



MEETING REPORT

**Consultation on Norovirus
prevention and control**

Stockholm, 12 September 2006

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1. Background

The founding regulation¹ establishing the European Centre for Disease Prevention and Control (ECDC) gives ECDC a mandate to strengthening the capacity of the EU for the prevention and control of infectious diseases, which may spread within or to the EU. Between 1 January and 5 July 2006, a total of 42 outbreak episodes on 13 different cruise ships sailing in European waters were confirmed or suspected to be caused by Norovirus (NoV). The outbreak investigation was coordinated by the EU funded surveillance network Divine-net, in collaboration with ECDC. Almost 1500 cases of gastro-enteritis were reported, but no common source could be determined. Two new NoV variants were identified through the microbiological analysis of patient and environmental samples during these outbreaks. Based on previous years' experience, it was considered likely that the emergence of new NoV strains coincided with increased virus activity in the community, which in turn reflected an increased activity on cruise ships.

Considering the international dimension and the extent of the NoV activity on the cruise ships as well as the resistance of the virus in the environment, ECDC called for a one-day consultation with experts in the field of NoV epidemiology and microbiology.

2. Objective of the consultation

The objective of the consultation was to review the NoV epidemiological situation in Europe, to assess the actions needed to prevent consecutive outbreaks in cruise ships, and to review the prevention and control measures for cruise ships and other settings (Annex 1).

3. Expert presentations

An update of the latest knowledge on the microbiological aspects of NoV was given, and the epidemiological situation of NoV in Europe was reviewed. The challenges encountered during the latest outbreak investigation and control on the cruise ships introduced the focus of the discussions on NoV on cruise ships. The broad experience of the US CDC Vessel Sanitation Programme (VSP) in terms of possible prevention and control strategies was shared, followed by an introduction of the European programme Shipsan (approval in process by the European Commission at the time of the meeting). Finally, the meeting focused on the strategy to follow with regards to NoV outbreaks on cruise ships and in the community. (Annex 2)

¹ Regulation 851/2004 of the European Parliament and of the Council

3.1. Norovirus microbiology

The basic characteristics of NoV were presented, including the emergence of new variant strains. The following points were raised during the discussions:

- There is currently no rapid test to diagnose or exclude NoV infection. ELISA tests are used on US ships; while these have limited sensitivity, they can be used in outbreak situations. However, they are not suitable for individual-case use.
- Saliva tests identifying antibodies to NoV are at the experimental stage. Considering the time needed before antibodies develop, the usefulness of this test in outbreak situations can be questioned. In addition, there are many different NoV genotypes and it is not known how broad the antibody response actually is. Research on the immune response to NoV is needed.
- In terms of vaccination, some clinical trials with an oral vaccine have been carried out. Although the vaccine proved to be immunogenic, the vaccine covers one genotype only. However, the role of pre-existing immunity in the prevention or modification of NoV illness is not clear. Further research is ongoing.
- Research is also ongoing with relation to alternative strategies, like the use of antiviral drugs based on the use of soluble glycans that inhibit attachment of NoV to its target.
- While rapid tests may provide a certain benefit in an outbreak situation, it is the implementation of strict hygiene measures, and hand washing in particular, that is the only effective control strategy.

3.2. Norovirus epidemiology in Europe

In Europe, the occurrence of NoV outbreaks of international relevance is monitored by Divine-net. The importance of linking epidemiological and microbiological data was emphasised. The main mode of transmission in European outbreaks is person-to-person, but the role of (diffuse) food-borne outbreaks related to the new variants needs to be determined. The following points were raised during the discussions:

- The major burden of NoV outbreaks is in nursing homes and hospitals. Genotype GGII.4 dominates in institutional settings.
- There is little reporting on NoV outbreaks from cruise ships in Europe: the outbreaks occur rather frequently and are considered “normal”; testing of patients represent a certain risk for the staff and often there is only a limited number or no medical staff at all on board; the frequency of the outbreaks results in them not being systematically investigated.
- It was mentioned that data from Ireland show that after 6 years of stricter implementation of control measures, the size of the outbreaks in hospital settings seems to decrease (although not the incidence of outbreaks). Similarly, the CDC

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Vessel Sanitation Program reported a measurable reduction in the average size of outbreaks, but not in the incidence.

