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Foodborne disease undermines consumers' confidence in the food they eat. It causes substantial morbidity in the population and can prove fatal in some cases. Prompt detection and defining the source is imperative if public health interventions are to be effective.

Safefood, the Food Safety Promotion Board has a statutory function to develop a strategy for the effective delivery of a specialised enteric laboratory service for the island of Ireland. The Board has established a multi-disciplinary group, composed of individuals from both jurisdictions with specialist knowledge of enteric pathogens, to consider how this might be taken forward.

The document contains a series of options for the development of specialised laboratory services on the island. The document and the consultation process that follows its circulation have the potential to improve public health, by ensuring that an effective and efficient reference laboratory service is established. The public health benefits that accrue will serve to increase confidence in the food supply on the island.

I commend this paper to you and look forward to your participation in the consultation process.

Dr. Tim Wyatt
Chairman
FSPB Expert Group on Enteric Laboratory Services
1 The Context and the Challenge

In this section we describe the role of the Food Safety Promotion Board and the purpose of this report.

1.1 The Role of the Food Safety Promotion Board (FSPB)

The FSPB was established in December 1999, under the terms of the Belfast Agreement. It is one of six implementation bodies set up under the Agreement. The North/South Ministerial Council gave the FSPB the key role of conducting a cost-benefit analysis of the different ways of meeting the island’s need for enteric reference laboratory services. The FSPB established a functional group on enteric laboratory services under the chairmanship of Dr. Tim Wyatt of the Mater Hospital, Belfast. There are nine other members of the expert group with FSPB providing the Secretariat. The opinions expressed in this document reflect the views of these individual members and are not necessarily representative of their parent organisations.

1.2 The Purpose of this Work

The remit of the group included:

(i) describing current arrangements for the typing of foodborne enteric pathogens in both jurisdictions

(ii) developing and evaluating options for the provision of an improved enteric reference service

(iii) indicating the costs and the benefits associated with each of these options

(iv) advising on the potential for the development of a comprehensive service for the typing of human, food and animal isolates with the aim of promoting better public health

(v) reporting back to the FSPB.

1.3 Our Approach

The expert group worked in the following way:

(i) it examined the current arrangements for identifying the more common microorganisms that cause foodborne disease

(ii) established the range of foodborne pathogens isolated in laboratories in both jurisdictions that require detailed identification

(iii) defined the basic principles and criteria governing an appropriate enteric reference service

(iv) outlined various scenarios for the service and examined the range of options and determined the strengths and weaknesses of each one.

The following report is a summary of the deliberations of the expert group.
2 Food Poisoning - A Serious Issue

In this section we identify the scale of the problem caused by foodborne disease and we give a brief description of the main organisms causing food poisoning.

An outbreak of food poisoning in Lanarkshire, Scotland in 1996 left 21 people dead and more than 100 others hospitalised, some with permanent damage to their health. The infection was caused by E. coli O157 and began when a group of pensioners ate contaminated meat and gravy at a church lunch. The outbreak spread and lasted for several months. A subsequent enquiry criticised the delays in taking and analysing samples from the butcher's shop at the centre of the outbreak. The lack of rapid results slowed down the public health response to the outbreak.

There was a time when gastroenteric illness was considered little more than an inconvenience rather than a cause for concern. The occurrence of a number of high-profile outbreaks of serious illness like the one outlined above has focussed more attention on this important issue globally and the true burden of gastroenteritis is being increasingly recognised.

Large-scale outbreaks have occurred on the island of Ireland too. During 2000 and 2001 in Northern Ireland, three outbreaks of cryptosporidiosis occurred as a result of public water supplies becoming contaminated. In total, there were 476 confirmed cases, 68 of whom required hospitalisation. In the Republic of Ireland also in 2000, Salmonella Typhimurium in a cooked ham product caused illness in 78 people; 27 were hospitalised. In the west of Ireland in 2001, 462 customers at a hotel suffered from viral gastroenteritis. The source of the outbreak was traced to Norwalk-like virus (NLV; also known as small round structured virus (SRSV)) contamination of the hotel's water supply. And in another outbreak in the Republic of Ireland in 2000, 125 people became ill after consuming shellfish contaminated with NLVs.

The evolution of new strains of micro-organisms, globalisation of the world's food supply, the increase in large-scale production and processing of food, increased international travel, and improved diagnosis and reporting of gastroenteric illness have all contributed to the rise in the reported incidence of foodborne illness globally.

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* e.g. Salmonella Typhimurium DT104 and E. coli O126
There is also a greater appreciation of the socio-economic impact of foodborne illness. Costs to be considered include treatment costs, product recalls in the food industry, the effect of the loss of public confidence on businesses in the food and tourism sectors and more recently, disruption to hospital services.

In this chapter, the main causes of foodborne enteric illness, the disease burden on the island and socio-economic impact of gastroenteric illness are outlined.

2.1 The Main Causes of Gastroenteric Illness

The main organisms implicated in gastroenteritis are listed below. You will find further details in Appendix 2.

2.1.1 Bacterial agents of gastroenteric infections

Many of the most clinically significant and prevalent organisms causing gastroenteritis are bacterial. These include well-recognised bacteria such as Salmonella and Listeria, as well as agents such as Campylobacter and Verocytotoxigenic E.coli (VTEC) O157. The latter two have emerged as significant causes of foodborne disease in recent years. Campylobacter is the now single biggest cause of food poisoning both in the north and south of Ireland. Outbreaks attributed to Campylobacter, however, are uncommon. Conversely, Salmonella, another major cause of food poisoning, has been implicated in several foodborne disease outbreaks but its significance is declining in the last couple of years. While the number of cases of VTEC and Listeria infections are low, these organisms can cause severe illness and death can occur. The numbers of reported cases in 2000 of these bacterial causes of enteric illness are listed in Table 1.

<table>
<thead>
<tr>
<th>Causative Agent</th>
<th>Number of reported cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter spp.</td>
<td>2621</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>1084</td>
</tr>
<tr>
<td>Verocytotoxigenic E. coli O157</td>
<td>89</td>
</tr>
<tr>
<td>Listeria spp.</td>
<td>11</td>
</tr>
</tbody>
</table>
2.1.2 Viruses as agents of gastroenteritis
There is increasing recognition of the role of viruses in gastroenteric illness. The most significant gastroenteric viruses in both Northern Ireland and the Republic of Ireland are NLVs, with rotavirus common among infants. As many as 27 outbreaks of gastroenteritis were caused by or were suspected to have been caused by NLVs in 2000.

While the illness itself is short with a rapid recovery, viral gastroenteritis outbreaks in hospitals can lead to closure of hospital wards to new admissions and can cause major disruption to hospital activities. The winter of 2001/2002 has proved particularly difficult in that 16 outbreaks of viral gastroenteritis in health care facilities have been reported in Northern Ireland in the period December 1st 2001 to 31st January 2002 alone, eight of which occurred in hospitals. Several more hospitals have been affected by viral gastroenteritis in the Republic of Ireland during Spring 2002.

2.1.3 Protozoa which cause gastroenteritis
A variety of protozoa are capable of causing gastroenteric illness, including Cryptosporidium parvum and Giardia lamblia. In Northern Ireland, the reported incidence of cryptosporidiosis has risen dramatically in the last five years with 417 cases recorded in the year 2000 and 361 cases in 2001. A number of outbreaks have occurred, primarily associated with water supplies, and it is perceived as an emerging problem. Collated data is not available for the number of cases in the Republic of Ireland, although two small outbreaks were reported to the National Disease Surveillance Centre (NDSC) in the year 2001.

2.1.4 Toxin-producing bacteria causing foodborne illness
Gastroenteritis may also result from the ingestion of bacterial toxins already preformed in foods or from the ingestion of bacteria that produce toxin in the gut subsequently. Such toxins can be produced by Staphlococcus aureus, Bacillus cereus and Clostridium perfringens and the resulting illnesses tend to be mild, of short duration and usually resolve within 24 hours. Botulism, caused by Clostridium botulinum, is a more serious but rare illness.

2.2 Gastroenteritis Disease Burden on the Island - The Challenge
The number of reported cases of food poisoning on the island of Ireland continues to rise as evidenced by the accompanying graphs. This may in part be due to improvements in diagnosis and reporting.
Figure 1. Food Poisoning Notification Rates in Northern Ireland for the period 1990-2000

Figure 2. Food Poisoning Notification Rates in the Republic of Ireland for the period 1990-2000

Figure 3. Salmonella Notification Rates in the Republic of Ireland for the period 1990-2000
Though reporting systems differ between Northern Ireland and the Republic of Ireland, it is estimated that in 2000, there were 4460 cases of food poisoning on the island of Ireland. An additional 4013 cases of gastroenteritis were recorded in children under two years of age. The latter primarily comprise cases of viral gastroenteritis although in the Republic of Ireland, this category also includes protozoal infections. Viral gastroenteritis in persons over two years of age is not notifiable in either jurisdiction.

It is important to note that these statistics represent only those cases that are microbiologically confirmed. Many cases of foodborne illness are not accounted for in surveillance statistics. This is particularly so for those illnesses that are mild and/or of short duration as they are not brought to the attention of medical authorities. To estimate the true number of gastroenteric illnesses, community-based studies are required. The FSPB is currently funding an all-island community-based survey of enteric illness, the results of which will be available in late summer 2002.

A similar study, however, of gastrointestinal disease conducted in England in the mid-nineties estimated that 20% of the population suffered from gastrointestinal disease annually, only a portion of which sought medical attention. Were these figures applicable to the population of the island of Ireland, and such comparisons should be treated with caution, then approximately one million people would suffer varying degrees of discomfort each year.

2.2.1 Outbreaks of gastroenteritis
In 2000, 56 outbreaks of gastrointestinal disease were reported, examples of some of which were outlined at the beginning of this section. Viruses were implicated or suspected in 29 of these and caused the greatest number of illnesses.
Due to the difficulty in confirming NLV outbreaks, many outbreaks are reported as ‘suspect viral’ based on epidemiological evidence. For two outbreaks, numbers of cases were not available. This number represents laboratory confirmed cases only, true number probably higher.

2.3 Socio-Economic Cost of Gastroenteritis

Few attempts have been made either in Northern Ireland or the Republic of Ireland to evaluate the socio-economic burden of gastroenteric illnesses. Studies undertaken in other countries, however, have shown that there is a significant economic cost to society.

The immediate health sector costs associated with a serious milk-borne E. coli O157 outbreak, in Scotland in 1994, were estimated to be Stg£649,167 (1,038,667), or Stg£9,143 (14,629) per case. However, when the costs were projected over 30 years, the total estimated cost of the outbreak rose to Stg£11,930,347 (19,088,699), or Stg£168,032 (268,851) per case.

