ROBERT KOCH INSTITUT

Framework Ebola Virus Disease

Intervention Preparedness in Germany

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Foreword

The current outbreak of Ebola virus disease (EVD) in West Africa is the largest recognized outbreak of this disease to date. It is also the first such outbreak including cases infected outside of Africa. The risk of an introduction of EVD to Germany (defined as an infected person entering Germany and passing the infection to others) is very low. But it cannot be totally excluded that in isolated instances infected persons could enter unrecognizably during the incubation period, potentially leading to a limited number of secondary infections in Germany.

Germany is well prepared for having cases of EVD. Treatment capacities for patients with highly contagious and life-threatening diseases are higher than in any other industrialized nation. Medical care can be provided to the highest standard. The German Public Health Service (ÖGD) works efficiently. In a crisis situation, national, state and local level authorities collaborate effectively, as has lately been thoroughly practiced in a large multi-state exercise (LÜKEX 2013). Levels of government regularly exchange information, and infection control recommendations are harmonized.

This framework sums up available information, recommendations and regulations regarding infection control and clinical management of EVD cases in Germany within the context of the current outbreak in West Africa. Biological safety rules and regulations regarding technical, logistical and personal protective measures have been taken into account. The framework is a work in progress, intended to further evolve over time.

Of note: The existing small risk the outbreak poses for the German population can only be minimized substantially and sustainably by combating the epidemic in West Africa urgently and effectively.

Berlin, December 1st, 2014

1. Aims

This framework is intended to guide recognition, assessment and management of cases of EVD in Germany. The earlier and better suspected cases can be assessed and infection control measure applied, the greater the chance to completely avoid secondary infections or at least limit their numbers.

This framework combines existing information, scientific recommendations, regulations and other publicly available documents regarding the management of EVD in Germany, put into perspective of the current outbreak in West Africa.

The framework describes standard operating procedures, tasks and responsibilities in any case of a patient with EVD being diagnosed in Germany, but especially within the context of the current outbreak in West Africa.

2. Intended Audience

This framework is written for members of the Public Health Service in Germany (local health authorities, high and highest state health authorities, high and highest national level authorities) as well as medical staff in hospitals, private practices and emergency medical services in Germany. Moreover, it covers the interface of the Public Health Service with other institutions (e.g. the fire service, police, the Federal Agency for Technical Relief and aid organizations).

3. Risk Assessment

The risk of an introduction of EVD to Germany (defined as an infected person entering Germany and passing the infection to others) is very low:

Among 100 air travelers from West Africa only about one person is headed for Germany. In the past months only very few infected persons have left the affected countries by regular air transport.

The affected countries conduct exit screening. However, it cannot be excluded that in isolated instances a person travels while incubating the infection (time between infection and symptom onset) and while exit screening is ineffective in recognizing infection. Such a case leading to a limited number of secondary infections would be possible in Germany.

However, further transmission of the Ebola virus within the German population appears even in light of a few imported infections practically impossible, since Germany fulfills all prerequisites to effectively break the chain of transmission and to safely care for those affected.

4. Pathogen Characteristics and Clinical Picture

4.1 Pathogen

Ebolavirus is a genus within the filovirus family. Three of the recognized Ebola virus species have caused large-scale outbreaks of human disease (Zaire, Sudan, Bundibugyo). Ebola virus infection can lead to the clinical picture of a viral hemorrhagic fever (VHF).

4.2 Endemic Area

EVD is a relatively rare disease. Large outbreaks of EVD have been recognized since 1976 in the Democratic Republic of Congo (formerly Zaire), the current South Sudan, the Republic of Congo, Uganda and Gabon. In March 2014 the West African country Guinea confirmed an outbreak caused by the Zaire species of Ebola virus. From there the epidemic spread to neighboring countries and now represents the largest known outbreak of EVD. By now (January 2015), exported cases of EVD have also been reported outside of Africa, namely in the United Kingdom and the USA, and secondary infections associated with the care for patients infected in Africa occurred in Spain and the USA.

Further information about the current outbreak in West African can be found in **appendix A** and

- http://www.ecdc.europa.eu/en/healthtopics/ebola_marburg_fevers/pages/index.aspx,
- http://who.int/csr/disease/ebola/en/

4.3 Routes of Infection

There are still doubts about the animal reservoir of Ebola virus. Zoonotic sources of infection are apparently great apes and bats (fruit bats, insectivorous bats). Humans can become infected by contact with infected animals, e.g. during hunting, butchering, preparation and eating of wild animals (so called "bush meat").

