

IN THE NEWS!

Thiomersal: IMB statement

Askeaton report on animal health

Salmonella infections in Ireland, 2000

Invasive Group A Streptococcal infection

Forum



Editorial Board:

*Dr D O Flanagan
(Managing Editor) NDSC*

Dr D Igoe, NDSC

Dr L Kyne, RCPI (Paed)

Dr D Nolan, ICGP

Mr J O Leary, AMLS

Dr N O Sullivan, ISCM

Dr J Quinn, NVRL

Dr L Thornton, FPHMI

Mr D Whyte (Editor) NDSC

**National Disease
Surveillance Centre,
Sir Patrick Dun's
Hospital,**

**Lr. Grand Canal St,
Dublin 2, Ireland**

Tel: +353 (0)1 6617346

Fax: +353 (0)1 6617347

info@ndsc.ie

www.ndsc.ie

IMB issues statement on Thiomersal

Thiomersal is a mercury-containing preservative used in vaccines to prevent bacterial contamination. Following several queries from general practitioners in relation to thiomersal in Tetravac [diphtheria, tetanus, acellular pertussis and inactivated polio vaccine] and Pentavac [as Tetravac plus *Haemophilus influenzae* type b(Hib)] the Irish Medicines Board, having consulted with the vaccine manufacturers, Aventis, has issued the following statement: "Thiomersal is present in both Tetravac and Pentavac in trace amounts. The trace amounts are equivalent to values below the limit of detection corresponding to less than 18 nanograms per vaccine dose. These trace amounts of mercury have no biologic effect and such products should be considered equivalent to thiomersal-free products.¹ As with any agent, hypersensitivity reactions can occur in sensitised individuals despite the very low concentration. However, previous experience with Tetravac and Pentavac in other countries has shown no evidence of any such reactions having occurred due to thiomersal." During the period 30/1/98 to 31/1/01, approximately 2 million doses of Tetravac were distributed. There were two reports of skin reactions. One was associated with an egg allergy and the other with the Hib vaccine. Almost 3.3 million doses of Pentavac were distributed from 14/11/97 to 30/11/00. A number of local skin reactions were reported. Following investigation these reactions were attributed to the Hib component of the vaccine.

1. Halsey NA. Limiting infant exposure to thimerosal in vaccines and other sources of mercury. *JAMA* 1999; **282**(18):1763-1766.

Investigations Of Animal Health Problems at Askeaton -Final Report

In the early 1990s, high levels of health problems in cattle were reported on two farms in West Limerick. Environmental pollution was suspected locally as being to blame. A nearby aluminium production facility and two Electricity Supply Board power plants further west were suspected locally as being likely sources of any pollution. Among the substances suspected to be involved were oxides of sulphur and nitrogen from all three point sources and aluminium, fluoride, dioxins and polychlorinated biphenyls (PCBs) from the aluminium processing facility. In 1998, these three facilities accounted for 56% of sulphur dioxide and 23% of nitrogen oxides emissions nationally.

A full assessment of all external factors that could have posed a risk to animal health in the area was carried out. Because of the concern about environmental pollution, the Government asked the Environmental Protection Agency to co-ordinate a multi-agency investigation. The Mid-Western Health Board became involved because of concerns that any environmental factors could have implications for human health. The formal investigation began in 1995.

The final report (released 9/8/2001 and available from the Environmental Protection Agency) concluded that pollution, toxic substances in the diet, soil and herbage composition anomalies were all unlikely causes of the animal health problems. The reasons for the severity of animal health problems on one of the farms could not be specifically identified – both because of the retrospective nature of the investigations and the very limited involvement of specialist veterinary pathology services during the period when the problems were at their worst. However, many of the problems reported were of a type commonly seen on farms elsewhere and there is evidence from the available historical information of the involvement of on-farm infectious, nutritional and management factors. The most likely causes of problems on the other farm were infectious and nutritional in nature.

While there was an unusually high incidence of animal disease on a small number of farms in the Askeaton area, neither the number of farms involved nor their geographical spread indicated a wider problem. Since the mid-1980s, air quality measurements in the area have complied with EU standards.