While these costs represent those for a serious food-poisoning outbreak, a recent general study in England, reported that the average cost for each case of gastrointestinal disease (including all those who did not seek medical care) was Stg£79 (126; 1993-1995 prices). If even these costs were extrapolated to the situation here, assuming a rate of 20% gastrointestinal disease cases are experienced (as in the UK) on this island per year, then the economies of the two jurisdictions lose Stg£79 (126) million between them annually.

<table>
<thead>
<tr>
<th>Causative organism</th>
<th>No. of outbreaks</th>
<th>No. of persons ill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses* (suspect and confirmed)</td>
<td>29</td>
<td>&gt;1137*</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>7</td>
<td>151</td>
</tr>
<tr>
<td>VTEC</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>C. perfringens</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>Shigella spp.</td>
<td>2</td>
<td>55</td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
<td>2</td>
<td>246†</td>
</tr>
<tr>
<td>S. aureus</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
<td>215</td>
</tr>
</tbody>
</table>

* due to the difficulty in confirming NLV outbreaks, many outbreaks are reported as ‘suspect viral’ based on epidemiological evidence
† for two outbreaks, numbers of cases were not available
‡ this number represents laboratory confirmed cases only, true number probably higher
Moreover, outbreaks can lead to significant opportunity costs. A series of viral gastroenteritis outbreaks in the winter of 2001-2002 occurred in hospitals both in Northern Ireland and in the Republic of Ireland. Hospital outbreaks often lead to closure of wards to new admissions and can cause major disruption to hospital activities. Thus, while the direct health effects of a viral gastroenteric outbreak are relatively minor and short-lived, the knock-on effects to the health service can be more substantial.

2.3.1 Economic impact on trade
Foodborne disease outbreaks can also impact on the food industry, resulting in expensive product recalls and the ensuing loss of public confidence. Foodborne disease outbreaks among holidaymakers can also threaten businesses in the tourism sector that are implicated in outbreaks.

In Summary
The number of reported cases of food poisoning on the island of Ireland has increased substantially over the last ten years.

Studies, such as that conducted in England and Wales, have established that the true incidence of gastrointestinal disease in the community is much higher even than the numbers reported to surveillance centres.

A variety of organisms are implicated in gastrointestinal disease and their relative importance changes with time, e.g. there have been substantial increases in the number of cases of Campylobacter and NLV infection reported in recent years.

In some cases, the link between severe illness and food poisoning has only recently been established, e.g. Haemolytic Uremic Syndrome with VTEC infection, and Guillain Barre Syndrome with Campylobacter infection.

The socio-economic impact of foodborne illness is substantial including: treatment costs, product recalls in the food industry, the effect of the loss of public confidence on businesses in the food and tourism sectors, and most recently, disruption to hospital services.
3. The Importance of an Enteric Reference Laboratory Service

This section of the report describes the role of an enteric reference laboratory service.

3.1 The Context

Definitive diagnosis and laboratory analysis of foodborne illness, together with comprehensive surveillance of foodborne illness, focussed research and education in appropriate areas, and the implementation and monitoring of strategic control programmes in food safety are the key elements in the prevention and control of foodborne disease. These activities fall under the responsibility of a variety of government departments and agencies in both jurisdictions.

The Departments of Health and the health boards, through the hospital services, laboratories and health professionals, the Departments of Agriculture through the veterinary laboratories and the veterinary inspectorate, the local authorities and district councils, the Drinking Water Inspectorate and the Environmental Protection Agency, the Communicable Disease Surveillance Centre (CDSC) and the NDSC, and agencies such as the FSPB, the Food Standards Agency Northern Ireland (FSA NI) and the Food Safety Authority of Ireland (FSAI), all contribute to the protection of the public against enteric illness.

In the protection of public health, foodborne disease surveillance is a vital element that permits outbreaks to be identified, disease trends to be tracked, new and emerging diseases to be spotted, and the impact of food safety control measures to be evaluated. It transforms clinical diagnostic data, and food and food animal test data, into useful information that enlightens and prioritises food safety policy. The deliberations of a group of surveillance experts on the island, chaired by Dr. Brian Smyth, were recently published by the FSPB in a consultation paper entitled ‘Towards the Enhancement of Foodborne Disease Surveillance’. A series of recommendations were made for the development of surveillance systems and the harmonisation of surveillance data on the island. The recommendations particularly relating to laboratory activities include:

- harmonisation of methodologies for specimen processing, organism identification, sub-typing and sensitivity testing
- establishment of formal interdisciplinary and inter-jurisdictional communication links between surveillance and laboratory personnel
- formal sharing of surveillance data on foodborne organisms between jurisdictions with a view to publishing on an all-island basis
joint participation of personnel from both jurisdictions in training programmes

establishment of joint research programmes that address goals common to both jurisdictions.

The report also highlights that good quality surveillance is highly dependent on the availability of detailed, comparable and timely information on pathogenic isolates. A specialist laboratory service, which can support the role of hospital, public health and veterinary laboratories in pathogen identification and characterisation, and which can provide leadership and co-ordination in the harmonisation of laboratory practices and in research, is crucial to the process.

3.2 Essential Roles of an Enteric Reference Service

3.2.1 Strain identification

Precise information on the strain of an organism causing disease helps inform the treatment of certain illnesses. Such information can also help avoid the potentially dangerous overuse of treatments such as antibiotics where they are inappropriate or unnecessary. An enteric reference service supports the role of the hospital laboratories in the exact identification of the strain and type of pathogen causing the illness. The reference laboratory uses typing and sub-typing techniques referenced to international standards and practices. For rare pathogens or those that are difficult to detect, an enteric reference service can provide the primary diagnosis. The level of support required will vary depending on the degree of expertise available in the primary laboratory.

3.2.2 Outbreak recognition and investigation

To obtain a clinical diagnosis of infection, limited typing of strains may be required. More detailed typing, however, provides a public health perspective and an understanding of the epidemiology of an organism.

When required, an enteric reference service, using more extensive typing, investigates the relatedness of clinical isolates to one another. Establishment of the relationship between clinical strains can provide early warning of outbreaks and can identify diffuse outbreaks not recognised by other means. Demonstrating relatedness allows authorities to rapidly determine the scale and intensity of any particular outbreak. It also focuses epidemiological investigation towards those cases that are part of the outbreak, allowing distinction from sporadic cases that may be occurring simultaneously in the community and thus preventing wastage of resources.

1 an expanded description of typing methods is provided in Appendix 3.
Investigation of the relatedness between clinical isolates and isolates from potential sources of the outbreak helps determine how the outbreak is being spread. An enteric reference service achieves this as quickly and as accurately as possible and delivers its results to those responsible for public health measures. Accurate, timely and detailed information ensures that the authorities adopt the appropriate response to any challenge. An effective service helps ensure that resources are not wasted either through under- or over-reaction to a specific challenge. The service also provides the information necessary to contain the outbreak, reassert good hygiene practices and, where required, prosecute those guilty of contraventions of public health regulations.

3.2.3 Harmonisation of laboratory practice
There are many variations in the methods and practices used by laboratories in identifying and typing pathogenic organisms. Meaningful comparison by surveillance personnel of data submitted by primary diagnostic laboratories is only possible through the practice of harmonised methods for detection and typing of organisms. An enteric reference service provides leadership and direction in the harmonisation of laboratory methods, guides best practice and monitors standards at primary laboratories to ensure the comparativeness of data generated.

3.2.4 Recognition of emerging threats and bioterrorism
Food poisoning is not static. Over time, new strains and types of pathogens develop constantly and new threats emerge. In the current climate, there is the additional threat of outbreaks due to enteric pathogens deliberately released as acts of bioterrorism. An enteric reference service provides information that can be used by surveillance centres and central government to establish trends, which in turn can be used to inform and prioritise food safety policy. A reference service also supports and conducts research in partnership with primary laboratories so that authorities are equipped to meet future as well as current threats.

3.2.5 Central culture collection
The preservation of pathogenic isolates permits future review and comparison of strains as and when required for research or surveillance purposes. An enteric reference service can provide the facilities to archive a library of representative isolates from different sources. In this way, it can be in a position to supply cultures of selected pathogens when required as reference or research material.
3.2.6 International reporting requirements
Greater harmonisation in foodborne disease surveillance is being sought by the European Union. Both the Republic of Ireland and Northern Ireland will have to ensure that they have the processes in place to meet these requirements. The establishment of the new European Food Safety Authority will ensure that more proactive food safety measures are taken in the future. The new Authority has indicated that it will seek greater information on all aspects of foodborne illness. The European Commission itself wants more frequent and more effective checks on foodstuffs in the Union and is currently drafting a new zoonosis regulation that will require Member States to set pathogen reduction targets and to increase reporting to the EU. This will require better data collection and more detailed sample analysis from Member States and in this, an enteric reference service is essential.

3.2.7 Antimicrobial resistance (AMR)
The Department of Health, Social Services and Public Safety (DHSSPS) in Northern Ireland and the NDSC in the Republic of Ireland have both recently published documents on this subject. The emergence of antibiotic resistant strains of common foodborne pathogens is causing concern among clinicians. An example of this is a strain of Salmonella called S. Typhimurium DT104 that is resistant to several antibiotics and has become established as the main cause of S. Typhimurium infections both in Northern Ireland and in the Republic of Ireland. When presented with a patient infected with an antibiotic resistant strain of bacteria, clinicians are limited in their choice of therapeutic agents. Both reports recommend continued and enhanced AMR surveillance of foodborne pathogens, and linkage and interpretation of data from human, food and veterinary isolates. An enteric reference service plays a role by collating data in a database of antibiogram profiles.

3.2.8 International liaison
Foodborne disease outbreaks do not recognise international boundaries and a number of international outbreaks have been identified in recent years. Increased international travel and globalisation of the world food supply mean that people from a number of countries may be exposed to a single outbreak source. For example, oysters harvested in Irish coastal waters were implicated in a foodborne disease outbreak in Hong Kong in the spring of 2002. An enteric reference service provides a contact point for liaison with similar organisations internationally.
In Summary

Essential Roles of an Enteric Reference Service:

Delivers rapid typing and sub-typing of organisms. Services include epidemiological typing (serotyping, phagetyping and molecular typing) as well as antibiogram trend analysis, toxin detection and serodiagnosis.

Provides diagnostic services for rare pathogens or those which are difficult to isolate.

Investigates the relationship between different isolates from food, water, clinical and animal samples.

Provides data and expert analysis to the laboratories and agencies for the control and prevention of foodborne disease outbreaks.

Facilitates, promotes and leads research with partners on the island.

Monitors laboratory standards and encourages best practice.

Keeps pace with emerging issues and threats in enteric illness.

Provides expert scientific advice on enteric pathogens.

Provides training and undertakes development programmes in microbiological methods and techniques associated with enteric pathogens.

Collects, preserves and supplies cultures of enteric organisms.