- The level of outbreak investigations in hospitals, airplanes or similar closed settings is not always optimal, considering the frequency of NoV outbreaks, as well as the occurrence of other disease outbreaks. In addition, the investigation of potential food- or water-borne introduction of the virus is extremely complex, and rarely successful.
- European data from the past 5 years show that about 12% of the NoV outbreaks are food-borne, while this is up to 40% in the US. Experts agreed that this difference is likely to be due to the definition used rather than to a true difference in main transmission mode.
- In order to detect outbreaks that were initiated through food-borne transmission, a distinction needs to be made between the *cause* of the outbreak, i.e. the transmission mode for the primary case(s) versus the *magnitude* of the outbreak, i.e. the transmission mode for the secondary and tertiary cases. The combination of the epidemiological and microbiological data also gives an indication of the true size of food-related cases.
- Investigations within the Vessel Sanitation Programme (VSP) in the US only include food analysis if the epidemiological investigation reveals a potential common source associated with a particular meal. Hypothesis-generating interviews are the basis before any further steps are taken. Experience in US has shown that outbreaks on cruise ships usually are caused by a person who is infected or symptomatic upon embarking. And even if contaminated food is involved, multiple transmission modes usually occur

3.3. Challenges for investigations on cruise ships

The challenges encountered during the investigation of the outbreak episodes on the cruise ships were presented. The following points were raised during the discussions:

- The two new NoV strains have been identified over a vast geographic region (Australia, Hong Kong and Europe). In addition to the role of person-to-person transmission, and the possible role of contaminated food, the possible role of the ship's crew in dissemination of such new variants over a vast geographic region should be taken into account, since crew members often come from different countries.
- The implementation of hygiene measures and the reporting of outbreaks are different depending on whether the ships go to US ports or not. Regulations in the US are stricter and the occurrence of outbreaks is reported on the internet in a transparent way. The US CDC publishes scores based on sanitation inspections of the affected ships, and outbreaks are published within a voluntary VSP activity. In Europe, analysis of Hazard Analysis Critical Control Point (HACCP) in cruise ships could be carried out.

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- Collaboration by the public health agencies with and between the different ship owning companies is recommended. The good cooperation between the medical staff could be a good start. In the US, sanitary inspections are paid by the companies themselves, considering the benefits of not having outbreaks during the cruises.
- In Europe, it is not clear if and where reports of epidemics on the cruise ships are registered. While some ships keep their own logs for outbreak episodes, there is a need for an international registry for cruise ship outbreaks.
- There is a need to identify ground rules with regards to what the response to a NoV outbreak on cruise ships should exactly entail, how fast the response should be triggered and how to coordinate the activities if needed on an international level.

3.4. Vessel Sanitation Programme in the US

The US Vessel Sanitation Programme (VSP) was established in the early 70's. The role and functioning of the VSP was presented, as well as the results of an analysis of the programme's findings in the past 10-15 years. The following points were raised during the discussions:

- According to the US data, background incidence is at four cases per cruise, while during an outbreak, around 100 cases usually occur. A sudden increase in viral outbreaks on cruise ships was detected in 2002 compared to the previous years. The annual number of outbreaks has remained at a relatively high level since then.
- In the US, all outbreaks are investigated under the supervision of the same (CDC) team and samples are assayed by one laboratory. In contrast, in the European cruise ship investigation, differences were observed between protocols used in different laboratories, which made comparison of results less straightforward.
- While NoV is a common cause for outbreaks on cruise ships, it needs to be stressed that multi-pathogenic outbreaks occur, involving multiple modes of transmission. Other viruses and bacteria need to be considered as well.
- A discussion is ongoing whether to use a threshold to investigate the outbreak based on an incidence rate or on an attack rate: the incidence rate includes the duration of the cruise whereas the attack rate doesn't.
- There is a need to work with the industry for the implementation of environmental control measures, and extend this to the land-based operators who deal with hotels and tour operators as well.
- One issue to be addressed is until which point public health authorities need to be involved. Should every outbreak be thoroughly investigated? What is the appropriate threshold before an investigation is launched? If the threshold is too high, there is a risk that other outbreaks, with lower attack rates (e.g. *Salmonella*) will be missed. One influencing factor may be whether it concerns a single outbreak, or whether a number of sequential outbreaks on the same ship are involved.