Studies carried out as part of this investigation showed human health in the area to be as good or better, in general, than that in the mid-west region. Mortality experience was better overall, than that regionally. Incidence of cancer was considerably lower in the Askeaton area: two-thirds and one-third the regional level for males and females respectively. GPs reported no excessive illness and twinning and congenital abnormality studies showed no difference from expected prevalence of these conditions. Health status measurement using SF 36 (a standardised instrument for measuring self-perceived health status) showed some statistically significant differences in self-reported health. The actual impact of many of these differences is debatable but is not consistent with any known pollution source. Specific questioning about miscarriages showed that reported levels were similar to elsewhere. There was however an increase in self reported illness not requiring medical attention in the study area.

As a result of specific recommendations made by the four investigating agencies, a Government protocol for investigating human health and animal health problems was put in place in 1997. This protocol has been used on a number of occasions since then – specifically in the Silvermines, (Tipperary) investigation and the Leixlip area of Kildare.

Dr Paul McKeown, NDSC

Content of EPI-INSIGHT should not be reproduced without permission. © NDSC, 2001 All Rights Reserved.

Epidemiology of Salmonella infections in Ireland, 2000

Introduction

Salmonella is a bacterial pathogen that is a common cause of foodborne illness in Ireland and worldwide. There are over 2,300 known serotypes of salmonella. However in recent times *Salmonella enterica* serotype Enteritidis and *S. enterica* serotype Typhimurium have accounted for the majority of cases of human salmonellosis. *S. enterica* infections present as an acute self-limiting gastrointestinal illness, characterised by diarrhoea, abdominal cramps, fever, vomiting, and occasionally bloody diarrhoea. In vulnerable populations, such as the immunocompromised and the elderly, the illness may pose a more serious health risk. *S. Typhi* and *S. Paratyphi* can cause enteric fever, a severe systemic life threatening condition, but this is very rare in Ireland and mainly associated with travel.

Salmonella has been identified as the causative organism in many outbreaks in Ireland¹, and prevention, surveillance and control of infection is a public health priority. As salmonella is a zoonotic agent, control measures must focus on the animal reservoir as well as on humans. On a European level, control of salmonella infections and other zoonoses is currently being targeted as a major priority in a new EU food safety policy² launched by the EU Health and Consumer Protection Commissioner, Mr David Byrne on 1st August 2001.

This article reviews data available from the Interim National Salmonella Reference Laboratory (INSRL), weekly clinical notifications and outbreak surveillance data for the year 2000. These data enable us to provide an overview of the epidemiology and burden of disease caused by salmonella infections in Ireland and highlight in particular, the high levels of antimicrobial resistance among *S. enterica* isolates, particularly *S. Typhimurium*.

Information from INSRL

The Interim National Salmonella Reference Laboratory is based in the Department of Medical Microbiology, University College Hospital, Galway. This laboratory accepts *S. enterica* isolates from all clinical and food laboratories for serotyping, phage typing and antimicrobial sensitivity testing.

Demographic information: There were 665 clinical isolates of *S. enterica* referred to INSRL in 2000. The male: female ratio was 1:1. The age groups and sex of those affected are shown in Table 1.

Table 1: Age group of clinical isolates of *S. enterica* (n=665) referred to INSRL, 2000.

Age group (yrs)	No. of isolates (%)	Male	Female	Unknown
0-4	110 (17)	60	47	3
5-14	67 (10)	34	33	0
15-24	81 (12)	43	38	0
25-34	97 (15)	47	50	0
35-44	69 (10)	29	38	2
45-54	42 (6)	14	28	0
55-64	47 (7)	16	29	2
65+	47 (7)	20	26	1
Unknown	105 (16)	52	45	8
Total	665	315	334	16

Serotyping and phage typing: At present *S. Typhimurium* and *S. Enteritidis* are the dominant serotypes associated with human salmonellosis in Ireland (Table 2). The next most commonly isolated serotypes were *S. Bredeney*, *S. Kentucky*, and *S. Dublin*. There were no isolates of *S. Typhi* or *S. Paratyphi* detected in 2000.

The number of reported cases of *S. Enteritidis* appears to be on the increase, however it should be noted that the ascertainment process has varied from 1998 to 2000.

Table 2: Serotypes of *S. enterica* referred to INSRL.

