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WHO Guidance for the Use of Annex 2 of the INTERNATIONAL HEALTH REGULATIONS (2005)

Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern

International Health Regulations Coordination

World Health Organization

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1. Introduction

Under the International Health Regulations (2005) (IHR (2005)), States Parties are required to carry out an assessment of public health events arising in their territories utilizing the decision instrument contained in Annex 2 of the Regulations, and then to notify WHO of all qualifying events within 24 hours of such an assessment. The purpose of the WHO guidance on Annex 2 is to help national authorities to use the decision instrument in assessing public health events that may require notification to WHO.

1.1. Guidance for the utilization of Annex 2

The guidance document for the use of Annex 2 of the IHR (2005) is targeted to National IHR Focal Points (NFPs) and others responsible for assessing the need to notify WHO of public health events under the Regulations. The procedures described in this document are designed to support States Parties in the legally required use of Annex 2 but are not themselves of a legally binding nature. In the absence of scientific analysis upon which to base such guidance the approach taken was to explain the role and function of the decision instrument and to describe when and how to use it. Importantly, a number of case scenarios were included to illustrate the application of the assessment criteria. Through these scenarios, the four criteria set out in the decision instrument are tested against fictional events, while applying established epidemiological and public health principles.

1.2. Development of the guidance document

This guidance for the use of Annex 2 was prepared by the WHO Secretariat and builds on input from experts and WHO staff, including WHO Regional Offices, experienced in the development and application of the decision instrument. The previous WHO interim guidance was refined by a group of experts and users from around the world during a technical consultation held in Geneva at the end of October 2008 (please see http://www.who.int/ihr/summary_report_annex2.pdf). This present version incorporates the changes advised during the consultation.

1.3. The origins of Annex 2

In May 2001, the World Health Assembly expressed its support for ongoing work on the revision of the International Health Regulations, including the notification of events of urgent and international importance by countries to WHO instead of disease specific notification. To assist in the development of a new reporting mechanism, WHO commissioned the Swedish Institute of Infectious Disease Control to conduct a consultation process among public health experts in order to (1) define what constitutes an urgent international public health event and (2) develop an operational framework to be used at country level when assessing the international importance of public health emergencies.

Following an expert meeting in January 2002, criteria were developed, including an algorithm, to be used by countries to assess the urgent and international character of public health events. Based on an international evaluation that tested the usefulness of the notification assessment tool at country level, changes were made to the algorithm and to the explanatory section that supports the application of the four decision instrument criteria. In 2004-2005, the content and format was negotiated, amended and agreed by an Intergovernmental Working Group established by the 56th World Health Assembly. This process was informed by the report of an Ad Hoc Expert Group on Annex 2 of the draft revised International Health Regulations in February 2005. Finally, the International Heath Regulations (2005), including the decision instrument in Annex 2 were adopted by the 58th World Health Assembly on 23 May 2005 (Resolution WHA 58.3)

1.4. Other types of reporting to WHO

In addition to notification under Article 6 and Annex 2, other provisions in the IHR (2005) require reporting to WHO. An additional important option for States Parties assessing events is to **consult** with WHO in circumstances not at the time requiring notification or where related guidance is needed (Article 8). This consultation process can be appropriate when there is insufficient available information to complete the decision instrument assessment, or if a State Party seeks advice on appropriate public health investigative or response measures, or otherwise wishes to keep WHO informed.

Under Article 9.2, **other reports**, States Parties must inform WHO within 24 hours of receipt of evidence of a public health risk identified outside their territory that may cause international disease spread, as manifested by imported or exported human cases, infected or contaminated vectors or contaminated goods.

In contrast to communications initiated by States Parties such as notification and consultation, States Parties are required under the IHR (2005) to respond to **WHO Requests for Verification**. WHO has an expressed mandate to obtain verification from States Parties concerning unofficial reports or communications, received from various sources, about events arising within their territories which may constitute a Public Health Emergency of International Concern (PHEIC). These reports are initially screened by WHO prior to a decision in some cases to request verification. States Parties must acknowledge verification requests by WHO within 24 hours and provide public health information on the status of the event, followed, in a timely manner, by continued communication of accurate and sufficiently detailed public health information available to the notifying State Party.

1.5. Public health benefits of early notifications or consultations

A) **collaborative risk assessment** between WHO and the notifying State Party to determine whether further action is required; and

B) **assistance by WHO** to the notifying State Party in potential public health investigation and response.

Notification initiates an exclusive dialogue between the notifying State Party and WHO concerning the event at issue, and it does not mean that the notified event will necessarily be determined to be a public health emergency of international concern (which will be quite rare), or that WHO will take any specific leadership in the response.

2. Objectives of this guidance

This guidance is written to assist States Parties to implement the International Health Regulations (2005) ("IHR (2005)" or "Regulations") with regards to assessing public health events that may require notification to WHO. Under Article 6 of the IHR (2005), States Parties are required to carry out an assessment of events occurring within their territories using the decision instrument provided in Annex 2 of the Regulations. Any event that meets the decision instrument's criteria must be notified to WHO within 24 hours of assessment by the State Party. Consistent application by States Parties of the assessment and notification requirements under the IHR (2005) is crucial to ensure prompt communication to WHO of those events which may need immediate coordinated international public health assessment and response. Accordingly, this guidance emphasizes the use of the decision instrument on a routine basis as part of an essential risk assessment approach to notification to WHO. A consistent application of the processes used by States Parties for event communications will support WHO global surveillance and response functions for international public health security.

This guidance aims to provide all State Party personnel participating in decision-making relating to notification to WHO with a clear understanding of:

A) the **role and function** of the decision instrument, and

B) **when and how to use it** in the process of assessing events.

This guidance and the instrument itself are primarily designed for use by the NFPs and other national level public health professionals involved in the identification, assessment and reporting of events within the national system and in international notification to WHO. This guidance may also be valuable in providing a better understanding of States Parties' obligations under the Regulations for the different sectors involved in the implementation of the IHR (2005) at national level.

Official event-related communications under the IHR (2005) are carried out between the NFP and the WHO IHR Contact Point by the most efficient means of communication available. Both the NFP and WHO Contact Point are officially designated and required to be available on a 24 hour a day and 7 days a week basis. Whilst NFPs are responsible for notification, they will not necessarily be responsible for actually carrying out the assessment of events and public health risks. Guidance for the designation or establishment of NFPs, including terms of reference and an explanation of their core functions, is provided in the **National IHR Focal Point Guide** (http://www.who.int/csr/ihr/nfp/en/index.html).

The IHR (2005) specify different ways in which States Parties can initiate event-related communications with WHO. Notification is one component of a collaborative process between States Parties and WHO; this process includes the detection, (joint) risk assessment of and the potential response to public health risks. WHO considers a communication as a notification when it is specified as such by the reporting State Party, assuming an assessment is made by the country using the decision instrument. For events not requiring formal notification to WHO, particularly when information is not sufficient enough to complete a definitive assessment with the decision instrument, States

Parties may nevertheless consult WHO (under Article 8) and seek advice on evaluation, assessment and appropriate health measures to be taken. Irrespective of the type of communication, WHO's ability to effectively support States Parties in responding to public health risks and emergencies is critically dependent on the timeliness in sharing information.

3. Scope for notification under the IHR (2005)

Under the IHR (2005), notification is based on the assessment by a State Party of an "event" within its territory "that may constitute a public health emergency of international concern". While notification under the previous International Health Regulations (1969) focused only on 3 "quarantinable diseases", the obligation to notify WHO under the IHR (2005) is therefore much broader and covers a wide range of potentially international public health risks, be they communicable diseases, "contaminated" food (substance or microbial contamination), chemical contamination of products or the environment, release of radio nuclear material, or other toxic release.

The definitions of "event" and "disease" in the IHR (2005) are the building blocks of the expanded surveillance and notification obligations for States Parties. The term “event” is defined as "a manifestation of disease or an occurrence that creates a potential for disease". "Disease" means “an illness or medical condition that presents or could present significant harm to humans, irrespective of origin or source".

Accordingly notification may be required for:

- Events, irrespective of their origin or source, including those caused by biological (of infectious or non-infectious nature) chemical agents or radio nuclear materials;
- Events where the underlying agent, disease or mode of transmission is new, newly-discovered or as yet unknown at the time of notification;
- Events involving transmission or potential transmission through persons, vectors, cargo or goods (including food products) and environmental dispersion;
- Events that carry potential future impact on public health and require immediate action to reduce the consequences;
- Events arising outside of their known usual occurrence patterns.

As mentioned above, such potentially notifiable events extend beyond communicable diseases and address concerns like contaminated food or other products including pharmaceuticals, and the environmental spread of toxic, infectious material or other contaminants. With respect to pharmaceutical products, it is important to emphasize that the notification obligations under the IHR (2005) do not seek to replace the existing pharmaco-vigilance systems and other activities relating to the detection, assessment and prevention of adverse effects of medicines.

The IHR (2005) do not require that the event under assessment involve a particular disease or an agent or even that the agent are known, nor do they exclude events based upon whether they may be accidental, natural, or intentional in nature. The broadened scope and the shift from the previous disease list to the paradigm of event based notification require an informed judgment according to the circumstances in which an event occurs.

It should be noted that this broad scope also applies in the context of two other types of reporting by States Parties to WHO: consultations (Article 8) and responses to WHO requests for verification (Article 10) of reports it has received concerning events within that State Party's territory. The

verification requirement and consultation option may also involve events that originate from biological, chemical or radio nuclear hazards or from unknown etiology at the time of consultation or verification request.

4. Overview: Role and function of the decision instrument

4.1. Role and structure of Annex 2

Annex 2 establishes the necessary criteria for States Parties to decide whether or not an event needs to be notified to WHO under the IHR (2005). The purpose of Annex 2 is to increase sensitivity and consistency of the notification process in the face of users' variable experience, knowledge and perception, to capture as many relevant events as possible globally. Following the assessment, if States Parties remain uncertain regarding the need to notify WHO they are advised to consider the option of consulting the organization as previously described.

Annex 2 comprises two basic parts: page one, the **decision instrument or algorithm** that directs the user in the assessment of an event; and subsequent pages that contain particularized **questions and examples** of contexts in which these criteria may arise. The further specific questions and examples in Annex 2 guide the State Party in the assessment process as the four criteria are fairly broad.

With reference to the different parts of Annex 2, in this guide the following definitions are used:

Table 1. Definitions of the terms "criteria", "questions" and "examples".

Term	Definition
Criteria	Four decision boxes and numbered in Roman numerals (I-IV) in Annex 2
Questions	The questions are in Italics and numbered from 1 to 11 with Arabic numerals in Annex 2
Examples	Examples are the bullets marked with a check mark appearing under some of the questions

4.2. Events requiring notification

Under the decision instrument there are two basic categories of events which must be notified:

A) **all events that fulfill any <u>two</u> of <u>four</u> situational public health criteria specified below.** Within this first category, events involving certain diseases must always be assessed against these criteria (see list below). The need to notify such events will depend upon the outcome of the assessment.

B) **any event involving one or more cases of four specific diseases (Small pox, SARS, Human Influenza caused by a new subtype, Poliomyelitis due to wild-type poliovirus),** irrespective of the context in which they occur, because they are by definition unusual or unexpected and may cause serious public health impact.

