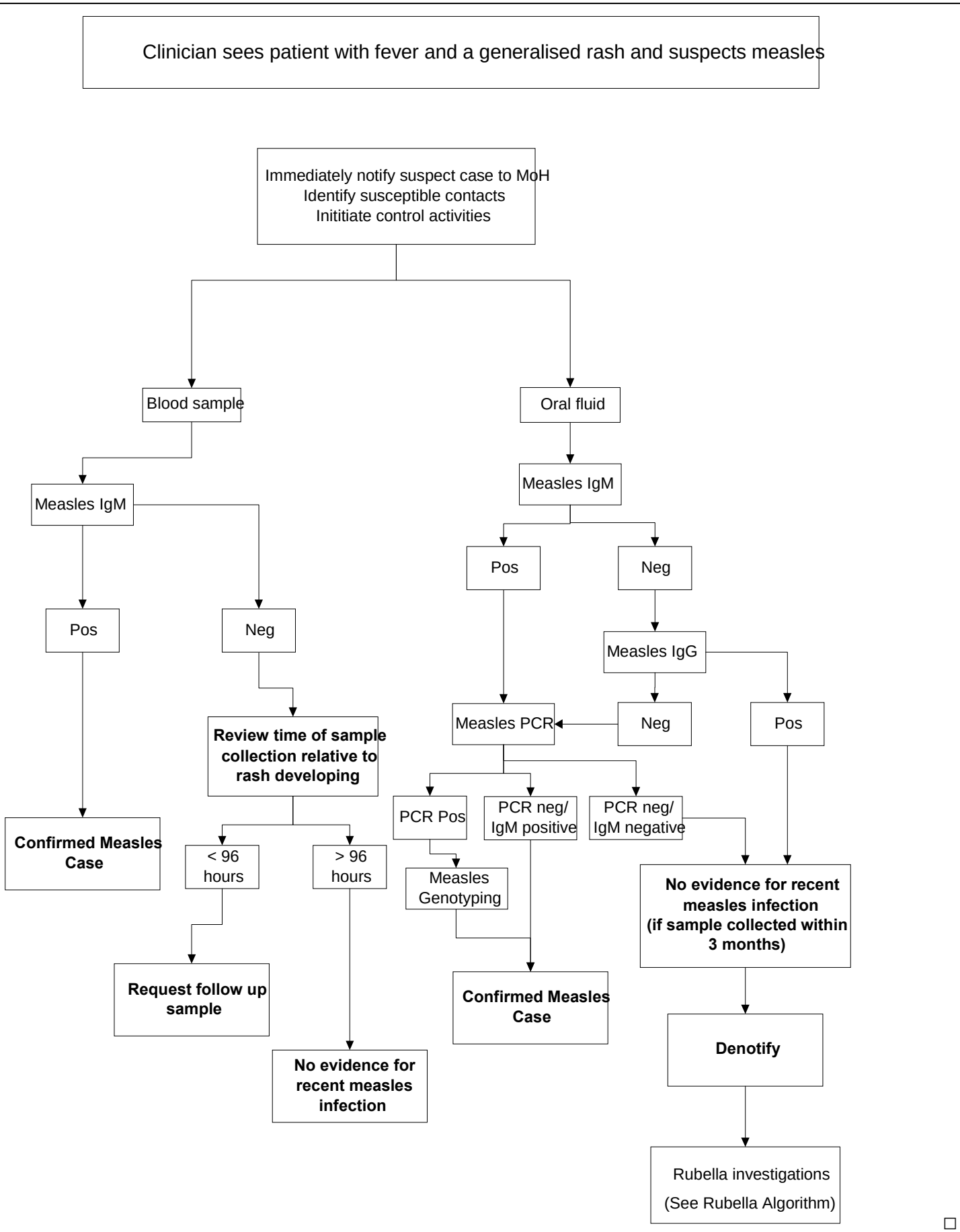
- Number of cases and incidence rate by month and year and geographical area
- Age-specific, sex specific and district specific incidence rates
- Measles vaccine coverage by year and geographical area
- DTP1 – measles or BCG measles drop out rate
- Completeness /timeliness of monthly reporting
- Proportion of known outbreak confirmed by laboratory
- Proportion of cases by age group and immunisation status
- Age groups suggested are
    - 0-8 months, 9-11 months, 1-4 years, 5-9 years, 10-14 years, 15-19 years, 20-24 years, 25 years and over