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- There is discussion about the operational use of a threshold: the use of attack rates is relevant for the implementation of control measures, targeting the exposed population. When using incidence rates, the exposed population is less clear.
- The existence of a legal authority has proven to be very helpful in ensuring the implementation of sanitation programmes on cruise ships.

3.5. The EU Ship Sanitation Programme (Shipsan)

The overall objectives of the European funded “Ship Sanitation Programme” (Shipsan) are the following:

- To describe the current situation on ship sanitation and control of communicable diseases related to cruise ships and ferries in the EU
- To assess the usefulness of an EU ship sanitation strategy
- To enhance the EU capacity to prevent outbreaks and control communicable diseases on cruise ships and ferries.

3.6. Prevention and control guidelines

Based on a review of the main NoV related guidelines available on the web, a basic set of hygiene principles to be implemented when an outbreak is identified, were developed and presented. The following points were raised during the discussions:

- Known efficient interventions for controlling person-to-person transmission (e.g. hand washing) should be systematically implemented. Guidelines should be kept simple and practical, and provide choices where possible, e.g. with regards to the disinfection product to be used, etc. In case of new developments, it should be possible to revise the guidelines easily.
- Most of the recommendations and measures are documented and have been compiled. It was proposed to centralise such information, and allow experts to give feedback and add suggestions. Useful recommendations from the industry should be considered.
- The implementation of measures needs to correspond to the local conditions on the cruise ships. Further evidence on the efficacy of measures and best practices is needed before strict implementation can be enforced.
- Training on the implementation of measures is important and needs to be continuous.
- Barriers to the implementation of guidelines need to be identified and addressed. Examples are the damaging effect of chlorine on materials, limited capacity and personnel, need for training, etc. From an administrative side, payment for the sick leave of affected crew needs to be considered. Finally, where can sick patients be isolated, if not on the ship? Experience has shown that hotels may not always be willing to collaborate.

4. Responding to the gaps

Based on the presentations, several gaps were identified in the current prevention and control strategy related to NoV epidemics on cruise ships.

4.1. Guidelines

- The diagnosis of an outbreak is based on clinical information, emphasising the need for an accurate case definition, which reduces to the minimum the “background noise”. A revision of the Kaplan diagnostic criteria was done by the US CDC. It would be useful to make sure they allow early detection of an outbreak, and therefore a rapid response.
- Criteria to report an outbreak need to be established. Should each individual case or cluster of cases of suspected NoV infection be reported?
- Criteria to start an outbreak investigation need to be established; research into the modelling of NoV transmission may be useful to define such criteria. A generic investigation protocol would be useful to allow for comparable data.
- Standardization with regards to the classification of the cause of a certain outbreak is needed, cf. mode of transmission for the primary cases versus for the secondary and tertiary cases.
- There is a need for European guidelines on generic and basic hygiene principles to control outbreaks. Specificities related to NoV control, or to certain settings should be added separately. The guidelines should be simple and practical, based on best practices. Based on the existing experience, certain scenarios can be anticipated, for which specific protocols should be developed.
- With regards to the use of disinfectants, the guidelines should provide the different options which disinfectants can be used according to the setting. The effectiveness of the use of hydro-alcoholic solution for hand washing needs to be determined.

4.2. Sanitary inspections

Variation exists between the Member States with regards to the implementation of sanitary inspections.

- Guidance is needed to standardize inspections on the ships in Europe, in order to better prevent outbreaks.
- NoV should not be the only target for inspection. However, it should be ascertained that specificities related to NoV are integrated in the existing inspection protocols.
- Similar principles of inspection can be applied in other institutions such as hospitals, nursing homes, etc.

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4.3. Surveillance and monitoring

Continuous monitoring of the incidence of gastroenteritis on cruise ships is needed in order to know when interventions are efficient.

4.4. Legal framework

There is currently no legal framework in Europe to respond to outbreaks on cruise ships.

- A European legal framework is needed to make clear where the responsibility lies for the investigation of outbreaks and the response to them. This framework should include the possibilities of sanctions to be imposed in case of non-adherence to the sanitation guidelines.
- Before such a legal framework is developed and can be implemented, voluntary implementation of the guidelines should be promoted.
- Legal guidance is also needed with regards to the involvement of facilities on land, e.g. in case a large number of symptomatic patients needs to be isolated or hospitalized.