Transmission from human-to-human is possible through direct contact with EVD patients or the corpses of those who have died of EVD, or by contact with their blood and other body fluids/excreta. Patient infectiousness increases along with viremia throughout the course of disease. A study on EVD patients in Liberia (Chertow et al. 2014) did not observe any transmission from patients within the early febrile phase (prior to onset of gastrointestinal symptoms). There is no indication that filo viruses can be transmitted airborne human-to-human via aerosols.

However, patients vomiting heavily or suffering from severe (explosive) diarrhea can generate infectious droplets. Thus, from a preventive point of view wearing of respiratory masks is required in close contact situations with these patients (see **chapter 7.2.3.2**).

Ebola virus can stay infectious outside of the body for a few days. Infection via fomites contaminated with body fluids, such as syringes, mattresses etc., is possible. On surfaces exposed to sunlight or under dry conditions the virus is being inactivated more quickly.

4.4 Clinical Picture

After an incubation period of between 2 and 21 days (median 8-9 days) EVD begins with non-specific symptoms such as fever, headaches, muscle aches, fatigue (early febrile phase) (**figure 1**).

After a few days, nausea, vomiting, gastroenteritis and epigastric pain typically appear (gastrointestinal phase) (**figure 1**). Some patients also suffer from conjunctivitis, pharyngitis, hiccups, delirium and a maculo-papular exanthema.

In later stages of disease, hemorrhagic manifestations including multiple bleeding sites are typical for EVD. Mainly the gastrointestinal tract, lungs and gums are affected. However, in the current outbreak hemorrhagic signs are seen only in a minority of patients.

From towards the end of the gastrointestinal phase patients either slowly recover or deteriorate towards metabolic acidosis due to severe hypovolemic shock.

Clinical Features of Ebola Virus Disease.

Phase of Illness	Time since Symptom Onset	Clinical Features
Early febrile	0–3 days	Fever, malaise, fatigue, body aches
Gastrointestinal	3–10 days	Primary: epigastric pain, nausea, vomiting, diarrhea Associated: persistent fever, asthenia, headache, conjunctival injection, chest pain, abdominal pain, arthralgias, myalgias, hiccups, delirium
Shock or recovery	7–12 days	Shock: diminished consciousness or coma, rapid thready pulse, oliguria, anuria, tachypnea Recovery: resolution of gastrointestinal symptoms, increased oral intake, increased energy
Late complications	≥10 days	Gastrointestinal hemorrhage, secondary infections, meningoencephalitis, persistent neurocognitive abnormalities*

* Secondary infections are presumptive diagnoses based on clinical features of distributive shock, oral or esophageal candidiasis, and oral ulcers; meningoencephalitis is a presumptive diagnosis based on clinical features of unconsciousness and stiff neck.

Figure 1: NEJM, Ebola Virus Disease in West Africa - Clinical Manifestations and Management, November 5th, 2014)

EVD lethality ranges between 30 and 90%, depending on virus species. In the past, in outbreaks of Ebola Zaire 70-90% of the patients died with the clinical picture of multi-organ failure. In the current outbreak in West Africa lethality is generally around 60%, however under optimal intensive care lethality appears to be clearly lower.

*For advice on therapy see **chapter 7.2.7**.*

4.5 Period of Transmissibility

Disease transmission within the incubation period has never been described.

EVD patients are contagious at least while they have symptoms and viremia. Infectiousness correlates with disease severity and is highest late in the disease, when viral load is peaking. It is unclear whether post-recovery protracted viral excretion (e.g. in urine) is relevant. In the main outbreak area, many infections apparently are due to contact with the bodies of deceased EVD patients (e.g. during funeral practices). In studies on Ebola virus infected macaques, viable virus was isolated up to 7 days after death (Prescott et al. 2015). The role of prolonged viral shedding, e.g. through urine, after Subsiding of symptoms, is not clarified (Moreau et al. 2015, Kreuels et al. 2014, Wolf et al. 2015).