Liaises with similar organisations internationally.
4 How the Service Currently Operates

We describe the current usage of and demand for enteric reference services in the two parts of the island.

The current framework in Northern Ireland and the Republic of Ireland for the diagnosis of human infections and the detection of enteric pathogens is quite complex as demonstrated in Figures 4 and 5. This section outlines current practice in each jurisdiction for activities relating to clinical, food, water, and food animal samples.

4.1 Current Usage of Enteric Reference Services by Laboratories in the Republic of Ireland

Figure 4 outlines the activities of the various laboratories in the Republic of Ireland and their interaction with enteric reference services.

4.1.1 Human isolates
Clinical hospital laboratories in the Republic of Ireland differ in their use of reference laboratory services. Small and medium sized hospital laboratories generally identify enteric pathogens to genus level. These laboratories then forward isolates directly to a reference laboratory or to a larger hospital laboratory within the Republic of Ireland for confirmation and serotyping, e.g. *Salmonella enterica*. The larger hospital laboratories, employing Clinical Microbiologists, usually identify all enteric pathogens to genus and species level before forwarding them to a reference laboratory for phagetyping, toxin detection, or further typing as appropriate.

Since the Interim National Salmonella Reference Laboratory (INSRL) at University College Hospital (UCH), Galway was established in 2000, hospital laboratories are using its services for typing and sub-typing of *Salmonella enterica* isolates. All isolates are serotyped and tested for antimicrobial resistance. *S. Typhimurium* and *S. Enteritidis* isolates are further characterised by phage typing, with pulsed field gel electrophoresis (PFGE) and plasmid profiling performed on request. Prior to 2000, the Laboratory of Enteric Pathogens (LEP) in Colindale, London was routinely used for typing and subtyping of clinical Salmonellae. There has been a decline in the number of salmonellosis cases since 1998. In 2000, 681 clinical Salmonellae were typed at the INSRL, decreasing to 554 in the year 2001.

Campylobacter is the foodborne pathogen most frequently isolated in the Republic of Ireland. Campylobacteriosis, however, is not an individually notifiable disease and the organism is not normally referred for further identification. In 2001, only 12 isolates were sent to the LEP for typing. This has resulted in limited information being available on the epidemiology of Campylobacter in the Republic of Ireland.
Since October 2000, the Public Health Laboratory at Cherry Orchard Hospital Dublin has commenced provision of an E. coli O157 and non-O157 reference service for clinical and food samples. This service includes E. coli serotyping and verocytotoxin detection. This has improved diagnostic facilities for VTEC infections in the Republic of Ireland and diminishes the prolonged turn-around-times for services available from the United Kingdom. Phage typing for clinical VTEC isolates is still accessed at the LEP.

In 2001, the Microbiology Department at Waterford Regional Hospital commenced ribotyping of Listeria isolates and to date some 150, mainly food isolates, have been typed. A joint research programme has been set up with the molecular diagnostic unit at the Cork Institute of Technology (CIT) to provide, in addition to ribotyping, serotyping and PFGE typing of Listeria.

The Virus Reference Laboratory, University College Dublin is responsible for the diagnosis of all human viral pathogens. In the area of foodborne disease, it provides a routine diagnostic service for the identification of agents of viral gastroenteritis primarily NLVs; rotavirus diagnosis is usually available in hospital laboratories. This service is used in the main only by hospitals in the eastern region.

Serodiagnosis of yersiniosis is also frequently sought at the LEP. The LEP received 88 specimens from Republic of Ireland laboratories in 2001.

Molecular typing is now a key tool in microbial characterisation. Clinical laboratories generally use the LEP for molecular typing of human enteric isolates other than Salmonella enterica. In addition to Salmonella enterica, the INSRL has recently begun offering PFGE typing of Listeria, Shigella and Campylobacter spp. Meanwhile, the PHL, Cherry Orchard is developing a molecular typing service for VTEC. Other research laboratories in the Republic of Ireland, e.g. the Molecular Diagnostics Unit of Cork Institute of Technology, have significant experience in molecular typing, and are also routinely sub-typing foodborne pathogens.

Surveillance of foodborne illness in the Republic of Ireland is the responsibility of the NDSC. Specific data is collated on selected enteric pathogens. The statutory notification system provides for the notification by General Practitioners of salmonellosis separately from other causes of bacterial food poisoning but information is also provided on clinical Salmonella isolates by the Interim National Salmonella Reference Laboratory, detailing the...
serotype, phage type (for S. Typhimurium and S. Enteritidis) and antibiogram profile. The NDSC is also informed by hospital laboratories of all laboratory confirmed E. coli O157 cases, under the Enhanced Surveillance Scheme. Information on Campylobacter and Listeria laboratory confirmations is also compiled by the NDSC on an annual basis. No data is currently collated from hospital laboratories on Cryptosporidium, S. aureus, B. cereus, Adenovirus, Calicivirus, Rotavirus or Clostridium species.

4.1.2 Animal isolates

In the case of animal isolates of foodborne pathogens, the situation is less complex. The EU recognises the Central Veterinary Research Laboratory (CVRL) of the Department of Agriculture and Food (DAF) as the National Salmonella Reference Laboratory for animal isolates in the Republic of Ireland.

The DAF has a statutory responsibility to monitor poultry flocks for Salmonella enterica and conducts serotyping and antibiotic sensitivity testing on all isolates found. There are 21 DAF-approved private laboratories which also submit Salmonella isolates to the CVRL for serotyping and antibiotic sensitivity testing. PFGE is also available and is used selectively. In total, approximately 2500 isolates are serotyped annually. All animal Salmonella enterica isolates are stored in a culture collection and a comprehensive database is maintained.

In order to obtain more detailed typing, including phage typing of S. Typhimurium and S. Enteritidis strains, isolates are forwarded to the INSRL Galway. Rare serotypes are also submitted to reference laboratories for confirmation of serotype. Prior to 2001, the LEP was used for phage typing of S. Typhimurium and S. Enteritidis isolates and is still used on occasion for research isolates. In 2001, 611 Salmonella isolates of non-human origin were typed at the INSRL. During the same time period, 356 Salmonella isolates of non-human origin were referred to the LEP for serotyping and 537 for phage typing from Republic of Ireland laboratories.

All Campylobacter, Listeria and E. coli O157 test data from work conducted by the CVRL and by the approved private laboratories is captured in the Foodmicro Database at the CVRL. Surveillance research projects are also ongoing for Campylobacter and enterococci, however, the veterinary services do not generally refer these organisms for further typing to enteric reference services. These isolates are stored in the hope of developing typing capabilities in the near future.
4.1.3 Food isolates
There are seven EU Official Food Microbiology Laboratories (OFMLs), specified in SI 95 of 1998, in the Republic of Ireland conducting microbiological testing of foods on behalf of the health boards. These laboratories are accredited by the National Accreditation Board of Ireland to ISO 17025 standards. In 2000, 512 strains of the four main bacterial foodborne pathogens (Salmonella spp. (59 isolates, 10 of which were S. Enteritidis or S. Typhimurium), Campylobacter spp. (165 isolates), Listeria spp. (285 isolates) and E. coli O157 (3 isolates) were isolated at these laboratories. Since 2000, laboratories are using the INSRL for typing and sub-typing of Salmonella isolates. Isolates of other organisms are forwarded to the LEP as required.

DAF also has statutory responsibilities for testing meat and meat products, milk and milk products, and egg and egg products for microbiological safety. Salmonella enterica isolates obtained are forwarded to the CVRL for serotyping and antibiotic sensitivity testing, and onwards to the INSRL for further typing as required.

Local authority laboratories also conduct microbiological analyses on samples taken during inspections of domestic abattoirs and small meat and meat products premises. Salmonella enterica isolates obtained are forwarded to the CVRL for serotyping, and onwards to the INSRL for further typing as required. Furthermore, the Department of the Marine and Natural Resources conducts microbiological surveillance activities in relation to raw shellfish and fish.

4.1.4 Water isolates
Water is increasingly being implicated as the vehicle of transmission during outbreaks of gastroenteric illness. Monitoring of the microbial quality of drinking water (public water supplies and bottled waters) and water used in the manufacture of food is the responsibility of a number of organisations. The Environmental Protection Agency (EPA) has overall responsibility for the monitoring of drinking water supplies, including public water supplies and group water schemes. Testing is conducted in local authority and OFMLs. Furthermore, the DAF and the OFMLs both have responsibilities in monitoring water used in the manufacture/processing of meat and other foods respectively. Currently in the Republic of Ireland, there is no laboratory service for detection or enumeration of Cryptosporidium in water. During recent outbreaks samples had to be referred to the United Kingdom for analysis.
Figure 4. Outline of current practice in the Republic of Ireland
4.1.5 Research isolates

A large number of surveys are ongoing in the Republic of Ireland examining various food commodities and food animals for specific microbial pathogens. These include surveys commissioned/sponsored by the FSAI, the DAF and other organisations. For example, during the year 2000 in which 3000 domestic and imported poultry samples were examined during the FSAI/DAF Enhanced Poultry Monitoring Programme, 60% were found positive for Campylobacter spp. and 11% for Salmonella spp. Demand for detailed typing of pathogenic strains isolated during this type of research activities will increase in the future.

4.1.6 Turn-around-times (TATs)

Rapid TATs are crucial during outbreak investigations. TATs are calculated as being from the time of submitting isolates to obtaining the final results.

Laboratories using the INSRL for phagetyping Salmonella isolates recorded average TATs of five days for telephoned results as compared with 14 days when strains had been referred to the LEP. Confirmed results are available in ten days.

The TAT for VTEC confirmation at PHL, Cherry Orchard is 48 hours for a phoned result, giving serotype and verotoxin status. A stool sample takes a minimum of 72 hours and a food sample five days. Written authorised reports are issued within a week. This is a major improvement on accessing United Kingdom services with a prolonged turnaround of up to two weeks.

The TATs vary for other organisms submitted to the LEP. Two public health laboratories experienced average TATs of seven days for S. aureus enterotoxin testing. In an emergency, LEP will give test results, by telephone, two days in advance of the final report.

TATs for molecular typing results from LEP also vary. TATs of one month and longer for the molecular typing of E. coli O157 are common for referring laboratories in Republic of Ireland. For example, 25 days elapsed between submission of a suspect E. coli O157 isolate to the LEP by a local authority laboratory and return of the toxin and phage typing results. As the case was regarded as an emergency, the CIT also conducted molecular analysis of the isolate and returned confirmation within two working days.
4.2 Current Usage of Enteric Reference Services by Laboratories in Northern Ireland

The current framework for the diagnosis of human infections and the detection of enteric pathogens in food, water and food animals is also quite complex as demonstrated in Figure 5.

4.2.1 Human and food isolates

There are nine hospital laboratories conducting microbiological tests on clinical specimens in Northern Ireland. The Northern Ireland Public Health Laboratory (NIPHL) conducts microbiological tests on food and is part of the Belfast Link Laboratories (BLL) located at Belfast City Hospital.