4.3. Public health criteria for assessment using the decision instrument

Whether an event is notifiable under the first category depends on a State Party's assessment using the following four essential and mandatory criteria:

1. **Is the public health impact of the event serious? (yes/no)**
2. **Is the event unusual or unexpected? (yes/no)**
3. **Is there any significant risk of international spread? (yes/no)**
4. **Is there any significant risk of international travel or trade restrictions? (yes/no)**

4.4. Timing of assessment and notification

Within a State Party all public health events which may meet any one of the four criteria have to be assessed for potential notification within 48 hours of the State Party becoming aware of it at the national level.[1] This regular and routine assessment of national events should be based upon the public health information available and the application of established epidemiological principles by experienced public health professionals. The same event may be reassessed over time as necessary as further relevant information about the event becomes available. If a State Party assesses an event and finds it notifiable using the decision instrument, it is required to notify it within 24 hours to the WHO IHR Contact Point, and through the State Party's NFP. Where an initial assessment of an event is negative but a subsequent assessment meets the notification requirement, then it has to be notified to WHO within 24 hours following this positive re-assessment.

The decision instrument is designed to be sensitive enough to minimize the risk that a public health event with serious international implications be notified too late for a critical early assessment and response that could contain the event before it spreads internationally. For this reason, there is no automatic publication with respect to notifications under the IHR (2005); it is the starting point for a dialogue between WHO and the notifying State Party on further event assessment, potential investigation and any appropriate public health response measures.

[1] The obligations to develop the public health capacities to detect, assess, respond to, and internally report public health events - and to report as required to WHO - are contained in Annex 1A. Under paragraph 6(a) of Annex 1A, States Parties are required to have and strengthen capacities to assess at the national level all domestic reports of urgent events within 48 hours.

5. Assessment of events according to the decision instrument

5.1. Notifiable events

The decision instrument classifies the notification of events into the above mentioned two basic categories.

The **first category of notifiable events** are those which fulfill any two of the four situational public health criteria. Consequently, all domestic public health events which may fulfill any of these criteria should be assessed using the decision instrument, including those where the cause or origin has yet to be identified.

Moreover, Annex 2 provides in the upper right box that events involving certain epidemic prone diseases must always be assessed using the decision instrument to see if any two of the four assessment criteria are fulfilled, and therefore require notification of the event: Cholera, pneumonic plague, yellow fever, viral haemorrhagic fevers (Ebola, Lassa, Marburg), West Nile fever and other diseases of special national or regional concern, e.g. dengue fever, Rift Valley fever and meningococcal disease. During the revision process, this list was purposefully left open to add additional diseases of national or regional concern. Unlike the second category of diseases, the mere presence of cases of these diseases does not automatically require notification or automatically fulfill any of the four criteria.

The **second category of notifiable conditions** comprises those events involving one or more cases of four critical diseases, listed in the box at the upper left corner of the decision instrument on page one of Annex 2: **smallpox, poliomyelitis due to wild type poliovirus, human influenza caused by a new subtype and severe acute respiratory syndrome (SARS).** These four infectious diseases have been established as being unusual or unexpected and may have serious public health impact. For this reason, even a single case of these four disease entities (as defined in WHO case definitions) must always be notified to WHO, irrespective of the context in which they occur. For events involving suspected cases of the four notifiable diseases (e.g. in the absence of laboratory confirmation of cases suspected for smallpox), States Parties must conduct an assessment of such events according to the decision instrument criteria, and then eventually notify WHO of all qualifying events within 24 hours of the assessment.

5.2. Assessment criteria and specific guidance in Annex 2

With the exception of cases of the four designated diseases, the decision whether or not an event must be notified to WHO requires an understanding by the user of four public health criteria (see table one).

Criterion 1: **Serious public health impact** weighs both the immediate and potential future consequences of an event on the health of human populations.

Questions that should be considered when assessing an event against this criterion:

- Is the number of cases and/or number of deaths for this type of event large for the given place, time or population?
- Has the event the potential to have a high public health impact?
- Is external assistance needed to detect, investigate, respond to or control the current event, or prevent new cases? (This includes inadequate human, financial, material or technical resources).

If the answer to any of these questions is affirmative, the first criterion should be deemed fulfilled for purposes of the decision instrument.

Examples of specific circumstances that contribute to a high public health impact include:

- Pathogen with high potential to cause an epidemic
- Indication of treatment failure, e.g. an infection that used to be treatable and is now not responding to commonly available antimicrobial agents
- Significant public health risk even if no or few human cases have been identified
- Cases among health staff
- Population at risk is especially vulnerable, e.g. refugees and internally displaced persons (IDPs)
- Factors that may hinder or delay public health response (war, disasters, weather, multiple foci)
- Area with high population density
- Spread of toxic, infectious or otherwise hazardous materials naturally or otherwise (potentially) contaminating a population or large area

Criterion 2: **Unusual or unexpected** nature of the event seeks the atypical character of an event within the epidemiological context.

Questions to be considered include:

- Is the event unusual, such as involving unusual aspects or features of an event which may be of special public health concern or cause for alarm?
- Is the event unexpected from a public health perspective?

As above, if an event is either "unusual" as described in this criterion, or the event itself "unexpected" from a public health perspective, then this second criterion should be deemed fulfilled for purposes of assessment and notification.

Examples that should be considered in this context include:

- Unknown causal agent, or an unusual or unknown source, vehicle or route of transmission (**unusual**)
- Evolution of cases more severe than expected or unusual symptoms (**unusual**)
- Event unusual for area, season, population (**unusual**)
- Disease/agent already eliminated or eradicated from State or not previously reported (**unexpected**)

Criterion 3: **Significant risk of international spread of disease** assesses if the event either presents significant risk of dissemination of disease across national borders, or if the disease has in fact already spread.

Questions to be considered under this criterion are:

- Is there evidence of an epidemiological link to similar events in other States?
- Is there any factor that should alert WHO to the potential for cross border movement of the agent, vehicle or host?

Examples that users of the decision instrument should also consider include these contexts in which this factor may typically arise:

- Where there is evidence of local spread, an index case (or other linked cases) with a history in the previous month of international travel, participation in an international gathering, or close contact with an international traveler or highly mobile population
- Event caused by environmental contamination with potential to spread internationally
- Event in area of intense international traffic with limited capacity for sanitary control, environmental detection or decontamination

Criterion 4: **Significant risk of international trade or travel restrictions** refers to the event's potential to prompt other States or entities to adopt measures that limit or ban trade or travel with the State(s) experiencing the event.

Questions to be considered under this criterion include:

- Have similar events in the past resulted in international restrictions?
- Is the source suspected or known to be a food product, water or any other goods potentially contaminated and that are imported/exported internationally?
- Is the event associated with an international gathering or areas of intense international tourism?
- Are there requests for information by foreign officials or international media?

6. Important considerations in the context of assessment and notification

6.1. Considerations for the assessment process

Utilization of the decision instrument based on the four criteria is not simply a mechanical process, but also requires the expert knowledge and experience of public health professionals concerning national disease patterns, epidemiological principles and other relevant subjects. Answering the specific questions and determining whether the criteria have been met requires an informed judgment on the part of the user, such judgment is always influenced by the users' particular experience, knowledge and perception.

The four criteria in the decision instrument are “situational criteria”, meaning that the assessment of an event against the criteria should take into account the specific time, place, population and other important contextual elements in which the event is occurring. It follows that the public health risk from a case of a given disease may be assessed differently in another location or at another time. New information and developments in the event should prompt a reassessment if the initial assessment did not result in notification of the event. With additional information, the event may then become notifiable. It should be noted that such developments would also include changes in the situational context as well as the epidemiological characteristics of the event. For example, heightened interest in the event by foreign officials or international media might change the assessment, particularly with respect to criterion four.

6.2. Considerations for notification

In order to carry out a collaborative assessment between the notifying State Party and WHO notifications must always include or be followed by ongoing communication of accurate and sufficiently detailed public health information on the event in accordance with Article 6.2. This information may include, where possible, case definition, laboratory results, source and type of the risk, number of cases and deaths, conditions affecting the spread of the disease, the health measures employed and any difficulties faced or support needed in responding to the event. As the event unfolds, more information may become available and the dialogue with WHO should include this new information.

Notification to WHO is part of the global early warning function the purpose of which is to provide international support to affected countries and information to other countries if needed. Notification will be associated with the following consequences, all of which intend to benefit WHO Member States:

1. Joint risk assessment with and offer of assistance by WHO to the notifying State Party

Under the IHR (2005), WHO must offer assistance to States Parties in assessing or controlling public health events occurring within their territories. This support can be in the form of technical advice and guidelines, specialized materials, deployment of international teams to affected areas and coordination

of international support from various sources. By virtue of its privileged access to national health authorities and institutions world-wide, WHO can bring the best technical skills to help manage public health threats quickly and effectively.

2. Provision of event related information to all States Parties

WHO seeks to manage event-related information in a responsible way in order to protect affected countries from any unjustified over-reaction by other countries. At the same time, WHO is obligated to provide event information to States Parties regarding public health risks whenever that information is necessary for them to protect their populations. States Parties should be aware that when WHO receives information on an event such information is not made generally available to other countries unless circumstances arise that justify dissemination in order to address the risk of international spread (Article 11). The context that justifies communication of the information to other States Parties include situations where the international spread of the public health risk is inevitable based on the evidence and known circumstances. When WHO intends to make such information available to other States Parties, it has an obligation to consult with the country experiencing the event. WHO may also make information available to the public, if other information about the event is already in the public domain, and if a need exists for public availability of information that is authoritative and independent.

3. Determination of a public health emergency of international concern

The IHR (2005) provide the regular framework for the timely and effective management of a broad spectrum of international public health risks. However, there are some rare events of particular importance for which the Regulations provide a basis for collective global action. Such serious events that endanger global public health are specified by the Regulations as public health emergencies of international concern. The term "Public Health Emergency of International Concern" (PHEIC) is defined in the IHR (2005) as "an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response". This definition implies a situation that is serious, sudden, unusual or unexpected, that carries implications on public health beyond one's national border and that may require immediate international action.

The responsibility of determining whether an event falls into this category lies with the Director-General of WHO and requires the subsequent convening of a committee of health experts - the IHR Emergency Committee. This committee advises WHO on the recommended measures to be promulgated on an emergency basis. It also gives advice on the determination of the event as a PHEIC in circumstances where there is inconsistency in this regard between the assessment of the Director-General and that of the affected country/ies. The Emergency Committee continues to advise the Director-General throughout the duration of the PHEIC, including advising on necessary changes to the recommended measures for control and on the termination of the PHEIC.

It is important not to equate notification with the very rare situation of a PHEIC since the vast majority of events assessed as requiring notification to WHO will not ultimately be determined to be PHEICs. The early notification of events fulfilling the decision instrument criteria is however essential to address those frequent events effectively under the solid framework of the IHR (2005); it is also essential to prevent the spread of disease across international borders.