In cured male patients, Ebolavirus could be detected in seminal fluid up to six months after symptom onset. Hence these patients should be advised for necessary protective measures and receive condoms. Please note the corresponding statement of the Permanent Working Group of Competence and Treatment Centers for highly contagious and life-threatening diseases (STAKOB) (www.rki.de/stakob-statements) and of the WHO (http://www.who.int/reproductivehealth/topics/rtis/ebola-virus-semen/en/). It is currently unclear whether cured female patients can transmit Ebolavirus sexually.

One study showed that in a female convalescent pregnant patient Ebolavirus was present in amniotic fluid after the virus was no longer detected in blood (Baggi et al. 2014). People present during birth or abortion are thus at an increased risk of infection, even though the pregnant woman is technically cured. During a former Ebola Virus Disease outbreak, in one mother the virus could be detected in breast milk after clinical recovery (Bausch et al. 2007). Before breastfeeding is resumed, breast milk should be analyzed for Ebolavirus.

In one cured patient, live replicable Ebolavirus could be detected in ocular fluid nine weeks after Subsiding of viremia (Varkey et al. 2015). Eye surgery thus comprises, long after clinical recovery, the

risk of Ebola Virus Disease transmission. Please note the corresponding statement of the Permanent Working Group of Competence and Treatment Centers for highly contagious and life-threatening diseases (STAKOB) (www.rki.de/stakob-statements).

5. Recognition

5.1 Clinical Procedure upon Suspicion of EVD and Early Measures

Any suspicion of EVD has to be thoroughly assessed. Ruling out differential diagnoses of other tropical diseases, especially malaria, is complicated by the non-specificity of early EVD symptoms (see **chapter 5.2**). Taking a comprehensive travel and exposure history thus is critical.

Procedure

Assessment of suspected cases of EVD is conducted based on the clinical picture as well as travel and contact history. In most cases, an anamnestic interview conducted from at least one meter distance from the patient should suffice to rule out whether the patient is a "well-founded suspect case" (the German term is comparable to the EU "probable case" definition; therefore in the following document it is referred to as "probable case") (see **appendix B**).

The patient needs to be made aware, that the information provided in the assessment of the EVD risk is of vital interest for him/her as well as any contacts including family and friends: The earlier appropriate medical care can commence, the more likely life threatening complication can be avoided.

Upon receipt of anamnestic information supportive of probable case status, the local health authority is to be called in (see **chapter 7.1**). The final decision, whether a patient represents a probable case of EVD is to be taken between the physician and the local health authority, under advise from an appropriate Medical Competence and Treatment Center (see **appendix C**) and the State health authority. Until the decision is taken whether the patient represents a probable case, any stable patient is to remain in his/her current environment (at home, in private practice, hospital emergency room).

Protective measures to be taken during assessment of suspected cases

The following protective measures apply when taking anamnestic history of a patient suspected of having EVD:

- Distance of >1m from the patient;
- Minimizing contact;
- Routine hygiene measures.

In case the patient's health status warrants physical examination, or if contact to body fluids seems likely (e.g. when the patient is vomiting), the following protective measures (PPE) are recommended:

- Disposable suit Category III, Type 3B or Type 4B, or as an alternative long-sleeved, liquid-tight disposable gown (preferably floor-length and with back lock);
- Two pairs of gloves;
- Protective goggles or face protective shield;
- FFP3 mask;
- Foot protection.

*For additional advice on PPE see **chapter 7.2.3.2** and **appendix D**.*

*For advice on therapy see **chapter 7.2.6**.*

*For advice on disinfection measures and waste management see **chapter 7.2.7**.*

Criteria defining the "well-founded suspicion of EVD" (like a probable case in the EU case definition)

A patient with fever (>38.5°C), or elevated temperature combined with other symptoms (e.g. diarrhea, nausea, vomiting, bleeding),

- who in the 21 days pre symptom onset had contact* with an EVD patient, a patient suspected of having EVD or a person who died of EVD,

or

- who in the 21 days pre symptom onset worked with Ebola virus, Ebola virus containing materials, or Ebola virus infected animals in a laboratory or any other institution. in Germany or elsewhere,

or

- who in the 21 days pre symptom onset spent time in a known Ebola virus endemic area (country reporting repeated cases in the past) or in an area which recently reported EVD cases for the first time,

  and

- who there had contact to fruit bats, other bats, or non-human primates (e.g. as bush meat, direct contact to live animals or their feces).