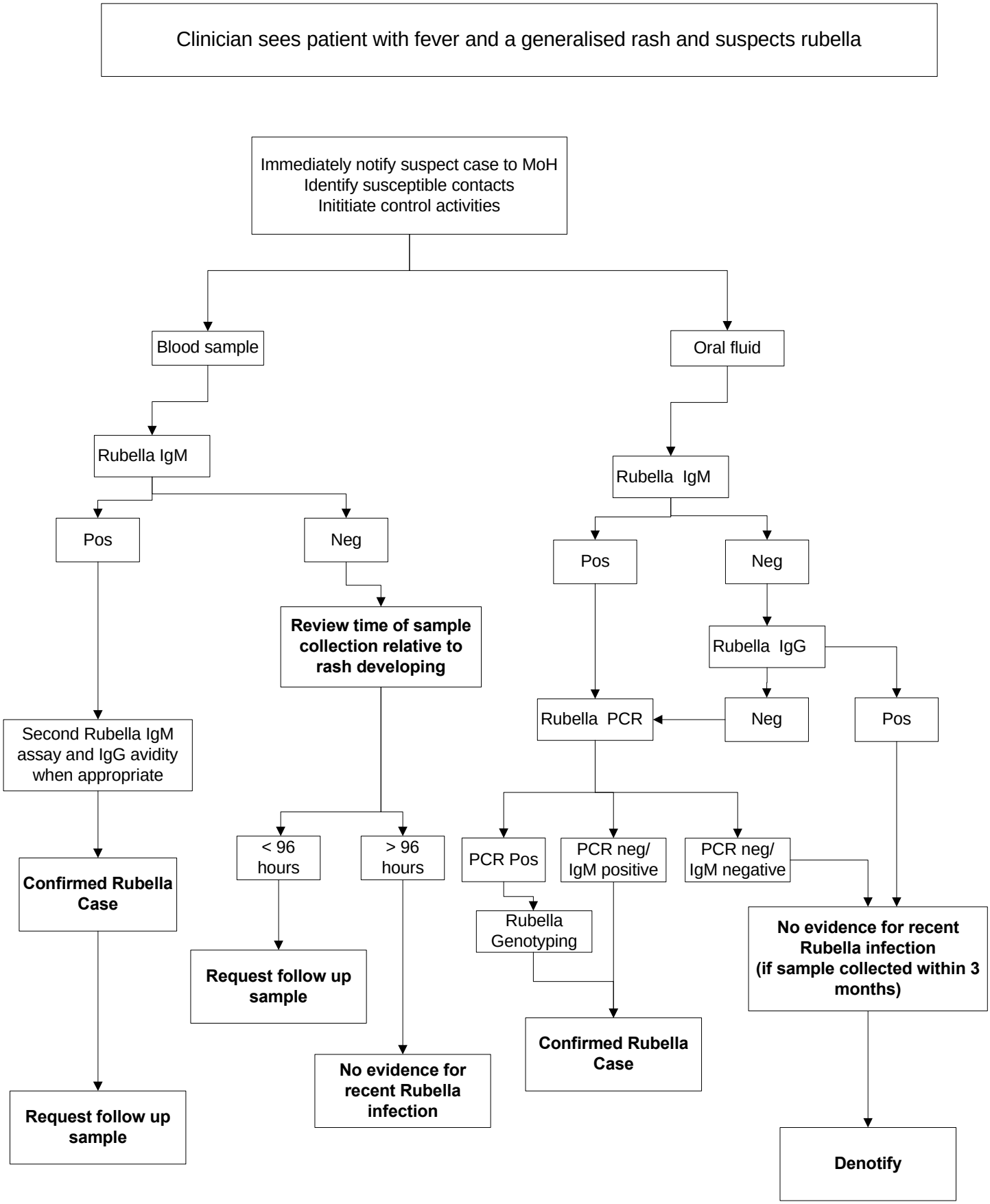
Elimination phase (Stage III)