Serotype	No. of cases (%)		
	1998	1999	2000
<i>S. Typhimurium</i>	578 (80)	200 (42)	286 (43)
<i>S. Enteritidis</i>	60 (8)	155 (33)	239 (36)
<i>S. Bredeney</i>	15 (2)	55 (12)	24 (4)
<i>S. Kentucky</i>	14 (2)	12 (3)	15 (3)
All other serotypes	54 (7)	52 (11)	101 (15)
Total	721	474	665

The predominant *S. Typhimurium* phage type isolated by INSRL in 2000 was DT104 (81%), and the predominant *S. Enteritidis* phage type detected was PT4 (70%).

Antimicrobial resistance: The antimicrobial susceptibilities of the most commonly isolated serotypes in 2000 are presented in Table 3. High levels of resistance were found among *S. Typhimurium* isolates, particularly *S. Typhimurium* DT104. Many of these isolates were found to be resistant to at least five antimicrobial agents, viz: ampicillin, chloramphenicol, streptomycin, sulphonamide and tetracycline (ACSSuT).

Table 3: Antimicrobial susceptibilities of human *S. enterica* serotypes isolated in Ireland in 2000.

	n	% resistance						
		Amp	Chl	Str	Sul	Tet	Tri	Nal
<i>S. Typhimurium</i>	286	83	73	78	90	83	16	2
<i>S. Enteritidis</i>	239	8	0	1	2	3	0.5	15
<i>S. Bredeney</i>	24	0	0	0	8	0	8	0
<i>S. Kentucky</i>	15	7	0	13	80	13	67	13
<i>S. Dublin</i>	12	0	0	8	0	0	0	0
<i>S. Hadar</i>	11	73	0	82	0	91	0	73
<i>S. Schwarzengrund</i>	10	0	0	0	10	0	10	0
<i>S. Virchow</i>	9	22	0	0	11	0	0	56

Amp=Ampicillin, Chl=Chloramphenicol, Str=Streptomycin, Sul=Sulphonamide, Tet=Tetracycline, Tri=Trimethoprim, Nal=Naladixic Acid

Clinical notification data

Salmonellosis is a notifiable disease. Medical practitioners are legally obliged to report all suspected cases. Information on trends in salmonellosis notifications shows that the crude incidence rate of salmonellosis rose in the 1990s to peak in 1998, and has been decreasing since then (Figure 1). The total number of notifications in 2000 was 640, compared to 960 in 1999. The crude incidence rate for 2000 was 17.6/ 100,000 population. To date in 2001, (weeks 1-30, week ending 28/7/01), the number of notifications was 215 as compared with 372 in the same period in 2000, illustrating the continuing downward trend.

Outbreak surveillance information

The Food Safety Authority of Ireland (FSAI) was notified of thirty-six outbreaks of gastrointestinal illness in 2000 that had been investigated by health boards. Salmonella was identified as the causative organism in five of these outbreaks (14%).

- A community outbreak of *S. Typhimurium* DT104 occurred in February in the north eastern region. At least seventy-eight persons were ill, of whom twenty-seven were hospitalised. The food vehicle identified was cooked ham.

- In March, an outbreak of *S. Enteritidis* PT4 was investigated in a nursing home in the eastern region. Patients and three staff members were ill but no specific food was identified.

- The Southern Health Board investigated an outbreak in a takeaway restaurant in April. *S. Enteritidis* was isolated and inadequately-cooked eggs were implicated. Eighteen people were ill, of whom four were hospitalised.

- An outbreak of *S. Typhimurium* DT104 was investigated in Midland Health Board in November in children attending a crèche. Four children and one staff member were ill. Unpasteurised milk was suspected as the source.

- The North Eastern Health Board investigated a small outbreak of *S. Kentucky* in three hospital in-patients in October.

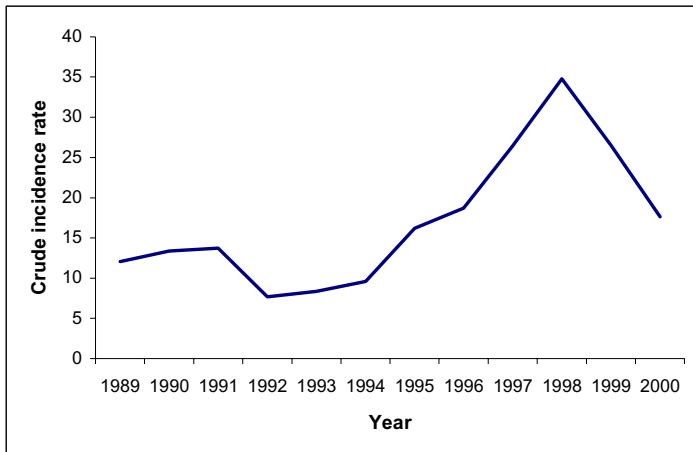


Figure 1: Crude incidence rate of salmonellosis in Ireland per 100,000 population, 1989-2000 (source: DoHC and NDSC).