7. Illustrations of the use of the decision instrument in selected case scenarios

In the following case scenarios, the four decision instrument criteria are tested against the description and potential implications of fictional events, while applying established epidemiological and public health principles. These examples illustrate that disease outbreaks or public health hazards detected by a State Party must be coupled with the context in which they occur to decide whether the event fulfils any two of the four assessment criteria and hence whether it must be notified to WHO or not. While helping to illustrate different kinds of events embedded in particular circumstances that would either lead to notification or not, it is in no way an exhaustive list of probable scenarios.

Table 2. Overview of case scenarios used for the application of the decision instrument

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Case scenario 1: Outbreak of cholera

An outbreak of cholera erupted in a remote municipality with 180,000 inhabitants in the centre of Country A. First cases were laboratory confirmed 2 weeks ago. Within the last three days only, 220 new suspect cases of cholera have been reported. Currently, 45 severe cases with laboratory confirmed Vibrio cholerae serogroup O1 biotype El Tor sensitive to Doxycycline are being treated at the isolation unit of the district hospital. In total, 4 deaths attributed to this cholera outbreak have been recorded. All the cases have been from this rural municipality with poor sanitation services. The cases have been attributed to recent rains setting in with human waste and other materials being washed into existing water sources leading to widespread contamination and environmental pollution. In response, chlorinated water supply and improved sanitation facilities are being established by public health workers in the affected municipality. Cholera is a reoccurring problem in the affected area, especially during the rainy season, resulting sometimes into case fatality rates higher than 2%.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public impact of the event:

- Insufficient sanitation capacities and the event's rural location may hinder or delay the public health response.
- The highly infectious pathogen has the potential to contaminate a large population in the municipality.
- External assistance may be required to control the event.

2. Is the event unusual or unexpected? **No**

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by a known agent that occurs usually in that area on a seasonal basis. Contaminating source and mode of transmission causing this cholera outbreak are also known.
- The case fatality rate of about 2% is high but not unusual for seasonal cholera outbreaks for the given area.
- The occurrence of the event itself is not unusual for the area and season, especially since flooding coupled with poor sanitation and hygiene potentiates the spread of water-borne diseases like cholera.

3. Is there a significant risk of international spread? No

Factors indicating that international spread is unlikely:

- No other cases have been reported outside of this remote municipality.
- The scenario does not indicate international travel of cases or contact of cases or other highly mobile people.
- It is unlikely that the waterborne agent of this event affects international waterways.

4. Is there a significant risk of international trade or travel restrictions? No

Factors indicating that the adoption of trade or travel restrictions is unlikely:

- No pointer to the export of food products potentially contaminated with *Vibrio cholerae* El Tor, nor to intense human traffic or interest from external media and/or officials regarding this event.

Based on the existing information, this cholera outbreak meets only one of the four criteria of the algorithm in Annex 2, and thus does not need to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Cholera is one of the epidemic prone diseases appearing in the upper right box that will always lead to utilization of the decision instrument to see if any two of the four assessment criteria are fulfilled.
2. The occurrence of a serious disease such as cholera does not necessarily constitute an unusual public health event or an actual risk to international spread.
3. The epidemiological context and risk of international spread posed by a disease event are important determinants of a potential public health emergency of international concern. Consequently, the public health assessment of the event must be coupled with circumstances, such as place (e.g. proximity to an international border or an airport), time, size of outbreak, as well as clinical and epidemiological characteristics of the pathogen.
4. Though an event might be assessed as not being notifiable there could be nevertheless good reasons for consulting WHO (e.g. limited local capacities, specific vulnerability of the population).

Case scenario 2: Cholera outbreak in a different setting

12 tourists become ill with acute gastrointestinal symptoms just prior to departing Country B. They had all been staying at the same popular tourist resort hotel from where they attended several organized group tours and excursions. Vibrio cholerae serogroup O1 was identified in the stool of six of these patients. Health authorities in Country B suspect a contaminated seafood salad as the source of infection. All symptomatic tourists consumed a seafood salad during a boat trip. During the previous years, sporadic cases of cholera have occurred in Country B but no epidemics. Country C has just reported to WHO two likely imported cholera cases in persons who have just returned from Country B.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? No

Factors indicating that a serious public impact of the event is unlikely:

- The number of cases caused by this cholera event is not large for the Country B.
- Though cholera has the potential to have a serious public health impact even if very few human cases have yet been identified, the event's circumstances minimize this likelihood in the given scenario.

2. Is the event unusual or unexpected? Yes

Factors indicating that the event is either unusual or unexpected:

- Though the event is caused by a known agent from a likely common source, the infection of a large group of tourists is very unusual.

3. Is there a significant risk of international spread? Yes

Factors indicating that international spread is likely:

- Evidence of an epidemiological link to similar events in other States exists.
- Given the recent stay of the cases at a popular tourist location and likely common source exposure, the risk of international spread from returning tourists is real.

4. Is there a significant risk of international trade or travel restrictions? Yes

Factors indicating that the adoption of trade or travel restrictions is likely:

- Implications on international travel are possible since the event has occurred in an area of intense international tourism activities.
- Though not specifically mentioned in the scenario, the contaminated seafood might have been exported to other countries.

Based on the existing information, this cholera outbreak meets two or more of the four criteria of the algorithm in Annex 2, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Cholera is one of the diseases that will always lead to utilization of the decision instrument. However events involving cholera or any other disease that require to be assessed do not necessarily have a serious character in the context of the given geography, population at risk and season.
2. The potential or actual export of even very few cases or their contacts present a risk of international disease spread.
3. In previous years, news of a disease outbreak in an area of intense international traffic have, often unjustified, led to restrictions of international trade and/or travel by other countries. Today, such restrictions need to comply with the IHR (2005).

Case scenario 3: Toxic chemical spill

Following an industrial accident in City D, 100 tons of benzene have spilt into a major river. This is the first time this type of accident has occurred in this area. The river is a main source of drinking water for both City D and also three other major cities in a neighboring country downstream of the river. Benzene is a known human carcinogen. Authorities in City D have shut off drinking water supplies to residents in response and alternative water resources are being mobilized. However decontamination efforts have been limited due to a lack of equipment and expertise.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public impact of the event:

- The event has potential acute health consequences because of: (i) consumption of contaminated drinking water and possibly food (e.g. fish); (ii) lack of water for consumption and hygiene; and (iii) poor water quality of alternative water. In addition, the event might have serious consequences on human health in the future because of delayed health effects of chemical exposures.
- The nature of exposition to this specific chemical agent may result in high proportion of severe cases
- The event has resulted in toxic contamination of a large geographical area with a high population density. Chemical might enter into the food chain.
- Inadequate existing response capacity requires external assistance to respond to the event (including laboratory support, exposure modeling, risk assessment and management).

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- This massive and wide-reaching environmental contamination with a chemical agent known to be carcinogen is relatively rare.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- Transboundary spread of the contaminant via the river to downstream cities in a neighboring country might have already happened or appears very likely. Contaminated food (e.g. fish) might be traded internationally.

4. Is there a significant risk of international trade or travel restrictions? **Yes/No**

Factors indicating that the adoption of trade or travel restrictions is unlikely:

- Only if contaminated food is traded internationally.

Based on the existing information, this chemical event meets two or more of the four criteria of the algorithm in Annex 2, and thus needs to be notified under Article 6 of the IHR (2005).

Learning points:

1. Notifiable events can extend beyond communicable diseases and may arise from biological and chemical agents or radio nuclear materials.

2. The seriousness of an event can be determined by its acute and delayed public health consequences. The assessment of the IHR notification obligation has therefore to consider whether an event carries a potential for future impact on public health and requires immediate action to reduce the potential consequences. For this example, assistance from WHO and other international partners might be requested, depending on existing national chemical emergency response plans and capacities.

3. The potential exportation of a public health hazard across international borders is a major concern.

Case scenario 4: Meningitis outbreak

Within the last two weeks, the National Institute of Public Health in Country E was informed that 105 patients with meningitis, mainly children and young adults from a suburb in City F, were hospitalized in several hospitals. 14 of these patients died after admission. Neisseria meningitis was isolated from cerebrospinal fluid and blood in several patients, and the serogroup has been serologically classified as type A by a conventional bacterial agglutination test.

During the past 24 hours, more than 400 geographically clustered patients with acute neurological syndrome were recorded in several district hospitals surrounding City F. A rapid investigation in the City F and 4 other affected districts indicates a substantial increase in the number of cases per week. Because of the rapid progression of the meningitis outbreak, the reporting system has broken down in some affected districts, making it difficult to assess the true attack rate and geographical size of the outbreak. Notably, Country E is considered part of the African meningitis belt, and one of the affected districts is adjacent to Country G that accommodates a refugee camp with highly mobile inhabitants. In addition, the national stockpile for meningococcal vaccine and related resources to launch an extensive immunization campaign are very limited.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public impact of the event:

- The event is caused by a pathogen with high potential to cause an epidemic.
- The substantial increase of cases in the event, the number of fatal cases since onset of the outbreak, the high population density and potential involvement of a highly susceptible refugee population might have a serious public health impact.
- Insufficient surveillance capacities may hinder or delay the identification of the epidemic threshold for mass vaccination.
- In view of the rapidly evolving outbreak and the lacking availability of vaccines and supportive equipment (logistics) in the country for a timely response, external assistance for public health investigation and response may be required.

2. Is the event unusual or unexpected? **No**

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by an endemic disease occurring in annual cycles in countries belonging to the meningitis belt.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- The risk of epidemics in the border areas of neighboring countries is increased because of similar environmental, climatic and bacteriological factors. The presence of a highly susceptible refugee population increases this risk.

4. Is there a significant risk of international trade or travel restrictions? No

Factors indicating that the adoption of trade or travel restrictions are unlikely:

- No precedent for international restrictions to be imposed. However, travelers to the area should be advised to be vaccinated against meningococcal disease and to avoid overcrowded places.

Based on the above information, this meningitis outbreak meets two or more of the four decision instrument criteria, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Meningococcal disease epidemics will always lead to utilization of the decision instrument.

2. An event with epidemic potential may pose a serious public health risk if the national capacities are not sufficient to respond and control it, and, as a result, external assistance is needed. The adequacy of the available resources (human, technical, financial) has to be determined in relation to the assessed event.

3. Geographical circumstances such as proximity to an international border might indicate the risk that the same event occurs in a neighboring country.

Case scenario 5: E. coli O157:H7 in spinach

In the highly industrialized Country H a total of 72 geographically widespread cases have Escherichia coli serotype O157:H7 infections with bloody diarrhea in relation to the consumption of fresh, bagged spinach in a timeframe of one week. Of the 63 hospitalized cases 7 patients developed hemolytic uremic syndrome (HUS) leading to the death of one child. E. coli O157:H7 with indistinguishable PFGE patterns were isolated from spinach samples and stool cultures of cases. The spinach product has been distributed nationwide and to five other countries. An additional country received the product through secondary distribution. Infection control measures for cases and their contacts have been applied, and a prompt recall of all the contaminated food products, has been issued to prevent further primary infection.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? Yes

Factors indicating a serious public impact of the event:

- The pathogen causing this event has a high potential to have a serious impact because of a strong aetiological association with HUS (in up to 10% of patients, particularly young children and the elderly).
- The broad geographical distribution (multiple foci) of the highly infectious pathogen through the contaminated food product has the potential to have a high public health impact in Country H.