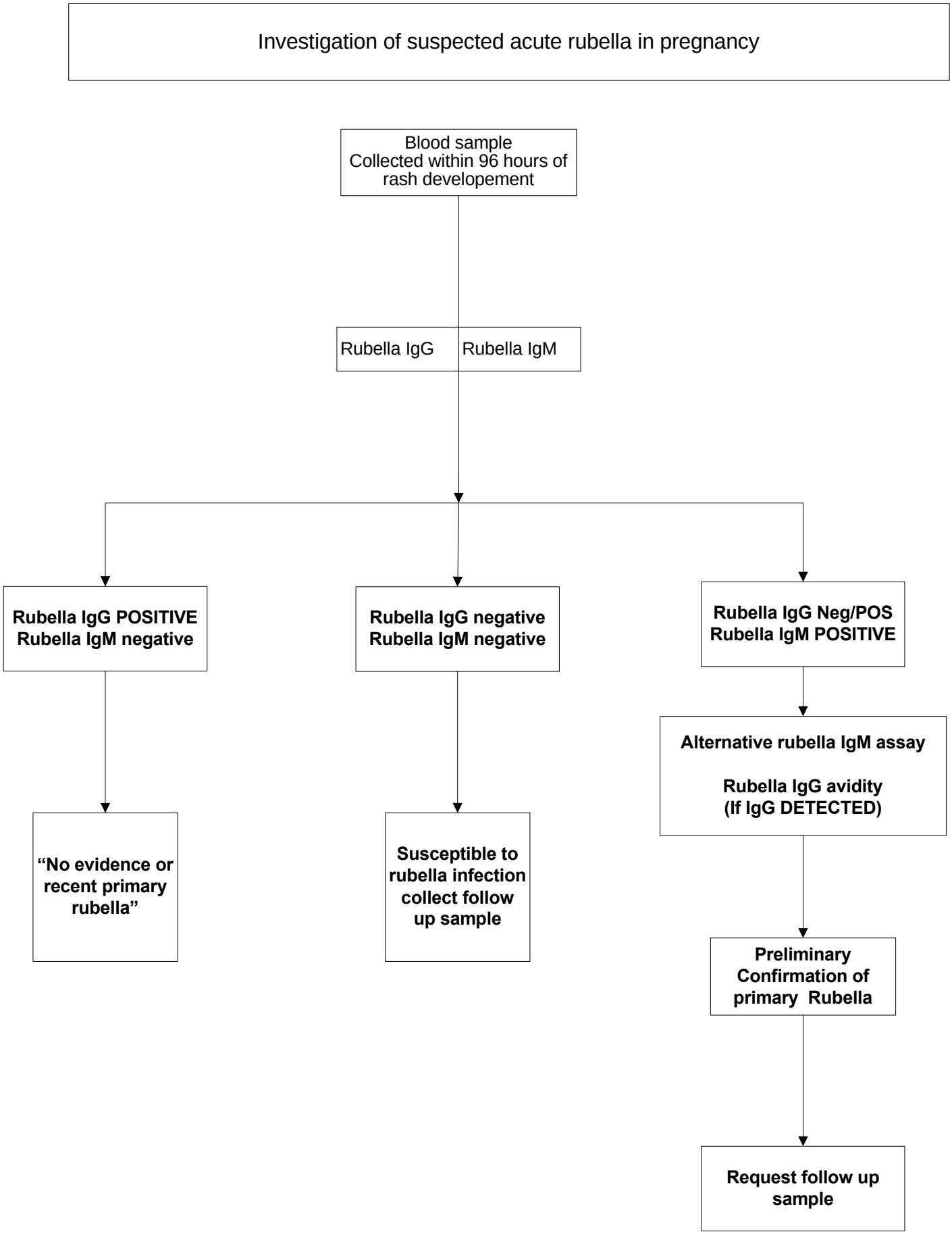
Reporting as for mortality reduction phase plus the following:

Programme performance indicators in elimination phase	Target
% weekly reports received	≥ 80%
% of cases* notified ≤ 48 hours after rash onset	≥ 80%
% of cases* investigated ≤ 48 hours after notification (with personal contact e.g. telephone or house visit)	≥ 80%
% of cases* with adequate specimen** and laboratory results within 7 days	≥ 80%
% of confirmed cases with source of infection identified	≥ 80%

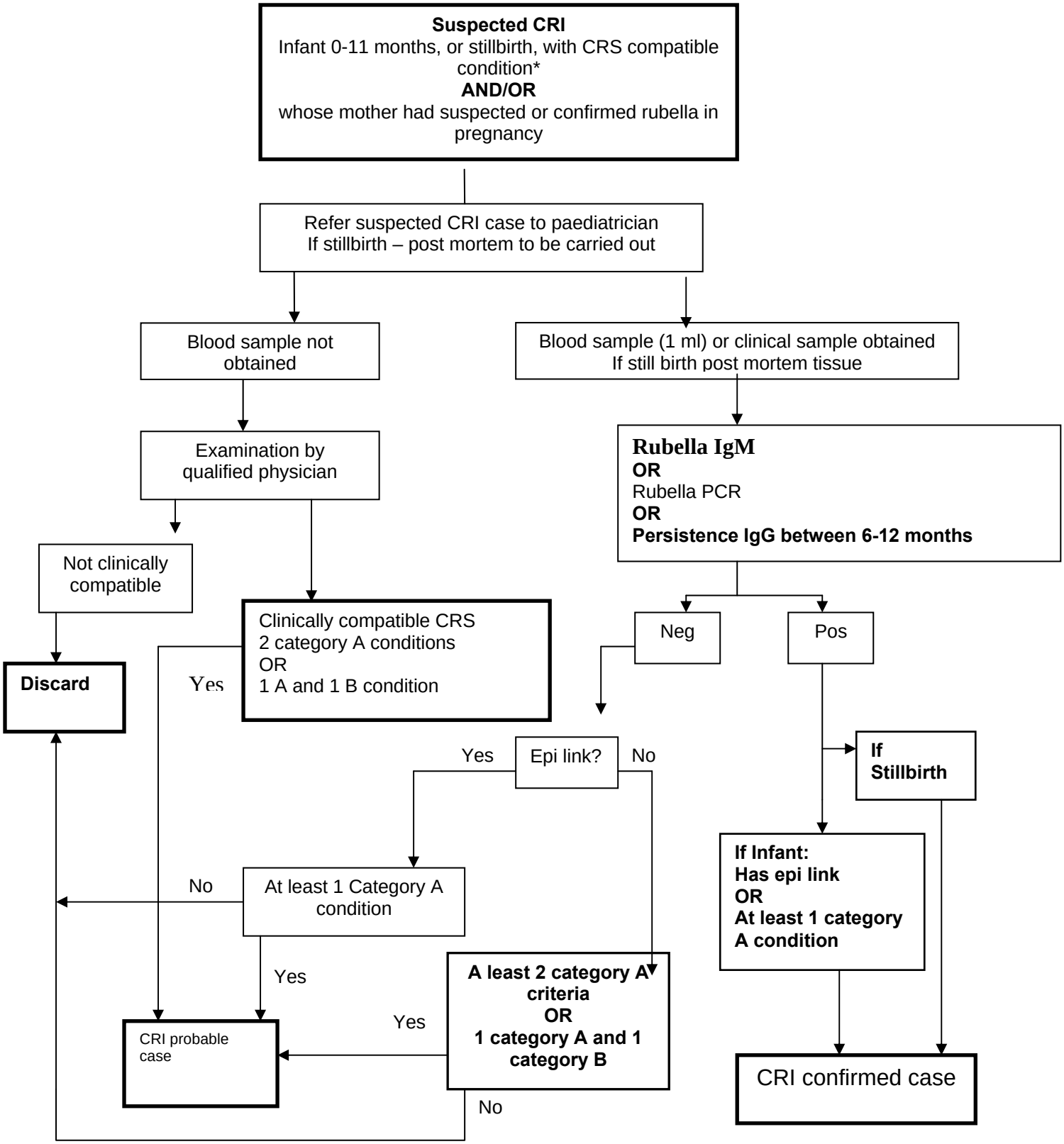
**all cases that meet the clinical definition*
*** an adequate specimen is a blood specimen or oral fluid sample (Oracol) collected within 28 days of the onset of rash*