Discussion

The importance of Salmonella as a foodborne pathogen in Ireland, and the burden of illness resulting from human cases is clearly highlighted by the data presented in this report. The incidence of salmonellosis however is decreasing, as evident from the clinical notification data (Figure 1). This finding was mirrored in the UK³ and Europe in 2000. This reduction may be attributed to the salmonella control programmes for *S. Enteritidis* and *S. Typhimurium* currently in place. Since 1999, eggs produced under the Egg Quality Assurance Scheme set up by An Bord Bia and the Irish Egg Association, with assistance from FSAI, are subject to enhanced salmonella controls in addition to the regulatory requirements. A national salmonella control programme in pig herds was developed in 2000, with FSAI, the Dept. of Agriculture, Food and Rural Development (DAFRD), food producers and processors. In this programme, pig herds are monitored and categorised according to the level of salmonella contamination present.

As time goes on, we will be able to monitor salmonella trends more accurately by examining the laboratory data generated by INSRL from the isolates submitted. It is hoped eventually with the advent of CIDR (Computerised Infectious Disease Reporting) that we will be able to merge clinical and laboratory data. *S. Typhimurium* remains the predominant serotype detected in Ireland, with an increase being seen in 2000 in the number of *S. Enteritidis* isolates that were detected (Table 2). The predominant serotype in England & Wales and Northern Ireland for the past number of years has been *S. Enteritidis*.³

A very interesting finding from analysis of the 2000 INSRL data set, is the scale of the problem of antimicrobial resistance (AMR) amongst salmonella isolates. This is a worldwide problem and has been highlighted previously⁴, however the data presented are extremely significant in relation to *S. Typhimurium* DT104. Multi-drug resistant

S. Typhimurium DT104 is now the most common variety of salmonella isolated in Ireland. Other strains such as *S. Hadar* also showed a significant level of resistance. It is extremely important to be able to link human, animal and food data in order to track the spread of AMR. Recent data from the US suggests that the use of antimicrobial agents in livestock may contribute to the problem of increased resistance in strains that cause human disease.⁵

The spread of AMR is a global issue that needs a strategic coordinated response to combat the problem. To this end, a subgroup of the Scientific Advisory Committee of NDSC recently launched the report on 'SARI' (Strategy for the control of Antimicrobial Resistance in Ireland).⁶

The DAFRD, FSAI and NDSC together aim to produce a "Zoonosis Report" for Ireland this year, presenting data collected on zoonotic agents in 2000 from clinical, food and animal isolates. This is seen as a priority at EU level as was highlighted by the report put forward by the Commission earlier this month.² A regulation is being proposed on the control of foodborne zoonotic agents. Salmonella is identified as the priority target, especially in poultry products and eggs. The aim is to cut the 166,000 annual cases of the illness in the EU by bringing in new controls that will affect producers of breeding poultry, laying hens, broilers, turkeys and breeding pigs. A fixed timetable has been put in place to meet these targets. To achieve these reductions, Member States will need to adopt national control programmes and encourage the private sector to collaborate.

The data presented on outbreaks of salmonella underlines the morbidity caused by this pathogen in Ireland. In the large community outbreak that occurred in the North-Eastern region, there were at least seventy-eight persons ill, twenty-seven of whom were hospitalised. This outbreak was caused by a multi-drug resistant isolate of *S. Typhimurium* DT104. Some of the foods implicated in the salmonella outbreaks included cooked ham, eggs and unpasteurised milk. It is crucial that efforts are made to trace the source of these outbreaks, so that preventive measures can be taken at every point in the food chain. Vulnerable groups were affected in three of these outbreaks that occurred in a hospital, nursing home and a crèche. It is extremely important to ensure that hygiene practices are of the highest standard in these settings.

Since July 1st 2001, the NDSC has initiated surveillance of all formally investigated outbreaks of infectious disease. There will be regular feedback to all the information providers to this system, and we encourage reporting of all investigated outbreaks, including family outbreaks.