All of these laboratories identify enteric pathogens to genus level and the larger laboratories work to species level. Most of the *Salmonella enterica* isolates are also serotyped in the primary laboratories. Two hospital laboratories send all *Salmonella* isolates while others send only the less common isolates to the BLL for serotyping.

All isolates of *S. Enteritidis*, *S. Typhimurium*, *S. Virchow*, *S. Hadar*, *S. Typhimurium*, *E. coli* O157 and *Shigella* spp. are sent to LEP for phagetyping. LEP phage typed approximately 600 isolates during 2001.

Belfast City Hospital laboratory carries out the molecular toxin typing of all *E. coli* O157 in Northern Ireland. Isolates are submitted to the LEP for phage typing. The laboratory maintains a complete database.

At this time, all hospital laboratories in Northern Ireland are participating in a Campylobacter Sentinel Survey. As a result, all Campylobacter isolates are currently submitted to the LEP for further typing. Normally, only a small number of isolates of Campylobacter spp. (approx. 20 in 2001) are submitted to the LEP for serotyping and phagetyping.

Serodiagnosis is sought at the LEP for approximately 100 specimens annually.

Belfast City Hospital identifies other food poisoning organisms, such as *S. aureus*, *Clostridium perfringens* and *B. cereus* to species level. Most of these are then forwarded to either the LEP or the Food Hygiene Laboratory (FHL) at Colindale for further typing. During 1998, 26 of these were referred to the LEP or FHL.
In the case of a large or persistent outbreak of Clostridium difficile, the organism is sent to the Anaerobe Reference Unit, Cardiff, for typing as appropriate.

Clinical samples of faeces positive for Cryptosporidium are submitted to the PHLS Cryptosporidium Reference Unit at Swansea for typing.

The Regional Virus Laboratory (RVL) Belfast provides a routine diagnostic service for the identification of viral gastroenteritis. PCR is available for the identification of SRSV, rotavirus, enterovirus, calicivirus, astrovirus, and faecal adenovirus.

Surveillance of foodborne illness in Northern Ireland is the responsibility of the CDSC NI. Hospital laboratories inform the CDSC NI on a voluntary basis of all laboratory confirmed enteric infections under the Laboratory Reporting System. Serotyping and phage typing information is included in the reported data for Salmonella isolates. Campylobacter, Cryptosporidium, Listeria, E. coli O157, S. aureus, B. cereus, Adenovirus, Calicivirus, Hepatitis A, Rotavirus, Clostridium perfringens, C. botulinum and Clostridium (other pathogenic species) laboratory confirmations are also reported.

4.2.2 Animal isolates in Northern Ireland

The Veterinary Sciences Division (VSD), Department of Agriculture and Rural Development, Northern Ireland (DARD NI) is a nominated National Reference Laboratory for animal salmonellosis under the European Directive on Zoonoses Control (92/117). In addition to typing Salmonella isolates from it's own surveillance programs and diagnostic veterinary investigation services, the laboratory is also responsible for serotyping isolates submitted from private commercial laboratories that are involved in testing animal samples. An extensive range of antisera is held and approximately 1,000 isolates serotyped annually. Antimicrobial resistance monitoring of Salmonella isolates has been on-going for a number of years at the VSD and a database maintained of results. All isolates of S. Enteritidis, S. Typhimurium and S. Virchowre referred to the LEP for phagetypeing with approximately 200 isolates being sent annually.

There is a joint research program on Campylobacter in food animals between the VSD and the Food Sciences Division (FSD), DARD NI. Facilities to speciate isolates of Campylobacter exist at both sites, while molecular typing of isolates is carried out at FSD, which has an international reputation for it's work on the molecular typing of Campylobacter isolates.
4.2.3 Water isolates
Monitoring of the microbial quality of drinking water and water used in the manufacture of food is the responsibility of a number of organisations. The Drinking Water Inspectorate has overall responsibility for the monitoring of drinking water supplies. Routine monitoring of drinking water is performed at Laboratories run by the Water Service of the Department of Regional Development. This usually consists of examination for bacteria. Examination for Cryptosporidium is also performed on filtrates of large volumes of water.

Sampling of private water supplies used in food businesses and drinking water where complaints/concerns have arisen is a local government responsibility. These samples are taken by EHOs and analysed at the NIPHL. Bacterial examination generally consists of enumeration of faecal and non faecal coliforms.

4.2.4 Turn-around-times
As explained earlier, TATs from the LEP vary, but overall they are shorter for samples from Northern Ireland than for the Republic of Ireland. Submitting laboratories appear satisfied. The shortest TAT for phagetypes of Salmonella isolates sent from the BLL was five days.
Regional Virus Laboratory
Diagnosis of viral gastroenteritis

Hospital Labs.
Isolation of organisms, limited serotyping of Salmonella, antibiograms

- Belfast Link Laboratories (BLL)
  - Belfast City Hospital Lab. and Public Health Lab.
    - Isolation of organisms from humans (Belfast City Hospital) and food (Public Health Lab).
    - Serotyping of Salmonella, molecular typing of E. coli O157

Belfast Link Laboratories (BLL)

LEP AT COLINDALE
- Serotyping Salmonella, Campylobacter, Shigella
- Phagetyping Salmonella, E. coli O157, Campylobacter
- Antibiogram
- Molecular typing
- Toxin testing

Research on Typing Methods
- Veterinary Science Division, DARD NI
- Food Science Division DARD NI
- Public Health Lab., Belfast
- City Hospital
- Queens University Belfast

VETERINARY SAMPLES

HUMAN SAMPLES

FOOD SAMPLES

Figure 5. Outline of current practice in Northern Ireland
5. Pros and Cons of Current Practice

This section attempts to evaluate current arrangements for enteric reference services taking into account the varying requirements of different laboratories, surveillance personnel, public health professionals and food safety managers.

Enteric reference services are accessed by clinical hospitals, food testing laboratories and veterinary laboratories. The current usage of enteric reference services for clinical isolates by hospital laboratories stems firstly from the need for confirmation of clinical diagnosis. Hospitals laboratories submit cultures and specimens to reference laboratories on an individual basis, when diagnostic and typing services are required that are not available to them locally. When outbreaks of enteric illness are suspected, cultures from linked cases and from suspected vehicles of infection are also submitted, to obtain the additional typing and sub-typing required to confirm association between strains and to institute public health control measures.

The demand for reference services by food and veterinary laboratories, however, is driven primarily by statutory monitoring and surveillance obligations.

The information generated by laboratory services is also used by surveillance personnel, public health professionals and food safety managers to develop strategies to prevent foodborne illness.

Any evaluation of the enteric reference services must consider the requirements of all users.

5.1 Quality and Range of Service

Enteric organisms emerge (e.g. Cryptosporidium) and decline (e.g. Salmonella enterica) in prevalence over time. An enteric reference service needs to provide services for a wide range of organisms and to be responsive to changing demands. The LEP is internationally renowned as a centre of excellence and the range of services provided is very comprehensive. Their strong research ethic ensures that the techniques used and the range of services provided keep pace with emerging issues in enteric illness. The INSRL provides typing services for Salmonella enterica. The range of typing services for Salmonella enterica match those provided by the LEP for Salmonella and a close relationship is maintained with the LEP.

5.2 Turn-around-times

Rapid TATs are not normally essential for typing enteric organisms isolated during food surveys or during veterinary monitoring programmes. However, during
investigations of enteric disease outbreaks, speed in typing organisms and toxins from clinical cases is a crucial component of an effective enteric reference laboratory service.

Although the LEP has responsibility first and foremost to service the public health needs of the people of England and Wales, Northern Ireland hospital laboratories receive a good service from the LEP. This is strengthened, in particular by contractual arrangements and satisfactory TATs are obtained.

TATs for Republic of Ireland laboratories from the LEP vary and information may not always be available at the time that it is required. Potentially, this can limit public health co-ordination and control, and it can particularly hamper the control and management of outbreaks. The current TATs for samples submitted to the LEP by Republic of Ireland hospital laboratories are a cause for some concern, and a service that could deliver reduced TATs would be of great benefit. Since the establishment of the INSRL, TATs for Salmonella isolates are lower than were previously experienced when isolates were referred to the LEP.

5.3 Harmonisation of Laboratory Practice

Meaningful comparison by surveillance personnel of data submitted by primary diagnostic laboratories is only possible through the practice of harmonised methods for detection and typing of organisms. There is currently little harmonisation in the methods and practices used by laboratories on the island in identifying and typing pathogenic organisms. There is a requirement for leadership and co-ordination in the harmonisation of laboratory methods and for a system for monitoring standards at primary laboratories on the island to ensure the comparativeness of data generated.

5.4 Data Collation and Trend Analysis

Epidemiological studies need high quality data to ensure accuracy. For Salmonella enterica, both veterinary and human isolates are generally subject to a substantial degree of typing, and thus comprehensive and centralised data collection is possible in each jurisdiction. These systems of data collection, however, remain fragmented between clinical, food and animal isolates and an integrated approach is seen as the way forward.

For other enteric pathogens, there is variable usage of the reference services at the LEP, in particular by hospital laboratories in the Republic of Ireland. This contributes to the lack of high-quality information on these pathogens for the jurisdiction.
For example, it may not be necessary to subtype Campylobacter routinely, however, knowledge of its epidemiology leading to preventative measures would be greatly improved by the subtyping of more isolates.

There are a number of factors which influence usage of reference laboratory services by hospital laboratories in the Republic of Ireland: forwarding of pathogenic isolates across international boundaries requires samples to be packaged according to International Air Transport Authority (IATA) regulations and this is a significant clerical burden on submitting laboratories; each hospital laboratory pays for the services it requires; and primary laboratories may see their role primarily as clinical diagnosticians and underestimate their role in public health protection.

These factors limit the number of isolates submitted to reference laboratories for further typing. There is a need to surmount these barriers in order to facilitate greater usage of enteric reference services. Greater usage of these services with concomitant data analyses would provide public health professionals and food safety managers with the necessary information to further develop strategies to prevent foodborne illness.

5.5 Need for More Detailed Information in Future

It is important that more isolates are typed and that surveillance programmes are established in order to compare strain types in animal populations with human populations. The EU will seek more detailed information from Member States on foodborne pathogens in the future. The creation of the European Food Safety Authority indicates the Union’s commitment to instituting more rigorous testing and controls to protect public health. The new zoonosis regulation currently being drafted will require Member States to set pathogen reduction targets and to increase reporting to the EU. This will require more detailed sample analysis and data collection from Member States. It will be expensive and difficult to meet the anticipated demand for increased and more detailed information under the present system.