2. Is the event unusual or unexpected? No

Factors indicating that the event is neither unusual nor unexpected:

- The occurrence of clusters of cases with *Escherichia coli* serotype O157:H7 infections is neither unusual nor unexpected. The pathogen is transmitted mainly through consumption of contaminated foods. The presence of enterohemorrhagic *E. coli* O157:H7 in food products is a known problem.
- The clinical evolution of cases is not more severe than expected for an event involving *E. coli* O157:H7.

3. Is there a significant risk of international spread? Yes

Factors indicating that international spread is likely:

- The scenario indicates that export of the contaminated food product already occurred.

4. Is there a significant risk of international trade or travel restrictions? Yes

Factors indicating that the adoption of trade or travel restrictions is likely:

- Similar events in the past have resulted in importing countries imposing trade restrictions to avoid importation of contaminated food products.
- Presence of contamination on the exported product may result in trade restrictions.

Based on the existing information, this outbreak of *E. coli* O157:H7 meets two or more of the four criteria, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Certain food safety-related public health events, including both food contamination and foodborne disease events, can have a high public health impact and international implications requiring notification and reporting under the IHR (2005).
2. Food safety events involving the international import/export of event-related goods have a significant risk of resulting in international restrictions on trade.
3. Beyond the lessons learned from this scenario, food safety events that require notification or reporting to WHO may relate to any of the three hazards which can occur in food: chemical, physical (sometimes know as foreign matter) and microbiological.

Case scenario 6: Outbreak of plague - part one

National authorities in Country J received reports of a suspected outbreak of bubonic plague from an area of the central highlands where housing and sanitation conditions are poor. The outbreak involving 68 clinically suspected and 12 presumptive[2] cases of bubonic plague started a few days after heavy rains occurred. The clinical picture includes sudden onset of high fever, general malaise, severe prostration with headache, and tense cervical, axillary or inguinal buboes. The symptoms among three patients, of which one died, indicate septicemic plague. However, no evidence suggests the manifestation of secondary pulmonary plague.

Due to the delay between the collection of the samples and their arrival at the reference laboratory in Country J, Yersinia pestis could not have been confirmed. Although plague has not been established yet as the definite cause of this outbreak, local health-care providers started antibiotic treatment with streptomycin after laboratory specimens were taken. In addition, public health education about how to avoid exposure to disease-bearing animals and their fleas has been issued for the general public. Local public health authorities and doctors are familiar with diagnosis, prevention and treatment of plague since bacteriologically confirmed or presumptive human cases (≈300/year) of bubonic plague occur annually in this enzootic area during the rainy tropical summer season.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **No**

Factors indicating that a serious public impact of the event is unlikely:

- The number of cases caused by this bubonic plague event is not elevated for the given place and the evolution of this outbreak does not indicate a serious public health impact, so far.
- The public health authorities responded appropriately to this event by early treatment of cases and by promptly disseminating information about the outbreak of plague.
- However, right after the detection this event had the potential to cause a serious public health impact since the natural course of bubonic plague can lead to secondary pneumonic plague. In addition, given the lack of bacteriologic confirmation, clinical diagnosis alone is not always straightforward for the identification of patients with bubonic or pneumonic plague, potentially leading to underestimation of the seriousness. Therefore, at that stage of first risk analysis, Country J might have faced difficulties to complete a definitive assessment with the decision instrument. As a consequence, national authorities could have then decided to start a confidential consultation with WHO, as provided by Article 8 of the Regulations, and to seek advice on evaluation, assessment and appropriate health measures to be taken.

2. Is the event unusual or unexpected? **No**

[2] Detection by microscopy of gram-negative bacillus with morphologic patterns of *Yersinia pestis*

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by a known agent for which Country J has a known enzootic reservoir. The occurrence of human cases of bubonic plaque in an enzootic region is therefore not unusual, nor is it unexpected.

3. Is there a significant risk of international spread? No

Factors indicating that international spread is unlikely:

- The event does not involve factors that make cross border spread likely.

4. Is there a significant risk of international trade or travel restrictions? Yes

Factors indicating that the adoption of trade or travel restrictions are likely:

- In 1994, the epidemic of plague (bubonic and pneumonic) in India showed what impact the media can have. The international reaction was very intensive though the outbreak remained limited as a result of rapid interventions. Several countries closed their borders to travelers from India, some airline companies cancelled all flights from India, and also trade embargoes were declared. Though this event does not encompass cases of pneumonic plague or any other characteristics that would justify any embargo of international travel or of imports of goods from Country J, the significant risk of those travel and trade restrictions as an overreaction can not be excluded.

Based on the existing information, this plague outbreak meets only one of the four criteria of the algorithm in Annex 2, and thus does not need to be notified under Article 6 of the IHR (2005).

Learning Points:

1. An event that potentially has a fulminant public health impact can evolve in a way that offsets its actual public health significance. The assessment of possibly notifiable events has to take into account the situational and operational context in which an event occurs. This also includes the analysis of national capabilities to respond to an event under assessment.
2. States Parties have an explicit opportunity to initiate a "consultation" with WHO to determine an appropriate response for events not requiring formal notification, or where information is insufficient to complete the decision instrument at the time of initial assessment. This consultation process allows States Parties to keep WHO informed and to have a confidential dialogue (similarly to notification) with WHO on further event assessment and any appropriate investigative or response measures. In addition, if an affected State can point out in relation with media to the fact that it is working in collaboration with WHO on a disease related event, then overreaction is not likely to occur.
3. Despite lacking evidence indicating international concern for transboundary transmission, certain disease outbreaks are perceived per se as global microbial threats and lead, though unjustified, in many instances to restrictions of international travel and/or trade.

Case scenario 6: Outbreak of plague - part two

After the laboratory confirmation of this controlled outbreak of bubonic plague, all Y. pestis isolates were screened for their in-vitro susceptibility to antimicrobial agents which are most commonly used for plague treatment. From one patient who presented with symptoms of bubonic plague a multidrug-resistant strain was detected. This wild-type strain was resistant not only to all the first-line antimicrobial drugs recommended for therapy and prophylaxis of plague, but also to antibiotics that may represent alternatives to classic therapy. For the last 10 days, no further cases of bubonic plague occurred in Country J.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating that a serious public impact of the event is likely:

- The discovery of a multiresistant Y. pestis strain causes major public health concern, especially in a disease for which no vaccine exists. The fact that a strain of *Y. pestis* acquired under natural conditions a resistance indicates the potential for continued undetected circulation among the natural hosts followed by the re-occurrence of such an alarming event (i.e. human infection with resistant strain) with its possible implications for treatment, especially in a pneumonic outbreak.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- Despite the fact that a multi-resistant strain was isolated once in Madagascar in 1997, *Y. pestis* is considered as being universally susceptible to antibiotics. Any new emergence of a multi-resistant strain is unusual.

3. Is there a significant risk of international spread? **No**

Factors indicating that international spread is unlikely:

- There are no indications for international spread.

4. Is there a significant risk of international trade or travel restrictions? **Yes**

Factors indicating that the adoption of trade or travel restrictions are unlikely:

- Though the scenario does not provide any details indicating the attention of international media, the risk of travel and trade restrictions cannot be excluded as seen during similar events (cf. India 1994).

Based on the above information, this plague outbreak meets two or more of the four criteria of the algorithm in Annex 2, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

- The appearance of multidrug resistance of a disease agent that involves an epidemic potential may have serious public health impact, even if multiresistance is suspected in a single case.

Case scenario 6: Outbreak of plague - part three

Two weeks after the detection of the suspected outbreak of bubonic plague in Province A described above, a total of 11 patients from Province B were suspected to have pneumonic plague, were isolated and treated with streptomycin, and reported to the national public health authorities in Country J. Since the early clinical symptoms of pneumonic plague are unspecific, pneumonic plague was not suspected until four patients had died and seven others were presenting with the same respiratory symptoms. The diagnosis of pneumonic plague was then ascertained from sputum samples by the rapid F1 dipstick assay and ELISA. In vitro testing showed susceptibility to antimicrobial agents.

Now, more than one week after the death of the index case, field epidemiological investigation and control measures have been initiated from the national level. The local public health infrastructure does not provide sufficient surveillance and laboratory systems, epidemiologic response capabilities, case management and infection control capacities. The epidemiological investigation revealed that the index case was a bubonic patient from the previous outbreak in the highlands (see outbreak of plague - part one) who travelled about 200 km to consult a traditional healer and died with a secondary pneumonic plague. The healer, his family, and a patient of the healer developed primary pneumonic plague. The other villagers became infected during their active participation in the funeral ceremonies. The local funeral practice includes the cleaning and kissing of human bodies. Outbreaks of pneumonic plague have never occurred before in Province B.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating that a serious public impact of the event is likely:

- The number of cases associated with this outbreak of pneumonic plague is high for the given place.
- This event, even if only very few human cases have yet been identified, has the ability to cause a high public health impact because of the potential for spread, high mortality if cases are left untreated, the expected panic in the population and the amount of response measures needed by public health authorities. The late identification of pneumonic plague cases increases the risk of public health impact since the immediate application of the control measures are decisive in preventing an epidemic of pneumonic plague. Thus, additional cases must be expected.
- The inadequate public health infrastructure might hamper the control.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- The occurrence of the event itself is unusual for the area.

3. Is there a significant risk of international spread? **No**

Factors indicating that international spread is unlikely:

- Noting the remote and circumscribed location of this event, there is no factor that implies the risk of cross border spread.

4. Is there a significant risk of international trade or travel restrictions? Yes

Factors indicating that the adoption of trade or travel restrictions are likely:

- As indicated in the first part, pneumonic plague is perceived by the public and some governments as a global threat for public health. However, in view of the epidemic potential and bearing the lasting impression of the Black Death in the Middle Ages in mind, international reactions are usually intense when an outbreak of pneumonic plague is discovered. Therefore, this event involves a significant risk of unjustified travel and trade restrictions imposed by other countries.

Based on the above information, this plague outbreak meets two or more of the decision instrument criteria, and thus does need to be notified under Article 6 of the IHR (2005).

Learning Points:

1. An event that at initial assessment was considered not to be notifiable can evolve over the coming days and weeks so that new assessments must be made, using the decision instrument criteria. And with additional information the event may then become notifiable. Knowing this possible evolution, preparedness for early detection and timely response is strongly recommended for the previous case scenario.
2. The timeliness of detection of and response to an event is an important consideration in assessing the immediate and potential future consequences of an event on human health and populations.
3. The impact of an event is also determined by concomitant issues which may delay or hinder an appropriate response such as geographic considerations or traditional burial habits.
4. Early notification will enable WHO to assess travel restrictions issued by other countries and provide appropriate recommendation for travelers going to and coming from the affected area.

Case scenario 7: Outbreak of unknown etiology

During the last four days, 23 cases of febrile encephalitis associated with respiratory illness (8 [35%] fatal) were reported to the Ministry of Health in Country L. The index case and eight additional cases occurred among abattoir workers of the same slaughterhouse, three cases are household members of one of those workers, and the other cases occurred among traders and customers exposed to cows and pigs at a cattle-market held 1.5 weeks ago. Meanwhile, two of the patients died; and two health-care workers caring for these fatal cases have also fallen ill. Concurrent with the human cases, illness and death occurred among swine from the same regions, 1-2 weeks before illness in humans. The disease in swine, which is so far of unknown etiology, is not well defined but appears to include rapid and labored breathing; an explosive nonproductive cough; and neurological changes, including lethargy or aggressive behavior.