It is evident from this report that there is very valuable information derived from analysis of the data collected by INSRL. Ongoing participation of laboratories in this system and the assistance of public health and environmental health in investigation of cases/outbreaks at health board level, will enable the epidemiology of salmonella infections in Ireland to be elucidated even further. Prevention of salmonella infections requires a strategic approach involving a wide range of professionals, to help to reduce the burden of illness caused by this pathogen.

**Dr Barbara Foley (NDSC), Prof Martin Cormican (INSRL),
Dr Margaret Fitzgerald (FSAI) & Dr Paul McKeown (NDSC)**

References

1. Bonner C, Foley B, Wall P, Fitzgerald M. Analysis of outbreaks of infectious intestinal disease in Ireland: 1998 and 1999. *Ir Med J* 2001; **94**: 140-144.
2. EU Health and Consumer Directorate. Press release. Available at <http://europa.eu.int/comm/dgs/health_consumer/library/press/press176_en.html>
3. PHLS Laboratory of Enteric Pathogens 1981-1991; PHLS Salmonella Dataset 1992 onwards. Available at <<http://www.phls.co.uk/facts/Gastro/Salmonella/salmHumAnn.htm>>
4. Cormican M, Butler C, Morris D, Corbett-Feeney G, Flynn J. Antibiotic resistance amongst *Salmonella enterica* species isolated in the Republic of Ireland. *J Antimicrob Chemotherapy* 1998; **42**: 116-118.
5. Tollefson L. & Miller M.A. Antibiotic use in food animals: controlling the human health impact. *J AOAC Int* 2000; **83**: 245-254.
6. Subgroup of SAC, NDSC. Strategy for Control of Antimicrobial Resistance in Ireland - SARI. June 2001. ISBN 0-9540177-0-6.

INVASIVE GROUP A STREPTOCOCCAL INFECTIONS

Group A Streptococcus (GAS) is a common cause of skin infections and pharyngitis. Invasive infections can occur occasionally and may be severe. These include bacteraemia, often without an identifiable primary focus, and infection at other normally sterile sites such as bone, central nervous system and other deep tissue sites. Severe soft tissue infections such as necrotising fasciitis, myositis and orbital infections may also occur.

Invasive GAS infections carry a significant mortality, particularly if they are complicated by streptococcal toxic shock syndrome (STSS). STSS is characterised by hypotension (systolic BP ≤ 90 mmHg or $< 5^{\text{th}}$ percentile for age in children) accompanied by at least two of the following signs:

- Renal impairment (serum creatinine ≥ 177 $\mu\text{mol/l}$ for adults)
- Coagulopathy (platelets $\leq 100 \times 10^9$ or disseminated intravascular coagulation)
- Liver function abnormalities (AST, ALT or total bilirubin more than twice the upper limit of normal for age)
- Adult respiratory distress syndrome (ARDS)
- A generalised erythematous macular rash, which may desquamate.

Invasive GAS infections are most common in young children and the elderly and are often associated with underlying chronic illness. Risk factors include diabetes, HIV infection, cancer and alcohol abuse. Secondary infection of chickenpox lesions has been identified as a risk factor in children.¹

The reported annual incidence of invasive GAS infections ranges from 1.5-3.5/100,000 population in North America and Europe. An increased incidence has been reported in Sweden for the first six months of 2001 (1.5/100,000 population, compared to 0.9 and 1.3/100,000 for the same periods in 1999 and 2000 respectively).²

Clinical concern has been raised regarding a number of recent cases of invasive GAS infection in Ireland. There are no national figures for invasive GAS infection but surveillance is carried out in some regions. There were nine cases of GAS bacteraemia reported to Infoscan, which covers the Southern, Mid-Western and South Eastern Health Board regions, for the first quarter of 2001. This compares to three cases for the first quarter of 2000 and no cases for the same period from 1997 to 1999. Thirteen cases of invasive GAS infection have been reported in the Eastern Regional Health Authority region for 2001 to date.