5.6 Force Majeure

The LEP has responsibility, first and foremost, to service the public health needs of the people of England and Wales. In the event of a force majeure (a disruptive event that cannot be anticipated), their responsibility lies with samples received from laboratories within their own jurisdiction. Isolates received from laboratories in Northern Ireland and the Republic of Ireland, understandably, would not receive equal priority. During a significant enteric outbreak on the island of Ireland, this risk may not be acceptable.
In Summary
Laboratories agree that the LEP is internationally renowned as a centre of excellence and the range of services provided is extremely comprehensive, keeping pace with emerging issues in enteric illness.

A force majeure in the jurisdiction of England and Wales, however, could result in disruption of the service to the island of Ireland.

While TATs are inconsequential to veterinary laboratories and current TATs from the LEP acceptable to Northern Ireland hospital laboratories, TATs for samples submitted from Republic of Ireland hospital laboratories to the LEP are longer than desirable.

There is variable usage of the LEP service by Republic of Ireland hospital laboratories, for pathogens other than Salmonella enterica, and consequently there is a lack of high-quality information on these pathogens there. In addition, the different levels of usage between Northern Ireland and the Republic of Ireland make it more difficult to compare data meaningfully and develop an all-island epidemiological view.

It is important that more isolates are typed and that surveillance programmes are established in order to compare strain types in animal populations with human populations. The EU will introduce regulations in the future aimed at achieving such an end.

There is currently little harmonisation in the methods and practices used by laboratories on the island in identifying and typing pathogenic organisms. There is a requirement for leadership and co-ordination in the harmonisation of laboratory methods and for a system for monitoring standards at primary laboratories to ensure the comparativeness of data generated.
6 Considerations in Planning an Improved Enteric Reference Service

This section of the report describes the principles, range and level of service required for an enteric reference laboratory service.

The main task of the expert group was to outline and evaluate options for an improved enteric reference service for the island, in light of the concerns expressed about the limitations of current practice. However, the group firstly needed to examine the role and purpose of an enteric reference service. In doing so, it analysed the basic requirements of an adequate reference service.

6.1 How an Enteric Reference Service Should Operate

While a key role of an enteric reference service is to provide a definitive diagnostic service, there are certain principles which are fundamental to the establishment of a high quality enteric reference service. These are:

- The service should have dedicated resources and staff so that full service is available to both jurisdictions at all times.
- It should be a public health resource being government-funded in order to encourage maximum use by all laboratories (hospital, food, veterinary, water and research laboratories).
- Users should be able to access the service quickly and easily.
- Public health needs should determine the service’s priorities.
- The data generated should be managed in such a way that it is readily and rapidly available to those submitting the isolates and to public health professionals as appropriate.
- It should operate with best practice, validated methodologies and state of the art technologies.
- It should guide best practice at diagnostic laboratories, encourage harmonisation of methodologies and monitor standards.
- As a centre of excellence, it should provide education and expert scientific advice to laboratory personnel.

6.2 The Range of Services Required

Based on current and emerging priorities on this island for the detection of foodborne diseases, the expert group considered that the minimum range of services that should be available to laboratories from an enteric reference service are listed in Table 3. These include typing services for Salmonella, Campylobacter,
Listeria, VTEC, S. aureus, B. cereus, viruses, Cryptosporidium, Giardia, C. difficile and C. perfringens.

It is cumbersome to routinely test for rare foodborne pathogens such as C. botulinum and other rare fermentative Gram-negative rods, also Shigella spp., Vibrio cholera and Yersinia spp. There are few isolates submitted to reference laboratories at present and it would be difficult to maintain the necessary level of expertise. Therefore, an appropriate international reference laboratory would be better placed to carry out this work.

6.3 The Level of Service Required

There are a number of factors that influence the demand for enteric reference services:

- the organism implicated and its potential threat to public health, e.g. severity of illness caused, ease of transmission to other persons
- the suitability of specific typing techniques and the value of information obtained
- whether the sample from which the organism was isolated was collected as part of an outbreak investigation or as part of a monitoring programme, e.g. molecular typing is required during outbreak investigations to assist decision-making on public health measures by outbreak control teams
- medico-legal or trade reasons
- the research need for epidemiological information
- EU and other statutory obligations.

The expert group indicated that an initial objective should be to identify all enteric pathogens to species level: Salmonella enterica and VTEC isolates should also be serotyped and phage typed routinely. Ideally, molecular typing would be performed for all outbreak strains and for a sub-set (20-25%) of remaining isolates (i.e. epidemiologically-unrelated clinical isolates and all food/water/food animal strains isolated during monitoring programmes) to assist in trend analysis and recognition of emerging threats. These figures should be reviewed after three years.
Table 3. The range of specialised laboratory services for foodborne pathogenic organisms that should be available to laboratories on the island of Ireland.

<table>
<thead>
<tr>
<th>Organism</th>
<th>specialist Reference Laboratory Services</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>species identification</td>
</tr>
<tr>
<td>Salmonella spp.</td>
<td>(+)</td>
</tr>
<tr>
<td>Campylobacter spp.</td>
<td>(+)</td>
</tr>
<tr>
<td>Escherichia coli O157 and other VTEC</td>
<td>(+)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>(+)</td>
</tr>
<tr>
<td>Listeria spp.</td>
<td>(+)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>(+)</td>
</tr>
<tr>
<td>Bacillus cereus</td>
<td>(+)</td>
</tr>
<tr>
<td>Anaerobes (C. difficile, C. perfringens, C. botulinum)</td>
<td>(+)</td>
</tr>
<tr>
<td>Enteric Viruses: NLV, rotaviruses, adenoviruses</td>
<td>+</td>
</tr>
<tr>
<td>Crytosporidium &amp; Giardia</td>
<td>+</td>
</tr>
</tbody>
</table>

While the ability to conduct species identification for all organisms should be available, in practice, the demand for organisms other than viruses and protozoa should be low as the capacity exists within most primary laboratories for species identification.

Many primary laboratories conduct serotyping of common strains of Salmonella spp. and E. coli. Demand for serotyping of these organisms will be concentrated on rare serotypes.

While phage typing of Campylobacter species has been developed, molecular typing is considered more appropriate for this organism.
7. An Examination of the Options

This section outlines and evaluates a variety of options for an enteric reference service.

The signing of the Belfast Agreement in December 1999 made possible the opportunity for an all-island enteric reference laboratory service. The establishment of such a service would address concerns relating to the current service and would allow for the development of an all-island understanding of common epidemiological problems.

The expert group agreed that there was a need to upgrade the current system and, thereby, benefit from better data and service. A number of alternatives were explored for the provision of enteric reference services for the island. Four possible options are outlined and evaluated in this section:

1. Use of the LEP for all specialist enteric services.

2. Establishment of a managed network of reference laboratories on the island servicing both jurisdictions, applying the same high level of service to each jurisdiction.

3. Development of a single site on the island for all specialist enteric services.

4a. Establishment of a managed network of reference laboratories in the Republic of Ireland, initially for use by Republic of Ireland laboratories.

4b. Development of a single site in the Republic of Ireland, initially for use by Republic of Ireland laboratories.

These options were evaluated based on the potential quality of the service that they would provide, their impact upon the professionals in the area, their management and their overall contribution to the knowledge base. Please note that no financial costings have as yet been undertaken of these options. A full economic appraisal of options will be undertaken after this consultation process and prior to publication of the final report.
7.1 Option 1 - An Enhanced Service from the LEP

This option proposes the sole use of the LEP for all specialist enteric services that cannot be provided locally, with the provision of standards for those tests that are conducted locally. The LEP is internationally renowned, produces work of a high quality, and laboratories in both jurisdictions have a long history of availing of its expertise.

Northern Ireland experts have expressed satisfaction with the service received from the LEP and are keen to retain use of its services. They have immediate access to a high-quality reference service that uses accredited methods with good TATs. Data for the jurisdiction can be compared or grouped with data produced for the remainder of the United Kingdom.

Medical experts from the Republic of Ireland have indicated certain concerns about the service from the LEP due mainly to slow TATs, lack of a central database for epidemiological analysis and lack of a central culture collection. Central culture collections are already maintained for veterinary Salmonella isolates in each jurisdiction.

7.1.1 Some of the key issues surrounding such a development

7.1.1.1 Institution of a service contract for the Republic of Ireland

Opting for this alternative would require the Republic of Ireland to have a service contract, similar to the one between the LEP and the DHSSPS. Such a contract would require improved TATs, and access to an all-island database and culture collection. The existing contract between Northern Ireland and the LEP would remain in operation.

7.1.1.2 Agreement with the LEP regarding number of isolates

In the future as more isolates are typed and surveillance programmes are established in order to compare strain types in animal populations with human populations, it is anticipated that a much larger demand will be made on reference services from both jurisdictions. This will increase current expenditure on reference services significantly and require agreement from the LEP regarding the increased number of isolates being typed. The LEP have indicated that providing services for an increased number of isolates from the island of Ireland would be possible.

7.1.1.3 International Air Transport Authority Regulations

The IATA have stringent packaging requirements for the transport of pathogenic isolates by air. Isolates must also be accompanied by substantial paper work, including emergency contact telephone numbers, etc. There is currently a
derogation in place within the United Kingdom, which means that these regulations are not fully applied between Northern Ireland and the LEP, but Republic of Ireland laboratories transporting isolates by air are required to comply with these regulations.

Main advantages of using the LEP exclusively:
- this option would allow for close links with United Kingdom expertise. The LEP is recognised internationally as a centre of excellence.
- all isolates would be submitted to the same laboratory and this would ensure consistency in the results achieved and the quality of the work.
- data for each jurisdiction could easily be compared or grouped on an all-island basis. Wider comparison would also be possible with Great Britain.
- users would be familiar with this practice.
- this option would not involve any capital outlay.
- this option allows for immediate start-up as no construction time would be required.

Main disadvantages of using the LEP exclusively:
- an enhanced service would be highly dependent on the introduction of a service contract between the Republic of Ireland and the LEP.
- it would require additional revenue to encourage wider use, particularly by Republic of Ireland laboratories.
- as a purchaser of services, laboratories on the island of Ireland would have little influence in directing the activities of the service.
- a force majeure in the jurisdiction of England and Wales could result in disruption of the service to the island of Ireland.
- IATA regulations would require more stringent packaging and paperwork than rail/road transport within the island. Transport to the LEP would also be more expensive than the cost of transport within the island.
- there are no established inter-laboratory communication channels and this could limit internal and cross-border communication with colleagues.
- the concentration of reference service expertise at the LEP could limit the development of technical expertise on the island. It has limited the development of the surveillance function and the epidemiological focus within the Republic of Ireland in particular. This is because data is difficult to collate.
7.2 Option 2 - Development of a Managed Network of Reference Laboratories on the Island of Ireland

A considerable body of expertise in typing methods is already available on the island. A description of the range of work performed by ten centres of expertise on the island is outlined in Appendix 4. Some have developed specialisations and are recognised for the quality of their work. This option explores the further development of some of these existing centres of expertise and their designation as reference laboratories forming a network for the entire island.