All human cases have occurred in the two rural areas (of two distinct Provinces) and are primarily adult men who had histories of close contact with swine. Illness has been characterized by initial fever and headache, followed by mild blurred vision, generalized seizures and disorientation that can progress to a coma within 24-48 hours, as well as development of respiratory failure in some patients. Most cases became ill 6 to 10 days after their last known exposure to swine. Initially, Japanese encephalitis (JE) virus was considered the probable etiologic agent for this outbreak since specimens from one early patient tested positive for infection with JE virus. However, the predominance of cases in humans who had close contact with swine suggested the possibility of another causative agent which laboratory diagnosis, despite numerous testing, has not been able to reveal yet. An epidemiological outbreak investigation team started a study to identify the source of human infection, to define specific risk factors associated with illness in humans, and to determine the risk for human-to-human transmission.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public impact of the event:

- The event is caused by an unknown pathogen which seems to have a high potential to cause a severe epidemic, in view of the relatively high number of cases and deaths since onset of the outbreak.
- It poses a significant public health risk since the definite source of infection (animal reservoir?); the infectivity among humans; possible routes of transmission; and the appropriate components of prevention and therapy (e.g. antiviral agents) are all still unclear. As a result, this event offers continuing opportunities for human infection with an obviously highly transmissible and pathogenic agent that might compromise control efforts.
- Cases reported among health-care personnel always represent a potentially serious public health event.
- The event has a great potential to impair effective control measures and external assistance may be required to further investigate the causal agent and control the ongoing event.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- The event is caused by a yet unknown infectious agent of uncertain origin causing an unusual clinical picture.
- The occurrence of the event itself is unusual, i.e. a potentially new emerging disease.

3. Is there a significant risk of international spread? **No**

Factors indicating that international spread is unlikely:

- Though cross-border movement of healthy carriers or animals contaminated with this newly recognized pathogen can never be ruled out, there are no indications for the risk of international spread in this scenario.

4. Is there a significant risk of international trade or travel restrictions? **Yes**

Factors indicating that the adoption of trade or travel restrictions are likely:

- The potential involvement of animals as the source of human infection may lead to an importation ban by other countries.

Based on the existing information, this outbreak meets two or more of the four criteria in the decision instrument, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Events with no or very few human cases yet identified may still represent a serious and notifiable public health event especially if associated with deaths in animals.
2. Cases among health-care workers should always prompt further investigation and indicate a potential high public health impact.
3. Events caused by unknown or unusual agent; source; route of transmission or vehicle may represent a potential public health emergency of international concern. Early consultation with WHO during an evolving outbreak of unknown origin is advised given the potential seriousness and lack of available information at this point.
4. The association of an event with food products potentiates the possibility of the imposition of trade restrictions.

Case scenario 8: Cutaneous anthrax in laboratory

A university hospital just reported one case of cutaneous anthrax in a worker at its laboratory. The lab worker presented with a painless ulcer on his right hand with surrounding vesicles along with massive edema and eschar formation accompanied by low-grade fever and sub-axillary lymphadenopathy. Skin lesion samples were sent to a specialized laboratory (with BSL-3 capability) for presumptive (by PCR) and for confirmatory (culture recovery) testing. PCR was positive. The patient is responding dramatically to the early course of ciprofloxacin administered right after the provisional diagnosis of cutaneous anthrax, and continued the treatment after proven susceptibility of the isolate; the patient's constitutional symptoms improved. Computed tomography of the chest was normal.

The epidemiologic and environmental investigation of this case indicated that the probable source of exposure was contact with contaminated surface of culture vials known to contain B. anthracis which the worker had handled without wearing gloves. Several vials containing B. anthracis had been stored in this laboratory freezer from investigation of a human cluster of cutaneous anthrax two years ago. A swab of the vial cap handled by the worker yielded a B. anthracis culture that was indistinguishable from the culture recovered from the patient's clinical specimen. For the case presented herein: there were no obvious links to any animal having tested positive; or any evidence for either naturally occurring or bioterrorism related anthrax during the identified timeframe of infection. Extensive environmental sampling from the patients' workplace (including the air filtration system), residence and travel destinations for the 60 days preceding symptom onset were negative for B. anthracis by PCR and conventional bacterial cultures. Nasal cultures taken from personal contacts and co-workers in the same workplace environment were also negative for B. anthracis. So far none of the other employees at the laboratory, who received immediate post-exposure prophylaxis, reported illness among themselves or their family members. Serologic studies for antibodies to B. anthracis among co-workers are planned.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **No**

Factors indicating that a serious public impact of the event is unlikely:

- The evolution of this event is not more severe than expected for cutaneous anthrax which is usually not a life threatening disease if treated adequately.
- Since the source of infection could be documented this event does not indicate the risk of further human infection with *B. anthracis*. In addition, anthrax is not very contagious among humans since the only potential for contagiousness exists through spore or organism-contaminated body fluids.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual:

- Human cases of anthrax are unusual, especially if occurring in a laboratory setting.

3. Is there a significant risk of international spread? **No**

Factors indicating that international spread is unlikely:

- The event poses no risk of disseminating across national borders.

4. Is there a significant risk of international trade or travel restrictions? **No**

Factors indicating that the adoption of trade or travel restrictions are unlikely:

- There is no risk of imposition of trade or travel restrictions.

Based on the existing information, this anthrax outbreak meets one of the four criteria of the algorithm in Annex 2, and thus does not need to be notified under Article 6 of the IHR (2005).

Learning Points:

1. The occurrence of an event involving a disease of public health importance, such as anthrax which usually requires notification to national public health authorities, does not necessarily constitute a notifiable event under the IHR (2005).
2. This scenario underscores the importance of safe laboratory procedures and alert for the potential infection of laboratory workers routinely handling biohazardous materials.

Case scenario 9: Outbreak of typhoid fever in endemic area

In Country O, engineers have been repairing water pipes in a densely populated city and have advised residents not to drink the water without first boiling it for the initial few weeks after the water service is restored. Despite these warnings there is a large outbreak of 600 cases of typhoid fever in the city. Residents from several suburbs have been infected and 14 people have died from the complications of the disease. Meanwhile, health officials have been testing the water supply which has now been deemed safe and the number of cases is rapidly declining. There are no reports of cases in neighboring cities. Typhoid fever is a commonly occurring disease in Country O.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **No**

Factors indicating that a serious public impact of the event is unlikely:

- The number of cases has already declined rapidly.
- Water supply has been deemed safe.

2. Is the event unusual or unexpected? No

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by a known agent from a known contamination source.
- The evolution of cases is not more severe than expected and the occurrence of the event itself is not unusual for the area.

3. Is there a significant risk of international spread? No

Factors indicating that international spread is unlikely:

- Local drinking water contamination is geographically restricted with low potential to spread across international borders.

4. Is there a significant risk of international trade or travel restrictions? No

Factors indicating that the adoption of trade or travel restrictions are unlikely:

- No precedent for international restrictions to be imposed. Travelers to the area should be advised to take necessary drinking precautions.

Based on the existing information, this typhoid fever outbreak meets only one of the four criteria of the algorithm in Annex 2, and thus does not need to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Each event must be assessed on its own context and on new developments over time as in some instances it will hold significant public health risk and in other situations it will not. In this case scenario the event might have appeared more serious at the very outset before the cause has been rectified.
2. A large outbreak of an endemic disease in itself does not, in all circumstances, constitute a notifiable event if the disease course is not unusual and there exists capacity to respond to the event.
3. Though notification is not required, consulting WHO might be considered for WHO's assistance in managing the response

Case scenario 10: Measles at an international athletics competition

The MoH in Country N was notified of one confirmed and eighteen suspected measles cases among participants of an international athletics competition. The primary case was an athlete from Country P who developed fever and coryza one day before the opening ceremony, severe conjunctivitis and cough followed, then the onset of a rash. Transmission must have occurred during extensive mingling of athletes from Country P in the prodromal stage before the competition and at several occasions in the domed stadium during the event. Seven suspected secondary cases had their only potential exposure at the opening ceremonies. Three cases with prodromal measles symptoms were unrelated spectators sitting in the same section of the upper deck, more than 30m above the athlete's entrance. Among those potentially at risk for measles were approximately 600 athletes; 500 coaches and managers from 68 countries; an estimated 2500 volunteers and staff; international media; and approximately 80,000 spectators from numerous countries attending the competition. In essence, the outbreak investigation team identified numerous groups with probable measles exposure.

All cases with the clinical picture of acute measles infection have measles IgM antibody in their acute serum specimens (greater than or equal to 1:40 by indirect fluorescent antibody (IFA) test). Nine cases have documented histories of measles vaccination between 9 and 12 months of age. Following onset of the rash, all patients were isolated in their hotel rooms. As live-virus measles vaccine could not have been administered within 72 hours of the most intensive exposure, the local health authorities recommended the use of immunoglobulin for contacts with high risks of complications. Quarantine or closing of this event was not feasible and, because exposure had already occurred, may not have limited secondary spread. Last year, a total of 546 confirmed measles cases and 92% vaccination coverage among children were reported in Country N.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating that a serious public impact of the event is likely:

- This event may represent a significant public health risk because of: the large-scale exposure to potentially susceptible persons gathered in a confined environment; the extreme infectiousness of the measles virus; the potential to generate serious measles illness; and the difficulty in obtaining timely evidence of measles vaccination from throughout the world.
- Though the high measles vaccination rate in Country N makes it unlikely that this event may cause high morbidity and/or mortality among its population, the event is potentially serious for other states whose residents return from the international competition.

2. Is the event unusual or unexpected? **No**

Factors indicating that the event is neither unusual nor unexpected:

- The event is caused by a known agent from a likely common source.
- Evolution of cases is not more severe than expected and the occurrence of the event itself is not unusual for the area.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- There is a high risk for cross border movement of measles through incubating participants returning to their home country, which endangers the elimination of measles in those countries that already achieved this goal or are on the brink of it.

4. Is there a significant risk of international trade or travel restrictions? **No**

Factors indicating that the adoption of trade or travel restrictions are rather unlikely:

- Though the measles outbreak has occurred in association with an international gathering, similar events in the past have not resulted in international restriction on trade and/or travel

Based on the above information, this measles outbreak meets two or more of the four criteria of the algorithm in Annex 2, and, thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Disease outbreaks at international events are potentially serious because of the risk of transmission to susceptible persons in large groups gathered in a confined environment.
2. An outbreak of a disease in conjunction with an international gathering may have a high public health impact as a result of exportation of the agent, vehicle or host to countries that have no or almost no indigenous transmission.
3. The public health risk of the occurrence of an infectious agent associated with international gatherings must be considered, even in areas without recent activity of that pathogen.
4. Following a joint risk assessment WHO might facilitate international contact tracing.