In the absence of national incidence figures it is not possible to say whether or not this represents a real increase in invasive GAS infection. However clinicians should be aware of the clinical features of invasive GAS infection and treatment options. Patients with invasive GAS infection must be treated in hospital and expert therapeutic advice should be sought from a clinical microbiologist or infectious disease physician. Non-penicillin allergic patients should receive a combination of high-dose penicillin and clindamycin. There is recent evidence that intravenous immunoglobulin (IVIG) can reduce the mortality in cases of invasive GAS infection associated with STSS.³

GAS carry surface proteins (designated M and T) which can be used to classify specific strains of GAS. Certain M-types, particularly M-1 and M-3, are associated with invasive infections and may cause outbreaks. It is important that any isolates of GAS from invasive infections are sent for typing to the PHLS Streptococcus and Diphtheria Reference Unit at Colindale.

Clinical microbiologists have been asked to provide information to NDSC on all cases of GAS identified over the past year. This information is being collated at present. From this will emerge the number of cases, demographic characteristics and information on strain types where available, seen over the past 12 months. This information will be used to determine the national incidence of GAS and will inform what further measures may need to be taken.

Dr Robert Cunney, NDSC

1. Davies HD, McGeer A, Schwartz B, Green K, Cann D, Simor AE, Low DE. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. *N Engl J Med* 1996;**335**:547-54.
2. Carrigu-Mas JJ. Increased cases of invasive Group A streptococcal infections in Sweden. *Eurosurveillance Weekly*, [Serial online] 2001 [cited, 24 May 2001] 21. Available at <http://www.eurosurv.org/>
3. Kaul R, McGeer A, Norrby-Teglund A, Kotb M, Schwartz B, O'Rourke K, Talbot J, Low DE. Intravenous immunoglobulin therapy for streptococcal toxic shock syndrome—a comparative observational study. The Canadian Streptococcal Study Group. *Clin Infect Dis* 1999;**28**:800-7.

Infant Botulism

On 14th August 2001, the FSAI confirmed that specific batches of an infant formula produced in Ireland were recalled as a precautionary measure. This followed an incident in the UK where a batch of the formula was linked to a case of infant botulism – the infant recovered. To date, no cases of infant botulism have been reported in Ireland. Disease facts on infant botulism are available on the NDSC website. Currently, antitoxin is not recommended for treatment of infant botulism.

Forum

Over the last eighteen months, the Editorial Committee of EPI-INSIGHT has endeavoured to cover a wide range of topics of interest to a diverse audience, in Ireland and internationally. The results from the first readership survey were collated in August 2001 and there has been a very positive response to the publication. The results of this survey are available now on the NDSC website;

http://www.ndsc.ie/epi_insight.htm

Thank you to all those who took part in the survey.

Information and reports on developments in infectious disease are welcomed from health professionals in all the health boards and further afield. The publication is distributed in a timely manner and may prove a good vehicle of communication of brief reports that would be of interest in other regions. If you have a report or would like to find out more, please e-mail epiinsight@ndsc.ie

Salmonella Monthly Report (July 2001):

Strains are allocated to months based on the date of receipt of the isolate from the referring laboratory. These figures are provisional as work may not be finished on particular strains at the time of publication. Data are provided courtesy of Prof Martin Cormican and Dr Geraldine Corbett-Feeney, INSRL.

Health Board	E	M	MW	NE	NW	SE	S	W	Total
S. Typhimurium	4	3	3	4	0	2	1	1	18
S. Enteritidis	8	6	2	0	0	3	10	1	30
S. Brandenburg	1	0	1	0	0	0	0	0	2
S. Bredeney	0	0	0	0	0	1	0	0	1
S. Corvallis	0	0	0	0	0	0	0	1	1
S. Derby	1	0	0	0	0	0	0	0	1
S. Dublin	0	0	0	0	0	1	0	0	1
S. Heidelberg	0	0	0	0	0	0	1	1	2
S. Newport	1	0	0	0	0	0	0	0	1
S. Saintpaul	2	0	0	0	0	0	0	0	2
S. Typhi	1	0	0	0	0	0	0	0	1
S. Virchow	2	0	0	0	0	0	0	0	2
S. Zanzibar	0	0	1	0	0	0	0	0	1
Total	20	9	7	4	0	7	12	4	63

The views expressed in this publication are those of the individual contributors and not necessarily those of the NDSC. The NDSC have made all reasonable efforts to ensure that all information in the publication is accurate at time of publication, however in no event shall the NDSC be liable for any loss, injury or incidental, special, indirect or consequential damage or defamation arising out of, or in connection with, this publication or other material derived from, or referred to in, the publication.