4.5. Involvement of the industry

Considering the fact that the cruise ship industry has an important interest in limiting and containing NoV outbreaks, there is an opportunity for a mutually beneficial partnership between the public health sector and the industry. The cruise ship industry should therefore be involved from the start in further regulatory developments, and the legal support for a possible collaboration should be considered. A first exploratory meeting with the medical directors of ship owning companies is to be organized by ECDC.

4.6. International network

Different organizations and stakeholders are to be involved in the further developments related to prevention and control of NoV outbreaks on cruise ships. Two main partners are identified: 1) Shipsan, considering the common goal of control of infectious diseases on cruise ships, and 2) the US CDC's Vessel Sanitation Programme, which has built a large expertise in the prevention and control of gastroenteritis outbreaks on cruise ships. In addition, the following stakeholders are to be considered:

- EU-wide surveillance network on viral food-borne outbreaks (Divine-net)
- Ship owning companies, including their medical directors
- Land operating companies, working in collaboration with the cruise ships.
- The European Commission
- European Maritime Safety Organization (EMSA)
- UN International Maritime Organization

5. Conclusions

The key points to consider for the future work on NoV are the following:

- On European level, there is a need for a generic set of guidelines on basic hygiene principles, the implementation of which has an effect on the incidence of infection in general. Specificities related to NoV, or to certain settings are to be added in a separate way.
- The need for intervention on European scale is most obvious for the control of outbreaks on cruise ships, trains, airports or airplanes, as well as large outbreaks with an international implication.
- In these settings, a clear commonly agreed protocol is needed with regards to the criteria before actions should be undertaken, the type of actions and the methodology to be used, as well as with regards to the responsibilities for those actions.
- Outbreaks in community settings, e.g. hospitals, nursing homes, etc, remain within the mandate of national authorities.

6. Annexes

6.1. Meeting participant list

Marion Koopmans	Divine-net – National Institute for Public Health and the Environment, the Netherlands
Pierre Pothier	Divine-net – University Hospital Centre Dijon, France
Markku Kuusi	Divine-net - National Public Health Institute, Finland
Paul McKeown	Divine-net – National Disease Surveillance Centre, Ireland
Jim van Steenberg	National Institute for Public Health and the Environment, the Netherlands
Ingrid Friesema	National Institute for Public Health and the Environment, the Netherlands
Jenny Kremastinou-Kourea	Shipsan – National School of Public Health, Greece
Christos Hadjichristodoulou	Shipsan – University of Thessaly, Greece
Elaine Cramer	CDC Vessel Sanitation Programme, United States
Eilif Dahl	Rikshospitalet, Norway
Boguslaw Suski	Sanco C3, European Commission

6.2. Agenda of the meeting

09:00 – 09:15	Opening of the meeting <i>Denis Coulombier - ECDC</i>
09:15 – 09:45	Latest knowledge on Microbiological aspects of NoV <i>Marion Koopmans – Divine-net, RIVM</i>
09:45 – 10:15	Review of the epidemiological situation of NoV in the EU <i>Marion Koopmans – Divine-net, RIVM</i>
10:15 – 10:30	Challenges of NoV outbreak investigation and control on cruise ships in Europe <i>Evelyn Depoortere - ECDC</i>
10:30 – 10:45	Coffee break
10:45 – 11:30	Current state on prevention and control on cruise ships: review of existing guidelines and identification of gaps <i>Elaine Cramer – Vessel Sanitation Programme, US CDC</i>
11:30 – 11:45	Introduction to the SHIPSAN proposal <i>Jenny Kremastinou - Shipsan</i>
11:45 – 12:30	Discussion and recommendations to the Member States related to outbreak investigations on cruise ships
12:30 – 13:30	Lunch
13:30 – 14:15	Current state on prevention and control in the community: review of existing guidelines and identification of gaps <i>Jim van Steenbergen – RIVM</i>
14:15 – 15:00	Main principles for European prevention and control guidelines in the community and on cruise ships
15:00 – 15:30	Recommendations to the Member States and plan of action
15:30 – 16:00	Conclusions of the meeting