Case scenario 11: Cases of clinically suspected smallpox

Local media report an outbreak of sick adolescents with rash in a high school of a large city in country CD. A week ago, a high school student visited the university hospital emergency room in the same town with fever, malaise, severe muscle aches and slight leukopenia, but the physical exam and laboratory results were otherwise normal. Two days later, the same student returned to the emergency room after collapsing in class. She now had a red, vesicular rash on the face and arms and appeared acutely ill. Her temperature was 38.5°C and her blood pressure was normal. She was admitted to the infectious disease ward with presumptive diagnosis of adult chickenpox. She had apparently no contact with others known to have chickenpox.

Over the course of the same week, 2 students from the same high school came to the university hospital emergency room with influenza-like symptoms and were sent home. These students returned to the emergency room with vesicular rash and severe prostration with headache. They were also admitted to the hospital with presumptive diagnosis of chickenpox. The day following their admission, the infectious disease consultant examined the students who had maculopapular rash on the face, forearms, hands and on the soles of the feet. The skin lesions were mostly deep-seated, hard and round well-circumscribed vesicles and pustules, which are partially umbilicated or confluent. Based on the clinical picture, the consultant raised the possibility of smallpox and the hospital epidemiologist declared a contagious disease emergency. Consequently, the 3 patients were moved to negative-pressure rooms with HEPA filters. Visitors and hospital staff not already caring for and in contact with patients are forbidden to enter the floor. Infection-control nurses begin interviewing staff to determine who has been in face-to-face contact with the patients during initial emergency room visits and admission.

Swab specimens from skin lesions had been sent to a laboratory, and requested to be examined by PCR for chickenpox, measles and smallpox. All samples tested negative for measles and chickenpox. Unfortunately, this laboratory and other laboratories in country CD do not have the laboratory capacity to rule out smallpox. In addition, the shipment of specimens by air to a specialized reference laboratory in country EF is delayed as the airline personnel have concerns about the possibility of becoming infected by the infectious material during transport. Moreover, the permission for import of specimens by recipient country EF is pending. Given that cases of smallpox are clinically suspected, a conference call between the hospital epidemiologist, the chair of the department of internal medicine, the hospital president for medical affairs, the National Institute of Infectious Diseases and city and state health authorities is set up. The group agrees that until definite laboratory diagnosis is obtained the affected hospital should be isolated. Accordingly, no one is allowed to leave the hospital until all persons with potential exposure are identified so that they can be quarantined and vaccinated in case specimens test positive for smallpox. A heated debate follows about the difficulties to obtain an approval required for specimen shipment. Over the course of today, public health authorities received a report of an additional case with skin rash of unknown cause from the original town.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating that a serious public impact of the event is likely:

- The event poses a significant public health risk since individual cases match the definition for suspected cases of smallpox provided under the IHR (2005) and no alternative diagnosis explains the illness.
- External assistance may be required to identify the causal agent and control the ongoing event.
- Irrespective of the suspicion for smallpox, the event seems to have a high potential to cause a severe epidemic given the relatively severe clinical outcome and increasing number of cases since onset of the outbreak. The event caused by a still unknown pathogenic agent offers continuing opportunities for human infection that might compromise control efforts.

2. Is the event unusual or unexpected? Yes

Factors indicating that the event is unusual or unexpected:

- In the absence of known smallpox disease, any detection of a case fulfilling the highly specific clinical case definition for smallpox is unusual and unexpected (see IHR (2005) case definitions: http://www.who.int/ihr/capacity/case_definitions/en/index.html).

3. Is there a significant risk of international spread? No

Factors indicating that international spread is unlikely:

- The event does not indicate a risk of disease dissemination across national borders.

4. Is there a significant risk of international trade or travel restrictions? No / Yes

Factors indicating that the adoption of trade or travel restrictions are unlikely/likely:

- So far, there seems to be no risk of imposition of trade or travel restrictions. However, media attention towards clinically suspected smallpox cases may increase the risk of travel restrictions.

Based on the above information, this event meets two or more of the four criteria of the algorithm in Annex 2, and, thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Though a notifiable case of smallpox is defined under the IHR (2005) as a clinically suspected case with laboratory confirmation, the detection of a serious suspected case of smallpox pending laboratory confirmation shall not preclude States Parties from immediately applying the 4 assessment criteria and notifying WHO of such a case. The clinical suspicion for smallpox could well lead to a notification even before laboratory confirmation is available.
2. Notification enables the notifying country to start a confidential dialogue with WHO on further event assessment and any appropriate investigative or response measures, including specific opportunities for the transportation and laboratory testing of specimens.

Case scenario 12: Fatal cases associated with yellow fever vaccine

A yellow fever vaccination campaign was conducted in a province of Country S following an earthquake. Four cases of vaccine-associated viscerotropic disease (YF-AVD), all fatal, were reported among approximately 40,000 individuals who received one particular lot of yellow fever vaccine. Because of this, the campaign was suspended by national authorities. The rate of YF-AVD was approximately 10/100,000 doses administered for this vaccine lot, compared to a rate of approximately 0.3/100,000 expected based on prior experience with yellow fever vaccines. An investigation is ongoing, which includes clinical and laboratory evaluation of the cases, epidemiologic evaluation of the adverse events, and a review of vaccine production at the manufacturing facility. Viral suspension used to make the vaccine lot administered in the province had also been used to produce seven other batches, which had been administered in three other countries in the region. There have been no confirmed adverse events following immunisation (AEFI) with the other batches.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public health impact of the event:

- The vaccine is used for routine infant immunization in endemic countries, and for population wide immunization in response to imminent or ongoing yellow fever outbreak. The vaccine is also approved by WHO for the use for international travel in accordance with Annex 7 of IHR (2005). The circumstances surrounding this particular event have the potential to generate a misunderstanding about the vaccine's safety and thereby to reduce its utilization.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual:

- Reports of vaccine associated viscerotropic disease cases have been published in 2001, but earlier cases have been identified since. The rate of the vaccine reaction in recent mass immunization campaigns has been 0-0.1/100.000 administered doses of medicine. Rates of YF-AVD associated with vaccine administration outside of mass campaigns has been estimated to be 0.3/100.000 doses.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- Specific vaccine lot has been distributed to four countries.
- The recall of the vaccine product could lead to supply shortages.

4. Is there a significant risk of international trade or travel restrictions? **Yes**

Factors indicating that the adoption of trade restrictions are likely:

- Temporary suspension of vaccine products following notification of safety concerns is common practice at the national and international level, until further clarification. National regulatory agencies in other countries are likely to follow suit with temporary suspensions or market recall as appropriate.

Based on the above information, this event meets two or more of the four criteria in the decision instrument, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Events potentially notifiable under the IHR (2005) extend beyond communicable diseases and may include issues related to public health interventions.

2. The notification requirements under the IHR (2005) provide an additional mechanism for vaccine vigilance and data sharing between national regulatory agencies.

Case scenario 13: Hazardous toy

A week ago, a 5 year old boy presented to a paediatric hospital in country GH with a decreased level of consciousness. There was no history of trauma, ingestion of medicines or plants. On arrival at the hospital, the boy was unconscious, bradycardic and severely hypotensive. Clinical laboratory investigations were all within normal limits. Computed tomography of the brain and an electroencephalogram showed no abnormalities. The urine toxicology screen returned with a negative result for illicit drugs. He was investigated and treated for suspected intracranial infection. Seven hours after presentation he became fully alert and cooperative. At this point he vomited a number of coloured beads and also passed a substantial number of beads in his stool. These were identified as beads from a toy. The boy had a further five episodes of vomiting and was persistently drowsy. With no obvious diagnosis, he was admitted to hospital for observation and further investigation.

A urine metabolic screen became available on Day 5 of admission and was positive for γ-hydroxybutyrate (GHB), which is a naturally occurring fatty acid found throughout the human body. The source of GHB in this patient was thought to be either exogenous (i.e. poisoning) or an inborn error of metabolism. The latter was excluded when a repeat metabolic screen from urine taken on Day 3 returned with a negative result for GHB. In searching for an exogenous source of GHB, toy beads from the boy's home, similar to those ingested, were sent for analysis and subsequently found to contain 1,4-butanediol (1,4-BD), which is metabolised to GHB in humans. After confirmation of GHB poisoning in this patient from 1,4-BD detected in the toy beads, the local Poisons Information Centre was notified. Meanwhile, the patient recovered completely and was discharged a week after admission with no residual sequelae of his poisoning. To date, no additional cases of poisoning associated with the use of the product have been reported. There is a dose–response relationship in GHB toxicity. Low doses may result in vomiting, drowsiness, visual disturbance and disinhibition, while higher-dose effects include confusion, coma, bradycardia and myoclonic (seizure-like) movements.

The national Consumer Product Safety Agency (CPSA) and the Ministries of Health and Trade have been alerted about the toy product. Because the toy presents a risk of poisoning to children, the CPSA is seeking to take action by removing the product from the marketplace in accordance with the National Hazardous Substances Act in country GH. When the manufacturer in country IJ was contacted, it supplied a list of ingredients in the production of the toy beads; this list did not include 1,4-BD. The toy product for children just came out three weeks ago. Meanwhile, two further samples of the beads tested positive for 1,4-BD. As a consequence, the Ministry of Trade issued an interim ban on the sale of the beads products in country GH. Similar products are marketed worldwide.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating that a serious public impact of the event is likely:

- Several tests revealed that the children's toy contains 1,4-BD which ingested can cause coma, respiratory depression, bradycardia and seizures.
- There is a great potential that other children using this toy would be exposed to a hazardous level of 1,4-BD. Additionally, this particular type of poisoning is difficult to diagnose since routine urine toxicology screens do not generally include GHB; this analysis would only be requested if there was reason to suppose that GHB poisoning was a possibility. This would be more likely in adolescents and adults with a history of possible drug exposure rather than in a young child at home. In this particular case the child was investigated for an inherited metabolic disease, which revealed the presence of GHB. Such a diagnosis might not have been made in a different hospital that did not have the same facilities, or where the attending physician did not take the same approach regarding differential diagnosis.
- It is indicated that possible that other products were manufactured by the same company that present a risk of 1,4-BD poisoning to children.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- A hazardous substance has erroneously been used in manufacture, while this product is marketed as being safe for children.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- Similar products are marketed worldwide.

4. Is there a significant risk of international trade or travel restrictions? **Yes**

Factors indicating that the adoption of trade or travel restrictions is likely:

- Worldwide media coverage and an international recall of this product are likely.

Based on the above information, this event meets two or more of the four criteria of the algorithm in Annex 2, and, thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Notifiable events can extend beyond communicable diseases and may arise from products containing hazardous chemical substances.
2. Timely notification of such an unusual finding enables WHO to alert at an early stage other countries to be on the lookout for similar cases.
3. It is important to consider the potential export of similar products that may contain hazardous substances.

Case scenario 14: Dengue Outbreak

An outbreak of a serotype (type 3) of Dengue has been identified in the tropical area of Country V. While this serotype had never been identified in Country V and other countries of the region, another serotype (type1) of dengue is endemic, and there have also been cases resulting from a second serotype (type 2). The introduction of a new serotype has the potential to establish itself in this and other areas. Residents have been urged to protect themselves from mosquito bites.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public health impact of the event:

- The introduction of a new serotype is associated with an epidemic potential and may represent a greater public health risk.