With Option 2, a number of strategically located laboratories would be selected for development as reference laboratories, reflecting the laboratories' current work programme on major foodborne organisms. This option suggests five key laboratories designated: the Salmonella Reference Laboratory, the Campylobacter Reference Laboratory, the Enteric Virus Reference Laboratory, the Listeria Reference Laboratory and the E. coli Reference Laboratory. Earlier, a need was identified for a reference service for ten groups of organisms. The reference services for the remaining organisms might be incorporated into the envisaged reference laboratories. Alternatively, they could be developed independently in other laboratories or they could continue to be referred to the LEP.

Under this option, each of the five reference service laboratories could be sited adjacent to either, the existing diagnostic microbiology facilities of a hospital, a veterinary pathology service, an academic institution or developed as a stand-alone facility. These reference services would be individually resourced and managed with dedicated funding.

7.2.1 Some of the key issues surrounding such a development

This option involves different sites and so adds an extra layer of complexity. The location of the sites, the maintenance of the dedicated facilities and the management of such a multi-site service will all require careful consideration and proper handling.

7.2.1.1 Location of laboratories

In order to take account of political sensitivities, perceived threats and the wide distribution of submitting laboratories, the reference laboratories would be strategically distributed between the two jurisdictions.

The group considered an open tender process for the supply of a multi-site reference service but judged it unfeasible due to the perceived political sensitivities.
7.2.1.2 Maintenance of a dedicated facility

The principles outlined earlier specify that in order to provide an equitable and rapid service, the reference facility should be a dedicated facility providing a service that is separately resourced and managed. When a reference facility is sited in conjunction with an existing diagnostic microbiology laboratory the facility should be funded and staffed independently of the existing diagnostic facility. This is particularly important, as during outbreaks and emergencies in the home laboratories region, demands could be made on the services of reference laboratory staff in helping with diagnostic services. This could result in the reference service being unable to carry out its normal work on behalf of all submitting laboratories.

7.2.1.3 Management

The management model of the multi-site reference service must reflect its collaborative multi-site structure. Such a model could be embodied in a Co-ordinating Management Committee, comprised of the managers of the reference services and the FSPB. The Committee would collectively audit performance, review standards, oversee the development of the service and collate the annual report. However, to ensure accountability and equity, the FSPB would allocate budgets to the reference sites. The Co-ordinating Management Committee could advise the FSPB on budget allocation and service developments.

**Main advantages of a managed network of laboratories:**

- this approach would have less negative impact on existing centres of expertise and would enhance regional centres of expertise. It would also improve access to, and co-operation with, local research institutes
- decentralisation of activities and the dispersal of laboratories would require and engender wider collaboration among the reference and referring laboratories throughout the island. This would encourage shared ownership of activities and greater flexibility
- locating at existing sites would require less capital investment to support their expansion into reference service sites
- it would take a relatively short time to develop
- submitting laboratories would not be required to adhere to IATA regulations if transporting samples to a service based on the island.
Main disadvantages of a managed network of laboratories:

- although the units would have lower capital costs, their operational and management costs would be higher
- consistency in quality and standards could be complex to maintain
- multiple sites require a potentially complex communications infrastructure linking individual laboratories and a central database
- submitting laboratories must package, label and transport samples to different reference laboratories and this would represent an additional clerical burden
- reference sites might not receive the critical number of samples needed to allow for more routine analysis and quick TATs
- there is potential for the duplication of expertise
- the development of these laboratories is highly dependent on key individuals. It could prove difficult to identify someone with similar expertise when replacement of one of these key individuals is required.
7.3 Option 3 - Establishment of a Single Site to Provide Enteric Reference Services to the Entire Island

Option 3 proposes the development of a single reference laboratory on the island, either as a greenfield site development, or through the expansion of an existing site. All of the reference work would then be located at this site. This site could be based in either Northern Ireland or the Republic of Ireland and would provide a full enteric service to both jurisdictions. It would develop links with the LEP and introduce compatible systems and methodologies. The centralisation of reference services in other countries is common. Centres like the LEP, for example, benefit from the concentration of expertise, ease of management of operations, and ease of data management.

The single site reference laboratory could be sited close to, or as part of, an academic institution, an existing diagnostic microbiology facility, a veterinary pathology service, or as a stand-alone facility.

This laboratory would receive enteric organisms of food, water, veterinary, human or environmental origin, isolated in primary or regional laboratories in both jurisdictions. It would also provide services for non-routine samples requiring specialist diagnosis or testing.

7.3.1 Some of the key issues surrounding such a development

The location of a single site reference laboratory and the perceived threat to current centres of expertise are sensitive issues.

7.3.1.1 Location of the reference laboratory

In the development of an enteric reference service, it is important to ensure cross-professional support from scientists, physicians and veterinarians from both jurisdictions and all disciplines. The choice of location will be particularly sensitive in this regard.

7.3.1.2 Current centres of expertise

There is a perception that research conducted at existing centres of expertise could be undermined and disadvantaged when a single site is developed.
Main advantages of single-site option:

- the centralisation of expertise would help develop a high quality reference service giving it a strong identity and an international reputation
- it would meet any current international requirements
- as a dedicated reference centre, with a critical mass of scientists, the laboratory could rapidly establish a culture of excellence and professionalism, and it would give staff improved career development opportunities
- a single-site service would avoid duplication of activities and expertise
- it would provide a single contact point and enable the convenient transport and delivery of multiple samples
- a single comprehensive database would be readily available for timely analysis and interpretation, providing greater public health protection
- the operational and management costs would be low relative to a managed network. A single site would allow for direct management and financial control
- submitting laboratories would not be required to adhere to IATA regulations if transporting samples to a service based on the island
- it could be flexible regarding additional functions such as bioterrorism detection and hospital infection control.

Main disadvantages of single-site option:

- it has a potentially long start-up time
- this option would necessitate a large capital outlay
- it would prove difficult to select a location
- a single site could be perceived as coming to dominate research in the area of foodborne disease, undermining research activities in already established centres of expertise
- existing laboratories could lose expertise
- highly qualified staff might not be willing to relocate
- a single site could become a terrorist target.
7.4 Option 4 - Establishment of an Enteric Reference Service in the Republic of Ireland to Provide Services Initially to Republic of Ireland Laboratories

Option 4 explores the introduction of an all-island enteric reference service on a phased basis. A comprehensive service would be developed in the Republic of Ireland to meet the Republic of Ireland’s immediate service needs. This service would be developed in consultation between representatives from Northern Ireland and the Republic of Ireland, developing facilities that met the unique needs of the entire island. This service would act as the referral site for the Republic of Ireland while offering the same service to the entire island.

In the short-term, Northern Ireland would continue to use the LEP but at an enhanced level. A revised contract between the LEP and Northern Ireland is envisaged allowing for more samples and the provision of detailed data on the submitted isolates that would be compatible with those for the Republic of Ireland. The new service in the Republic of Ireland would develop links with the LEP and introduce compatible systems and methodologies. In partnership with the LEP, an all-island perspective would be obtained. In the longer term, this service would also serve Northern Ireland laboratories.

This option recognises that Northern Ireland scientists have a professional and ethical responsibility to deliver the best service possible utilising the resources at their disposal. Laboratories would continue in the short-term to use a service that currently offers good protection to the public.

The government of the Republic of Ireland would fund the full capital costs and service costs for the Republic of Ireland.

The expert group considered two possibilities: a managed network (Option 4a) similar to Option 2, but all laboratories based in the Republic of Ireland; or a single site laboratory (Option 4b), similar to Option 3, but with the laboratory definitely located in the Republic of Ireland. The advantages and disadvantages of either Option 4a or 4b are similar to those described previously for Options 2 and 3.

7.4.1 Key issues surrounding Option 4

7.4.1.1 Location of reference laboratory and current centres of expertise

The choice of location, the impact on professionals currently working in the field and the management of the service remain the key issues. These have already been discussed under Options 2 and 3.
7.4.1.2 Communication

The development of communication/collaboration channels between an exclusive Republic of Ireland reference service and the LEP would be imperative. The use of compatible methodologies for organism identification and typing, and for antibiotic sensitivity testing, would be necessary so that in partnership with the LEP, an all-island perspective could be obtained.

Main advantages of Option 4:
• it meets the Republic of Ireland’s immediate service needs. It would gather comprehensive data on organisms causing foodborne disease in the Republic of Ireland, allowing the further development of epidemiological research and analysis, ensuring that the Republic of Ireland can meet its EU obligations in the future
• Northern Ireland scientists would gain access to a new, specialist service within easy reach of their own laboratories. It would provide an alternative service and may offer additional services currently not available or difficult to access
• in providing a single centre of expertise, the new service could co-operate more effectively with sister organisations such as the LEP and engage in joint research and data analysis. This would facilitate the evolution of an all-island epidemiological perspective. In time, it may be possible to develop combined services and pooled expertise in rare or specialised areas.

Main disadvantages of Option 4:
• it would lead only gradually to an enteric reference laboratory service which has an all-island basis
• this gradual development could affect the quality of the all-island data collected and it could reduce the potential epidemiological benefits that might otherwise have come from some of the other options
• the costs would be similar to those calculated for option 2 or 3 (depending on whether option 4a or 4b is selected) but would fall more heavily on the Republic of Ireland than envisaged for alternative options
• this option would not reflect the aspirations of the Belfast Agreement of closer collaboration between the two jurisdictions
• Northern Ireland would not be a full participant in the crucial development stages
• the location of the laboratory/ies would already be predetermined as being in the Republic of Ireland, leaving Northern Ireland without a potential site in the future.
8 Conclusions

An enteric reference service provides definitive identification of the causes of enteric illness. It is essential for outbreak recognition and for the identification of emerging issues and threats in enteric illness. An integrated enteric reference service for the island of Ireland would enhance public health protection by providing rapid identification of the causes of foodborne disease, by facilitating traceback to the sources of infection and by allowing sharing of comprehensive data on these organisms.

The expert group has considered differing ways in which the service now provided could be enhanced. Four options have been presented:

1. Use of the LEP for all specialist enteric services.
2. Establishment of a managed network of reference laboratories on the island servicing both jurisdictions with the same high level of service applying to each.
3. Development of a single site on the island for all specialist enteric services.
4a. Establishment of a managed network of reference laboratories in the Republic of Ireland initially for use by Republic of Ireland laboratories.
4b. Development of a single site in the Republic of Ireland initially for use by Republic of Ireland laboratories.