Clinician sees patient with fever and a generalised rash and suspects measles
Immediately notify suspect case to MoH
Identify susceptible contacts
Inititiate control activities
Blood sample
Oral fluid
Measles IgM
Measles IgM
Pos
Neg
Pos
Neg
Measles IgG
Measles PCR
Neg
Pos
Review time of sample collection relative to rash developing
PCR Pos
PCR neg/ IgM positive
PCR neg/ IgM negative
Confirmed Measles Case
< 96 hours
> 96 hours
Measles Genotyping
No evidence for recent measles infection (if sample collected within 3 months)
Request follow up sample
Confirmed Measles Case
Denotify
No evidence for recent measles infection
Rubella investigations
(See Rubella Algorithm)


Clinician sees patient with fever and a generalised rash and suspects rubella
Immediately notify suspect case to MoH
Identify susceptible contacts
Inititiate control activities
Blood sample
Oral fluid
Rubella IgM
Rubella IgM
Pos
Neg
Pos
Neg
Review time of sample collection relative to rash developing
Rubella IgG
Second Rubella IgM assay and IgG avidity when appropriate
Rubella PCR
Neg
Pos
< 96 hours
> 96 hours
PCR Pos
PCR neg/ IgM positive
PCR neg/ IgM negative
Confirmed Rubella Case
Rubella Genotyping
No evidence for recent Rubella infection (if sample collected within 3 months)
Request follow up sample
No evidence for recent Rubella infection
Confirmed Rubella Case
Request follow up sample
Denotify