2. Is the event unusual or unexpected? **Yes / No**

Factors indicating that the event is unusual or unexpected:

- The occurrence of a new serotype can be unusual.
- On the other hand, there is always a high possibility of introducing another serotype, especially when other types are already endemic.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- Given the intense movement of people across borders and the fact that there is a documented history of dengue epidemics leading to spread among countries further international spread of the serotype is probable.

4. Is there a significant risk of international trade or travel restrictions? **No**

Factors indicating that the adoption of trade or travel restrictions is unlikely:

- There are no indications for the risk of international trade or travel restrictions.

Based on the above information, this event meets two or more of the four criteria in the decision instrument, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

- The appearance of a new serotype involves an epidemic potential and may represent a serious public health risk for neighboring countries.

Case scenario 15: Outbreak of Rift Valley Fever

An outbreak of Rift Valley Fever (RVF) is sweeping through a province of country V affecting a large proportion of the country's livestock which is also exported to neighbouring countries. RVF has only occurred sporadically in country V in the last twenty years. Yesterday, two human blood samples yielded positive results on tests for RVF.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **Yes**

Factors indicating a serious public health impact of the event:

- RVF has demonstrated the ability to cause serious human disease.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- An outbreak of RVF involving a large proportion of country V's livestock is unexpected.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- RVF has demonstrated to spread rapidly internationally through the trade of live animals.

4. Is there a significant risk of international trade or travel restrictions? **Yes**

Factors indicating that the adoption of trade restrictions is likely:

- International trade restrictions are very likely because RVF is classified as an OIE List A disease (A080), which provides legitimacy to other countries for barriers to trade.

Based on the above information, this event meets two or more of the four criteria in the decision instrument, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

- Viral haemorrhagic fevers are diseases of special concern under the IHR (2005) and must always be assessed using the decision instrument to decide whether the event is notifiable.
- Annex 2 must be applied to animal diseases that have the capacity to infect humans in order to determine the notifiability of a given animal-associated event under the IHR (2005).
- Immediate notification to WHO upon detection of public health risks that spread rapidly internationally can be essential to provide timely public health information to other countries to allow them to assess and respond to such risks, as required in the IHR (2005).
- The presence of an animal disease which is part of the OIE disease list A provides trading partners with a sufficient reason to impose a trade embargo, posing a significant risk of international trade restrictions.

Case scenario 16: Radiopharmaceutical facility accident

An accident occurred at a facility producing radiopharmaceuticals for nuclear medicine purposes (diagnostics and research). The facility is located in Country B on the border between two other countries. The accident resulted in a release of radioactive iodine into the atmosphere that contaminated some agricultural areas in the vicinity of the radiopharmaceutical facility. Country B, like its neighbors, exports dairy products to several other countries.

Radioactive iodine emits beta radiation and has a short half-life (eight days). Radioactive iodine can be ingested when contaminated vegetables are consumed without proper washing or with contaminated milk and dairy products. When ingested or inhaled, radioactive iodine acts similar to stable iodine and is accumulated in the thyroid gland. High-dose exposures have been associated with an increased risk of papillary thyroid carcinomas in those exposed at a young age (0-18), as documented in Chernobyl studies. In this particular case, the radiation doses that resulted from the accident were substantially below the reference levels for an intervention with potassium iodide (KI) pills, hence the KI pills were not administered. The Federal Office for Radiation Protection confirmed that exposure to this level of released radioactive iodine will not increase the risk of thyroid cancer.

As a precautionary measure, the national competent authorities of country B informed the public about proper washing of vegetables and implemented restrictions in the use of rain water and local agricultural and dairy products for the duration of one month.

Under the IHR (2005), the presence of any two of the four criteria provided in the decision instrument of Annex 2 means that the event needs to be notified. While using the decision instrument, please answer the following questions:

1. Is the public health impact of this event serious? **No**

Factors indicating that a serious public impact of the event is unlikely:

- Level of radioactive iodine release is below the level deemed hazardous to human health.
- Low-dose exposures to local population, hence KI pills not needed.
- The population has been informed about the proper washing of vegetables, and restrictions were implemented within the country in the use of rainwater and local agricultural and dairy products.

2. Is the event unusual or unexpected? **Yes**

Factors indicating that the event is unusual or unexpected:

- An accidental release of radioactive iodine is always unusual and unexpected.

3. Is there a significant risk of international spread? **Yes**

Factors indicating that international spread is likely:

- The facility is located in proximity to international borders. International spread is therefore likely, especially under certain weather conditions.
- There is a risk that contaminated products have been exported.

4. Is there a significant risk of international trade or travel restrictions? Yes

Factors indicating that the adoption of trade or travel restrictions is likely:

- The risk of international trade restrictions against food products from Country B cannot be ruled out.
- High interest by international media and other countries' authorities are possible based on nature of incident.

Based on the above information, it is clear that this event meets two of the four criteria of the algorithm in Annex 2, and thus needs to be notified under Article 6 of the IHR (2005).

Learning Points:

1. Notifiable events can extend beyond communicable diseases and may arise from accidental exposure to radiation due to release of radioactive materials into the environment or a presence of a radioactive source in the vicinity of humans.
2. In the context of radiation accidents, there is always a great potential that other national authorities impose a ban on food products from the affected country until trust is restored.
3. For risk assessment in case a radiological event falls under the competence of other than national health authorities, it is imperative to establish operational and functional links with appropriate national competent authorities dealing with radiation emergencies and to coordinate the response of health authorities with these agencies.
4. Radiological events generate high media interest; hence early and transparent communication is a key component in the management of radiation emergencies.

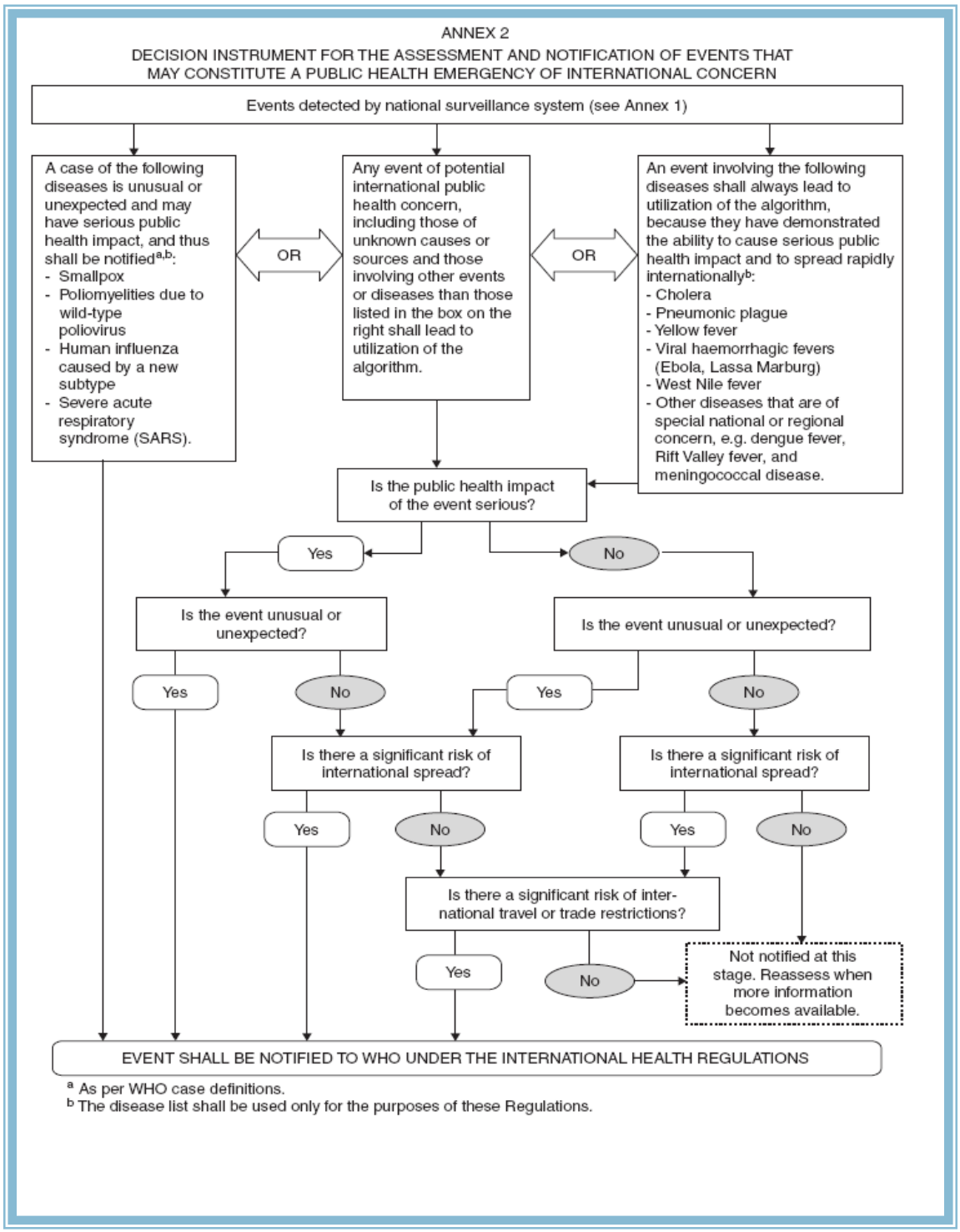
8. APPENDIX

8.1. Article 6: Notification

1. Each State Party shall assess events occurring within its territory by using the decision instrument in Annex 2. Each State Party shall notify WHO, by the most efficient means of communication available, by way of the National IHR Focal Point, and within 24 hours of assessment of public health information, of all events which may constitute a public health emergency of international concern within its territory in accordance with the decision instrument, as well as any health measure implemented in response to those events. If the notification received by WHO involves the competency of the International Atomic Energy Agency (IAEA), WHO shall immediately notify the IAEA.

2. Following a notification, a State Party shall continue to communicate to WHO timely, accurate and sufficiently detailed public health information available to it on the notified event, where possible including case definitions, laboratory results, source and type of the risk, number of cases and deaths, conditions affecting the spread of the disease and the health measures employed; and report, when necessary, the difficulties faced and support needed in responding to the potential public health emergency of international concern.

8.2. Annex 2 of the IHR (2005)



EXAMPLES FOR THE APPLICATION OF THE DECISION INSTRUMENT FOR THE ASSESSMENT AND NOTIFICATION OF EVENTS THAT MAY CONSTITUTE A PUBLIC HEALTH EMERGENCY OF INTERNATIONAL CONCERN

The examples appearing in this Annex are not binding and are for indicative guidance purposes to assist in the interpretation of the decision instrument criteria.

DOES THE EVENT MEET AT LEAST TWO OF THE FOLLOWING CRITERIA?