These options involve varying levels of change when compared to the operation of the current service. However, they represent ways in which some important deficiencies of the present system could be addressed. Each of these options needs to be carefully considered in the light of the maximum public health benefit to the population of the island.
Appendix 1

Membership of Expert Group

Chair
Dr. Tim Wyatt  Consultant Clinical Scientist
Mater Hospital Belfast

Members
Dr. Paul Rooney*  Consultant Microbiologist
Public Health Laboratory, City Hospital, Belfast
Mr. Ray Dolan  Finance Manager
FSAI, Dublin
Dr. Sydney Neill  Head of Bacteriology
Veterinary Science Division, DARD NI
Mr. Stanley McDowell  Veterinary Officer
Veterinary Science Division, DARD NI
Mr. Brian McKeever  Principal Environmental Health Officer
North Eastern Health Board, Cavan
Dr. Eleanor Mc Namara  Director
Public Health Laboratory, Cherry Orchard, Dublin
Mr. Noel Shanaghy  Chief Technologist
Regional Hospital, Waterford
Dr. Lorraine Doherty  Consultant in Communicable Disease,
DHSSPS, Belfast
Dr. John Egan  Head of Bacteriology
Central Veterinary Research Laboratory, DAF

Secretariat
Dr. Thomas Quigley  Food Safety Promotion Board
Dr. Patricia Garvey  Food Safety Promotion Board
Dr. Margaret Patterson  DARD NI and FSPB
Ms. Sonya Byrne  Food Safety Promotion Board

*Dr. Mary Crowe, St. Vincents Hospital, Dublin, retired from the expert group and was replaced by Dr. Rooney.
Appendix 2

The Main Causes of Foodborne Illness

Bacterial causes of gastroenteritis

Campylobacter
There is increasing concern internationally about Campylobacter and it is now the single largest cause of bacterial food poisoning in Ireland. Campylobacteriosis lasts from two to five days although it can last as long as ten days. The symptoms include abdominal pain, fever and profuse diarrhoea, with some patients experiencing bloody diarrhoea. Vomiting is uncommon. In 0.1% of cases, a serious complication known as Guillain Barre Syndrome (GBS) can occur that results in a temporary state of paralysis. In 2000, there were 2621 confirmed cases of campylobacteriosis on the island of Ireland.

Salmonella enterica
Salmonella enterica is a major cause of foodborne illness on the island of Ireland and has in the past been implicated in several foodborne disease outbreaks. The disease salmonellosis is an acute self-limiting gastrointestinal illness characterised by diarrhoea, abdominal cramps, vomiting and fever. In vulnerable populations such as the immuno-compromised and the elderly, it may pose a more serious threat. The average duration of illness is approximately seven days with 25% of patients requiring hospitalisation. In 2000, there were 1084 confirmed cases of salmonellosis on the island of Ireland. The number of cases has decreased from peaks in the Republic of Ireland in 1998 and in Northern Ireland in 1999.

Verocytotoxigenic Escherichia coli (VTEC)
E. coli O157:H7 is the most infamous of the group of bacteria known as VTEC. The severity of illness varies from mild diarrhoea to bloody diarrhoea with severe complications occurring in up to 10% of cases. The elderly and children under five years of age are most at risk of experiencing complications. Serious complications include acute renal failure, which may necessitate long term dialysis or kidney transplant. Mortality may be as high as 10% among those experiencing complications. While the number of cases of VTEC infection is low in comparison with other causes of bacterial foodborne illness, the severity of the illness makes it a significant public health concern. There were 41 and 48 reported cases in the Republic of Ireland and Northern Ireland, respectively, in 2000, including one child who died in the Republic of Ireland as a result of this illness.
Listeria
Incidents of listeriosis are rare by comparison with the major causes of foodborne illness. However, for susceptible individuals, morbidity and mortality are high. Up to 70% of the population may carry the organism in their intestines, and in healthy individuals, listeriosis presents as a mild flu-like illness. The main symptoms are nausea, vomiting and abdominal pain. Neonates, the elderly, pregnant women, those compromised by underlying illness and the immuno-compromised are susceptible to more serious disease such as septicaemia and meningitis. Mortality in these cases is in the region of 20-30%. There were eleven reported cases of listeriosis in Ireland in the year 2000.

Gastroenteric viuses
Many viruses such as NLVs, rotavirus, astrovirus and adenovirus can be foodborne, although person-to-person spread is generally a more common transmission route. The most significant viruses in foodborne terms, on the island of Ireland, are NLVs, with rotavirus common among infants (patients develop strong immunity following infection).

Norwalk-like viruses
NLVs are members of the Calicivirus family, but were formerly classified and are still often referred to as SRSVs. Symptoms of NLV infection include nausea, vomiting, abdominal pain, fever and occasionally diarrhoea. As many as 27 outbreaks of gastroenteritis were caused by, or were suspected to have been caused by, NLVs in 2000. Outbreaks as a result of food have been associated with shellfish and with foods contaminated by infected food handlers.

While in itself a short-lived illness with rapid recovery, viral gastroenteritis outbreaks in hospitals can lead to closure of hospital wards to new admissions and can cause major disruption to hospital activities. The winter of 2001/2002 has proved particularly difficult in that 16 outbreaks of viral gastroenteritis have been reported in health care facilities in Northern Ireland in the period December 1st 2001 to 31st January 2002 alone, eight of which occurred in hospitals. Numerous hospital outbreaks of viral gastroenteritis have already occurred in the Republic of Ireland during the first few months of 2002.

Rotavirus
Symptoms of gastroenteritis caused by rotavirus include diarrhoea and vomiting. Like NLVs, animals do not serve as reservoirs for rotavirus, and person-to-person
spread is the main transmission route. Rotavirus infection is common among infants but as patients develop a strong immunity following infection, it is a less frequent cause of illness in older age groups. The reported incidence of viral gastroenteritis caused by rotavirus has increased significantly in the latter half of the nineties in Northern Ireland with 509 cases reported in the year 2000, and is now the second most common gastroenteric pathogen reported. Collated data is not available for the number of cases in the Republic of Ireland.

Astrovirus and Adenovirus

Astrovirus and adenovirus are not frequently transmitted by food. Adenovirus, in particular, is associated with gastroenteritis in infants. There were 111 cases of gastroenteritis caused by adenovirus in Northern Ireland in the year 2000. Collated data is not available for the number of cases in the Republic of Ireland.

Protozoa which cause gastroenteritis

Cryptosporidium

The disease cryptosporidiosis is characterised by watery diarrhoea with vomiting and abdominal cramps. In most individuals the disease is self-limiting and is usually resolved within ten days. In immuno-compromised individuals, symptoms may last for up to six months and sometimes it can be fatal. In Northern Ireland, the reported incidence of cryptosporidiosis has risen dramatically in the last five years with 417 cases recorded in 2000. A number of outbreaks have occurred, primarily associated with water supplies, and it is perceived as an emerging problem. Collated data is not available for the number of cases in the Republic of Ireland.

Giardia lamblia

Symptoms of giardiasis include diarrhoea and abdominal cramps and the illness is self-limiting, resolving within a few weeks. There are between 21 and 69 reported cases annually in Northern Ireland although the number of cases is declining. Collated data is not available for the number of cases in the Republic of Ireland.

Toxin-producing bacteria which cause gastroenteritis

Staphylococcus aureus

S. aureus causes illness when enterotoxins preformed during storage or transit are consumed. Symptoms include nausea, vomiting, abdominal pain and prostration. Ten per cent of cases result in hospitalisation although mortality is low. Recovery is usually complete within 24 hours. There was one general outbreak of food poisoning linked to S. aureus in the Republic of Ireland for the period January 1998 - December 2000.
Bacillus cereus

B. cereus causes two forms of illness: emetic and diarrhoeal. The emetic illness is caused by the consumption of a heat stable toxin preformed in the ingested food. Nausea and vomiting result within 1-5 hours. Complications are rare and resolution is usually complete within 24 hours. A diarrhoeal illness occurs when spores of B. cereus germinate in the intestine, proliferate and a heat labile toxin is produced. In this case, symptoms, which include abdominal pain and profuse diarrhoea, are displayed 8-16 hours post ingestion. Similar to the emetic illness, complications are rare and resolution is usually complete within 24 hours.

Clostridium

Several species of Clostridia are implicated in gastroenteritis.

The main symptoms of food poisoning due to Cl. perfringens are diarrhoea and abdominal pain. Symptoms usually resolve within 12-24 hours. Illness is associated with the production of toxin in the intestine after eating food contaminated with the bacterium. Cl. perfringens has been implicated in a small number of gastroenteritis outbreaks in recent years.

Botulism is contracted by eating food containing the toxin produced by Cl. Botulinum. This is a life-threatening condition. Symptoms include dizziness, difficulty in swallowing, slurred speech and weakness of the limbs. Less frequently, patients may experience nausea, vomiting and diarrhoea. Respiratory problems can lead to death by asphyxiation. 10% of patients die even if they are administered botulism anti-toxin; a much higher number die without treatment. Concern has been expressed recently about the potential use of the toxin as a bioterrorist weapon.

Cl. difficile is an increasing problem for patients undergoing antibiotic therapy. The organism establishes itself and flourishes in the gastrointestinal tract producing two enterotoxins. These enterotoxins destroy the intestinal lining and cause diarrhoea. In Northern Ireland, 384 cases were reported in the year 2000. Collated data is not available for the number of cases in the Republic of Ireland.
Appendix 3

Typing Methods
The characterisation of agents responsible for foodborne illness is traditionally known as typing. The typing is conducted by examining the biochemical and molecular characteristics of the micro-organisms involved. The identification procedures initially rely on phenotypic methods, including serotyping, phagetyping and antiibiogram analysis. Genotypic methods are then used to identify the genetic composition of the organism by the study of chromosomal, plasmid or transposon DNA.

Serotyping
Serotyping is the characterisation of a number of antigenically distinguishable members of a single bacterial species. Serologically, bacterial strains may exhibit differences that are not apparent from the results of biochemical tests. One classical example where serotyping has been essential in epidemiology and the monitoring of disease is with Salmonella. With Salmonella, the subdivision of the genus is based mainly upon antigenic analysis. More than 2000 Salmonella types can be separated on the basis of somatic (O) and flagellar (H) antigens, using the Kauffmann and White scheme.

Phagetyping
Phagetyping is a typing method based on differences in the susceptibility of bacterial strains to a range of bacteriophages (phages). The method is successfully used to differentiate serotypes of Salmonella, Campylobacter and E. coli O157:H7. Each of the phages used for typing is lytic for one, or a limited number, of the strains of the species under test. A phage that lyses the particular strain being tested will form a clear macroscopic area against an opaque background layer of surface bacterial growth. The strain can then be defined and identified in terms of the phages to which it is sensitive. The observation of lysis is highly specialised, requiring a significant level skill and training.