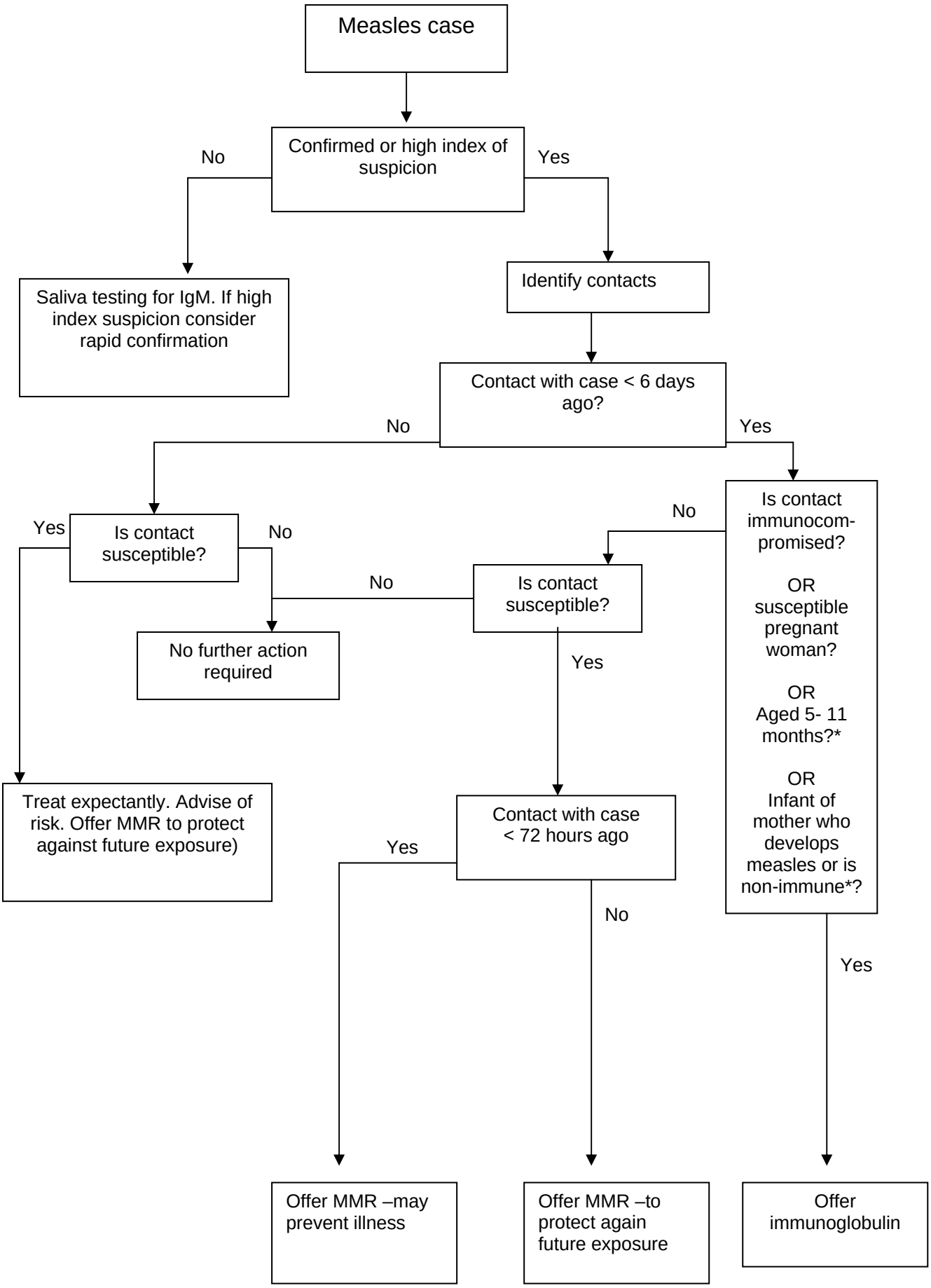

Investigation of suspected acute rubella in pregnancy
Blood sample
Collected within 96 hours of
rash developement
Rubella IgG
Rubella IgM
Rubella IgG POSITIVE
Rubella IgM negative
Rubella IgG negative
Rubella IgM negative
Rubella IgG Neg/POS
Rubella IgM POSITIVE
Alternative rubella IgM assay
Rubella IgG avidity
(If IgG DETECTED)
"No evidence or
recent primary
rubella"
Susceptible to
rubella infection
collect follow
up sample
Preliminary
Confirmation of
primary Rubella
Request follow up
sample

Surveillance of CRI/CRS - after rubella in pregnancy



* see ECDC case definition for Category A and Category B criteria for clinical CRS

Management of measles case contacts



*infants < 5 months usually protected by maternal antibody unless mother was also susceptible (index measles case, incomplete measles immunisation or no history of measles infection)

Guidance derived from National Immunisation Guidelines 2007

Abbreviations and acronyms

CCA	Community Care Area
CDC	Centers for Disease Control and Prevention (United States)
Cfi	Centre for infections (HPA, UK)
CFT	Complement fixation test
CNM	Clinical nurse manager
CRS	Congenital rubella syndrome
CSF	Cerebrospinal fluid
DoHC	Department of Health and Children
EIA	Enzyme-immunoassay
ELISA	Enzyme-linked immunosorbent assay
GP	General Practitioner
HHV6	Human herpes virus 6
HI	Hemagglutination inhibition
HPA	Health Protection Agency (UK)
HPSC	Health Protection Surveillance Centre
HSE	Health Services Executive
IFA	Indirect fluorescent antibody
IG	Immune globulin
IOM	Institute of Medicine
LA	Latex agglutination
LHO	Local Health Offices
MMR	Measles-mumps-rubella vaccine
mL	millilitre
MR	Measles-rubella vaccine
NDSC	National Disease Surveillance Centre (in 2004 name was changed to HPSC)
PCCC	Primary, Community and Continuing Care
PCR	polymerase chain reaction
PHN	Public Health Nurse
PMO	Principal Medical Officer
RNA	ribonucleic acid
RT-PCR	reverse transcription polymerase chain reaction
SPHM	Specialist in Public Health Medicine

SMO	Senior Medical Officer
SpR	Specialist Registrar in Public Health Medicine
SS	Surveillance Scientist
SSPE	sub-acute sclerosing panencephalitis
WHO	World Health Organisation
WHO EURO	World Health Organisation European Region

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