Is the public health impact of the event serious?	*I. Is the public health impact of the event serious?*
	1. **Is the number of cases and/or number of deaths for this type of event large for the given place, time or population?**
	2. *Has the event the potential to have a high public health impact?* THE FOLLOWING ARE EXAMPLES OF CIRCUMSTANCES THAT CONTRIBUTE TO HIGH PUBLIC HEALTH IMPACT: ✓ Event caused by a pathogen with high potential to cause epidemics (infectiousness of the agent, high case fatality, multiple transmission routes or healthy carrier). ✓ Indication of treatment failure (new or emerging antibiotic resistance, vaccine failure, antidote resistance or failure). ✓ Event represents a significant public health risk even if no or very few human cases have yet been identified. ✓ Cases reported among health staff. ✓ The population at risk is especially vulnerable (refugees, low level of immunization, children, elderly, low immunity, malnourished, etc.). ✓ Concomitant factors that may hinder or delay the public health response (natural catastrophes, armed conflicts, unfavourable weather conditions, multiple foci in the State Party). ✓ Event in an area with high population density. ✓ Spread of toxic, infectious or otherwise hazardous materials that may be occurring naturally or otherwise that has contaminated or has the potential to contaminate a population and/or a large geographical area.
	3. *Is external assistance needed to detect, investigate, respond and control the current event, or prevent new cases?* THE FOLLOWING ARE EXAMPLES OF WHEN ASSISTANCE MAY BE REQUIRED: ✓ Inadequate human, financial, material or technical resources – in particular: – Insufficient laboratory or epidemiological capacity to investigate the event (equipment, personnel, financial resources) – Insufficient antidotes, drugs and/or vaccine and/or protective equipment, decontamination equipment, or supportive equipment to cover estimated needs – Existing surveillance system is inadequate to detect new cases in a timely manner.
	IS THE PUBLIC HEALTH IMPACT OF THE EVENT SERIOUS? **Answer "yes" if you have answered "yes" to questions 1, 2 or 3 above.**

Is the event unusual or unexpected?	**II. Is the event unusual or unexpected?**
	4. *Is the event unusual?* THE FOLLOWING ARE EXAMPLES OF UNUSUAL EVENTS: ✓ The event is caused by an unknown agent or the source, vehicle, route of transmission is unusual or unknown. ✓ Evolution of cases more severe than expected (including morbidity or case-fatality) or with unusual symptoms. ✓ Occurrence of the event itself unusual for the area, season or population.
	5. *Is the event unexpected from a public health perspective?* THE FOLLOWING ARE EXAMPLES OF UNEXPECTED EVENTS: ✓ Event caused by a disease/agent that had already been eliminated or eradicated from the State Party or not previously reported.
	IS THE EVENT UNUSUAL OR UNEXPECTED? **Answer "yes" if you have answered "yes" to questions 4 or 5 above.**

Is there a significant risk of international spread?	**III. Is there a significant risk of international spread?**
	***6*. Is there evidence of an epidemiological link to similar events in other States?**
	7. *Is there any factor that should alert us to the potential for cross border movement of the agent, vehicle or host?* THE FOLLOWING ARE EXAMPLES OF CIRCUMSTANCES THAT MAY PREDISPOSE TO INTERNATIONAL SPREAD: ✓ Where there is evidence of local spread, an index case (or other linked cases) with a history within the previous month of: – international travel (or time equivalent to the incubation period if the pathogen is known) – participation in an international gathering (pilgrimage, sports event, conference, etc.) – close contact with an international traveller or a highly mobile population. ✓ Event caused by an environmental contamination that has the potential to spread across international borders. ✓ Event in an area of intense international traffic with limited capacity for sanitary control or environmental detection or decontamination.
	IS THERE A SIGNIFICANT RISK OF INTERNATIONAL SPREAD? **ANSWER "YES" IF YOU HAVE ANSWERED "YES" TO QUESTIONS 6 OR 7 ABOVE.**

Risk of international travel and/or trade **restrictions ?**	**IV. Is there a significant risk of international travel or trade restrictions?**
	8. *Have similar events in the past resulted in international restriction on trade and/or travel?*
	9. *Is the source suspected or known to be a food product, water or any other goods that might be contaminated that has been exported/imported to/from other States*?
	10. *Has the event occurred in association with an international gathering or in an area of intense international tourism?*
	11. *Has the event caused requests for more information by foreign officials or international media?*
	IS THERE A SIGNIFICANT RISK OF INTERNATIONAL TRADE OR TRAVEL RESTRICTIONS? ANSWER "YES" IF YOU HAVE ANSWERED "YES" TO QUESTIONS 8, 9, 10 OR 11 ABOVE.

States Parties that answer "yes" to the question whether the event meets any two of the four criteria (I-IV) above, shall notify WHO under Article 6 of the International Health Regulations.

8.3. Case definitions for the four diseases requiring notification in all circumstances under the IHR (2005)

A) Human influenza caused by a new subtype

Case definition for notification of human influenza caused by a new subtype under the IHR (2005)

State Parties to the IHR (2005) are required to immediately notify WHO of any laboratory confirmed case of a recent human infection caused by an influenza A virus with the potential to cause a pandemic. Evidence of illness is not required for this report.

An influenza A virus is considered to have the potential to cause a pandemic if the virus has demonstrated the capacity to infect a human and if the hemagglutinin gene (or protein) is not a variant or mutated form of those, i.e. A/H1 or A/H3, circulating widely in the human population.

An infection is considered recent if it has been confirmed by positive results from polymerase chain reaction (PCR), virus isolation, or paired acute and convalescent serologic tests. An antibody titre in a single serum is often not enough to confirm a recent infection, and should be assessed by reference to valid WHO case definitions for human infections with specific influenza A subtypes.

B) Poliomyelitis due to wild-type poliovirus

Case definition for notification of poliomyelitis due to wild-type poliovirus under the IHR (2005)

Under the IHR (2005), a notifiable case of poliomyelitis due to wild-type poliovirus is defined as a suspected case* with isolation of wild poliovirus in stool specimens[3] collected from the suspected case or from a close contact of the suspected case.

*A suspected case is defined as a child (under 15 years of age) presenting with acute flaccid paralysis (AFP[4]), or as any person at any age with paralytic illness if poliomyelitis is suspected.

[3] As a standard procedure, two stool specimens are collected from an AFP case within 14 days of paralysis onset. Since virus excretion in the stool decreases beyond two weeks after paralysis onset, and to increase the sensitivity of virus detection, additional stool specimens from up to five close contacts are taken from AFP cases for whom 2 specimens collected within 14 days of paralysis onset are not available.

[4] Poliomyelitis cannot be diagnosed reliably on clinical grounds because other conditions presenting with acute paralysis can mimic poliomyelitis. Surveillance for polio eradication therefore requires the reporting of all children < 15 yrs with acute onset flaccid paralysis, with subsequent laboratory testing of stool specimens.

Note concerning notification of wild or vaccine-derived poliovirus from sources other than AFP cases

In addition to notification of laboratory confirmed cases of poliomyelitis due to wild-type poliovirus (a disease which is designated in Annex 2 of the IHR (2005) as "unusual or unexpected and may have serious public health impact"), the isolation of wild or vaccine-derived poliovirus from other human or non-human sources (from persons without paralysis, or from environmental samples) must generally also be notified to WHO under the separate notification requirement for "events which may constitute a public health emergency of international concern" as they fulfill at least two of the four criteria for notification.

C) Severe Acute Respiratory Syndrome (SARS)

Case definition for notification of SARS under the IHR (2005)

In the SARS post-outbreak period, a notifiable case of SARS is defined as an individual with laboratory confirmation of infection with SARS coronavirus (SARS-CoV) who **either** fulfils the clinical case definition of SARS **or** has worked in a laboratory working with live SARS-CoV or storing clinical specimens infected with SARS-CoV.

Clinical case definition of SARS:

1. A history of fever, or documented fever

   AND

2. One or more symptoms of lower respiratory tract illness (cough, difficulty breathing, shortness of breath)

   AND

3. Radiographic evidence of lung infiltrates consistent with pneumonia or acute respiratory distress syndrome (ARDS) or autopsy findings consistent with the pathology of pneumonia or ARDS without an identifiable cause

   AND

4. No alternative diagnosis can fully explain the illness.

Diagnostic tests required for laboratory confirmation of SARS:

A) Conventional reverse transcriptase polymerase chain reaction (RT-PCR) and real-time reverse transcriptase PCR (real-time RT-PCR) assay detecting viral RNA present in:

1. At least two different clinical specimens (e.g. nasopharyngeal and stool)

   OR

2. The same clinical specimen collected on two or more occasions during the course of the illness (e.g. sequential nasopharyngeal aspirates)

   OR

3. In a new extract from the original clinical sample tested positive by two different assays or repeat RT-PCR/real-time RT-PCR on each occasion of testing

OR

4. In virus culture from any clinical specimen.

B) Enzyme Linked Immunosorbent Assay (ELISA) and immunofluorescent assay (IFA)

1. Negative antibody test on serum collected during the acute phase of illness followed by positive antibody test on convalescent phase serum, tested simultaneously

   OR

2. Fourfold or greater rise in antibody titre against SARS-CoV between an acute serum specimen and a convalescent serum specimen (paired sera), tested simultaneously.

Note:

In the absence of known SARS-CoV transmission to humans, the positive predictive value of a SARS-CoV diagnostic test is extremely low; therefore the diagnosis should be independently verified in one or more WHO International SARS Reference and Verification Network laboratories. A single case of SARS must be reported to WHO under the IHR (2005).

A detailed exposure history is an essential part of the diagnostic workup for any person under investigation for SARS. More information on SARS surveillance can be found at: http://www.who.int/csr/resources/publications/WHO_CDS_CSR_ARO_2004_1/en/index.html.

Infections with SARS-CoV that occur as a result of breaches in laboratory biosafety/biosecurity should be fully investigated.

Once an outbreak of SARS has been independently verified by one or more WHO International SARS Reference and Verification Network laboratories, WHO will make the appropriate case definitions for surveillance and reporting available through its well-established mechanisms.

D) Smallpox

Case definition for notification of smallpox under the IHR (2005)

States Parties to the IHR (2005) are required to immediately notify to WHO any confirmed case of smallpox. The case definition for a confirmed smallpox case includes the following:

Confirmed case of smallpox:

An individual of any age presenting with acute onset of fever (≥38.3°C/101°F), malaise, and severe prostration with headache and backache occurring 2 to 4 days before rash onset

AND

Subsequent development of a maculopapular rash starting on the face and forearms, then spreading to the trunk and legs, and evolving within 48 hours to deep-seated, firm/hard and round well-circumscribed vesicles and later pustules, which may become umbilicated or confluent

AND

Lesions that appear in the same stage of development (i.e. all are vesicles or all are pustules) on any given part of the body (e.g. the face or arm)

AND

No alternative diagnosis explaining the illness

AND

Laboratory confirmation.

Note:

In contrast to the varicella (chickenpox) infection with centripetal and more superficial lesions, the majority of smallpox cases present with a characteristic rash that evolves slowly over days (with each stage lasting 1-2 days) at the same rate and is centrifugal in distribution, i.e. predominantly concentrated on face and extremities with usual involvement of the palms and soles of the feet. More information and illustrative examples to differentiate smallpox from chickenpox can be found at http://www.who.int/csr/disease/smallpox/preparedness/en/index.html.

The risk of not identifying atypical presentations of smallpox is weighed against the extreme low risk of reintroduction of the disease and the very high risk of obtaining a false-positive laboratory result. In view of this, laboratory tests to confirm smallpox should be limited to individuals that match the above clinical case definition. Should a single, laboratory confirmed case of smallpox ever occur, it would then be considered an outbreak since smallpox no longer exists as a naturally occurring disease.

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