Antibiograms
Once an organism is isolated, its antibiotic sensitivity is usually determined. Micro-organisms vary in their resistance to antibiotics, and strains can show similar patterns of resistance to a range of antibiotics. This information is useful, not only in the selection of the appropriate antibiotic treatment, but also in fingerprinting the organism for epidemiological tracing. The antibiotic resistant patterns may be used to differentiate between strains of foodborne pathogens, particularly Salmonella spp. Generally, the isolated organism is tested for antibiotic resistance...
against a range of antibiotics and the resistance pattern (antibiogram profile) that emerges is used to distinguish it from other strains. Multiple antibiotic resistance appears to be frequently associated with certain phage types of Salmonella. Antibiotic resistance among foodborne pathogens appears to be increasing and the determination of antibiotic resistance patterns allows the analysis of trends in antibiotic resistance.

**Toxin Detection**

Demonstrating the presence of an enterotoxin in food and/or clinical material is used to rapidly identify toxin-producing microorganisms. Bacterial toxin detection is particularly important in confirming cases of Cl. perfringens, S. aureus and B. cereus related food poisoning. Toxin detection has the advantages of speed and specificity when compared with routine culture techniques. Serological differences are evident among some enterotoxins and these differences can also assist in epidemiological investigation of outbreaks of food poisoning.

Generally, toxin detection and serological differentiation are by immunoassay, although polymerase chain reaction (PCR) methods are being developed. Typically, toxin assays cannot be performed directly and procedures for extraction and/or concentration of enterotoxin need to be performed before the assay. These procedures require specialised services.

**Serodiagnosis**

The rapid detection of antibody in body fluids, such as blood, is used to detect some foodborne pathogens such as E. coli O157. The application of this technique is developing.

**Molecular Typing**

Molecular typing of isolates is now rapidly becoming an essential component of epidemiological investigation of infectious diseases. For some bacteria, neither serotyping nor phagetype systems exist. These drawbacks have prompted the development of new more discriminatory genetic techniques known as genotyping or molecular typing. Molecular typing methods are also used for further discrimination within known phenotypes, particularly those that possess the same phagetype or serotype.
Genotyping methods are currently available at the LEP and in some research laboratories on the island. The main methods include: plasmid analysis or ‘fingerprinting’ (with or without the application of restriction endonuclease cleavage), ribotyping, restriction fragment length polymorphism (RFLP) analysis, insertion sequence (IS) 200 fingerprinting and PFGE. At present the method providing the most discrimination is PFGE but in future this may be replaced by more rapid PCR-based methods. Other DNA-based methods include flagellar (fla) gene subtyping for Campylobacter, cholera toxin (ct) gene fingerprinting for Vibrio cholera and verocytotoxin (vt) gene subtyping for E. coli O157.
Appendix 4

Centres of Expertise
The group examined the expertise in enteric pathogen typing that is currently available on the island of Ireland. There are 10 centres of such expertise and the range of work carried out by these laboratories is documented below.

The centres are:

1. Department of Agriculture and Rural Development, Belfast (DARD NI)
2. Molecular Diagnostics Unit, Institute of Technology, Cork (MDU)
3. Interim National Salmonella Reference Laboratory, Galway (INSRL)
4. Public Health Laboratory, Cherry Orchard Hospital
5. National Diagnostic Centre, National University of Ireland, Galway (NDC)
6. Central Veterinary Research Laboratory, Abbotstown, Dublin (CVRL)
7. Bacteriology Department, Belfast City Hospital, Belfast (BH)
8. Regional Virus Laboratory, Belfast (RVL)
9. Virus Reference Laboratory, University College, Dublin (VRL)
10. Microbiology Department, Waterford Regional Hospital

Department of Agriculture & Rural Development, Northern Ireland
The science service of the DARD NI is responsible for the provision of research, statutory and diagnostic services in support of the aims and objectives of the Department as well as the provision of tertiary level education through the School of Agriculture and Food Science, Queen's University of Belfast. Work relating to foodborne pathogens is ongoing within two divisions of the science service: the FSD and the VSD.

The FSD has an established research record in the development and application of molecular typing methods for Campylobacter. A wide range of molecular typing methods is available including RAPD, PFGE, fla-typing, and automated ribotyping. The division also collaborate with a number of other centres both locally (e.g. Belfast City Hospital) and internationally through the CampyNet group.

The VSD is the nominated National Reference Laboratory for Salmonella under the Zoonoses Directive, EC Directive 92/117. Serotyping of Salmonella isolates, assessment and development of culture methods and the provision of scientific advice on Salmonella control to government and industry are among
its responsibilities. An extensive bank of Salmonella antisera are held and over 1000 isolates are serotyped annually. Antimicrobial resistance monitoring using NCCLS methods has been ongoing since 1995.

Molecular typing facilities for Salmonella, including plasmid profiling and PCR-based methods, are available within the VSD.

There is an active program of research on verocytotoxigenic E. coli at both the VSD and the FSD. The main focus of research is on improved methods of detection for all VTEC organisms and the development of antigen-capture based systems for the detection of vt1 and vt2. PCR based methods for the detection of vt1 and vt2 genes are also available.

Molecular Diagnostics Unit, Institute of Technology, Cork

The MDU, located within the Department of Biological Sciences, Cork Institute of Technology, was set up in 1995 for the application of molecular protocols in facilitating disease diagnosis and identifying significant bacteria in both clinical and food settings. Extensive molecular typing of Salmonella, Campylobacter and VTEC is conducted using PCR, ELISA assays and immunoblotting. A variety of techniques are used including non-culture DNA-based detection methods, electronic DNA fingerprint and molecular characterisation of antibiotic resistance genes. Unique databases have been developed for the assessment(s) of genetic relationships of bacteria in order to assist molecular tracking. DNA fingerprinting databases exist for S. Typhimurium, Campylobacter spp. and methicillin-resistant S. aureus (MRSA). Molecular characterisation of antibiotic resistance genes in several food pathogenic organisms is also performed. The MDU is currently collaborating with the Microbiology Department at Waterford Regional Hospital to provide reference and research facilities for Listeria.

MDU has also completed the construction of a national molecular epidemiology database for human rotavirus. There is close co-operation with the Bacteriology Department at Cork University Hospital on this work. Direct detection of rotavirus is also available.

Cell-culture facilities, which are used in the identification of viruses, have been developed within the Department of Biological Sciences at CIT.
Interim National Salmonella Reference Laboratory, Galway
The INSRL was established on January 1st, 2000. However, the laboratory has been conducting specialised research and routine diagnoses on Salmonella spp. since 1995. Serotyping, phagetyping and antibiogram profiling are all undertaken.

A near complete bank of antisera is held and the laboratory has offered a serotyping service to other hospitals throughout the Republic of Ireland for a number of years. A full range of sera for serotyping enteropathogenic/enterotoxigenic E. coli is also held by the laboratory.

Phage typing of strains of S. Typhimurium and S. Enteritidis has been undertaken since 1998.

Molecular typing of Salmonella using PFGE is used to subtype strains of Salmonella, especially S. Typhimurium involved in outbreaks of food poisoning. The INSRL has recently begun offering PFGE typing of Listeria, Shigella and Campylobacter spp.

The laboratory collaborates with the National Diagnostic Unit, NUIG, in the identification and epidemiology of Campylobacter.

The Public Health Laboratory, Cherry Orchard Hospital
This public health laboratory is one of the seven official food testing and accredited laboratories. In October 2000, it opened a Containment Level 3 laboratory primarily to facilitate the development of a verocytotoxin E. coli reference service, which was not available in the Republic of Ireland. The PHL is accredited for the isolation of E. coli O157 from food, and provides a clinical VTEC diagnostic service including serotyping and toxin status. The PHL has a development programme underway focusing on the application of molecular techniques to VTEC strains.

National Diagnostic Centre, National University of Ireland, Galway
The NDC is working in collaboration with the INSRL on the isolation and characterisation of human, animal and environmental isolates of Campylobacter spp. The research involves the epidemiology of human and animal Campylobacter isolates and the rapid detection of Campylobacter species in poultry flocks and processing plants.
All Campylobacter isolates are characterised by way of antibiotic resistance patterns, plasmid profiles, biotype and genotype. Both gene specific methods (ribotyping and PCR-RFLP of the \textit{fla} gene) and total genomic methods (PFGE and RAPD) have been established to study the epidemiology of strains. Work has commenced on the use of Amplified Fragment Length Polymorphism (AFLP) and the application of serotyping methods to discriminate strains.

Central Veterinary Research Laboratory, Abbotstown, Dublin
The CVRL of the DAF is the designated Republic of Ireland National Reference Laboratory for Salmonella testing under the Zoonoses Directive, EC Directive 92/117. Serotyping of Salmonella isolates, the assessment and development of culture methods and the provision of scientific advice on Salmonella control to government and industry are provided. An extensive bank of Salmonella antisera is held at the CVRL in order to type approximately 2000 isolates annually. Molecular typing facilities available at the CVRL include PFGE and PCR-based methods. DNA sequencing will be conducted in the near future. Antimicrobial resistance monitoring has been ongoing since 1998 and the laboratory is involved in an EU wide concerted action research project on antibiotic resistance. The CVRL participates in the EU Salmonella Reference Laboratory ring trials on isolation and serotyping. It also organises national ring trials for the DAF-approved labs. North-South cooperation is developing in this area. Research projects on Campylobacter, Salmonella and enterococci are ongoing.

Bacteriological Department, Belfast City Hospital
The NIPHL and the BCH Bacteriological Laboratory, which occupy the same site, conduct routine analyses and have an extensive research programme in the area of enteric, food and water microbiology.

Serotyping and antibiotic sensitivity testing of Salmonella are routinely carried out. Molecular detection of verocytotoxin genes and \textit{eae} determinants of \textit{E. coli} O157 is also undertaken. The laboratory has a molecular epidemiology research programme that is focused on the use of molecular methods in identification, epidemiology and the development of molecular diagnostic techniques. Molecular-based bacteriological techniques include PCR, RAPD, PFGE, RFLP, REA, SSCP and automated DNA sequencing.
The NIPH also carries out research on the diagnosis and molecular epidemiology of Campylobacter spp., E. coli O157, Cryptosporidium spp. and S. Enteritidis PT4.

The laboratory is currently working with DARD NI on typing and comparison of Campylobacter spp. from human, food and animal sources.

Regional Virus Laboratory, Belfast
The RVL handles approximately 115,000 specimens per annum. The service is based on electron microscopy, serology and viral culture along with a range of molecular diagnostic techniques.

A routine diagnostic service for viruses associated with gastroenteritis is available. PCR is available for the identification of NLV, rotavirus, enterovirus, calicivirus, astrovirus and faecal adenovirus.

Virus Reference Laboratory, University College, Dublin
The VRL provides a national diagnostic virology service for the Republic of Ireland, employing a wide range of methodologies for the identification of viral infection in humans and the determination of anti-viral immune status. The service is used in the main by hospital laboratories in the eastern region.

A routine diagnostic service for the identification of viral gastroenteritis is available. Direct electron microscopy, immunoassays, serology and molecular techniques are used.