***Contact:**

- direct contact with blood or other body fluids, or infectious tissue of a probable or confirmed case of EVD, or a person having died of EVD, or potential contact with Ebola virus contaminated clothing/objects;
- unprotected contact (<1m) with a probable or confirmed case of EVD, or a person having died of EVD (including household contacts, flight passengers having sat 1 seat in any direction from a case, including across the aisle and crew members tending to the case);
- presence in an African hospital, potentially treating cases of EVD.

Not classified as contact: Having been in the same room/transport vehicle, >1m away.

*A flowchart aiding in the assessment of these criteria can be found in **appendix B**.*

Initial measures to be taken in context of a probable case of EVD

For any patient assessed by the local health authority to meet the case definition of a probable case of EVD, said local health authority, involved physicians and potentially the Medical Competence and Treatment Centers (see **appendix C**) and the responsible state health authority should seek immediate transfer of the patient to a special isolation unit within one of the Medical Competence and Treatment Centers. This is especially urgent for more symptomatic patients (e.g. those vomiting and with diarrhea) and those in immediate need of advanced clinical care and laboratory diagnostics.

In the special isolation unit, routine laboratory diagnostics can be conducted according to point-of-care procedures, as well as diagnostics for Ebola virus infection and differential diagnoses including malaria (see **chapter 5.3**).

Especially for probable cases of EVD who are not yet very ill (early febrile phase), and without urgent requirement of any procedure or emergency laboratory tests, the local health authority can assess whether the probable case of EVD can remain in his/her current environment. This would be possible, if the locale (e.g. private residence, physician's office, hospital emergency room) is considered an "appropriate environment" according to § 30 IfSG.

Under these circumstances it can be considered jointly between the local health authority and the Medical Competence and Treatment Center to take a blood sample on location and to then initiate Ebola virus diagnostics.

*For additional advice on sample taking, sample transport and diagnostics see **chapter 5.3**.*

For any patient in preliminary isolation in their current environment (e.g. in a private room) barrier nursing procedures need to be followed (see **chapter 7.2.2**). The measure has to be upheld until the patient has been determined to be Ebola virus negative, or until the patient is laboratory confirmed and moved to a special isolation unit.

For any patient care, appropriate personal protective equipment according to **chapter 7.2.3.2** is to be worn.

*For further information see **appendix E**.*

Notification and transmission procedures regarding a probable case of EVD

Any probable case of EVD is notifiable as a suspected case of a viral hemorrhagic fever by the treating physician to the local health authority according to § 6 of the IfSG. For this purpose, the physician is permitted to breach of patient confidentiality.

These notifications need to reach the local health authority within 24 hours after the physician comes to raise the suspicion of EVD. From there they are further transmitted according to §§ 11,12 IfSG in electronic format to the appropriate state health authority and the RKI.

*For further advice see **chapter 7.1.1**.*

5.2 Differential Diagnoses

Assessment of differential diagnoses is essential to avoid therapy delays for other potentially life-threatening diseases (e.g. malaria) and to prevent false alarms with far reaching consequences.

Procedure

Clinical differential diagnosis is the consideration of other diseases presenting with similar clinical pictures. Regarding tropical infections, for any patient with unexplained fever malaria has to be strongly considered. Due to the high lethality of untreated malaria tropica and available treatment options, malaria diagnostics must be sought without delay. Advice on malaria diagnostic options for patients outside of special isolation units can be found in **appendix F**.

But differential diagnosis also includes the following infections: Other viral hemorrhagic fevers (such as yellow fever, Lassa fever, dengue fever, some Hantavirus infections, crimean-congo fever, Marburg fever), hepatitis A virus infections, typhoid, plague, rickettsioses, meningococcal and other septicemias, leptospirosis, hemorrhagic forms of relapsing fever, shigellosis and even some

intoxications. Early phase non-specific symptoms can be caused by influenza, noro virus or harmless infections. Co-infections with multiple pathogens are possible.

Differential diagnosis should be considered jointly with the specific National Reference Centers and Consultation laboratories.

5.3 Laboratory Diagnostics

In the event of a probable case of EVD (see **chapter 5.1**) local health authorities order appropriate isolation of this patient, if necessary after consultation with Medical Competence and Treatment Centers. For probable EVD cases, laboratory diagnostics should be carried out in a BSL-4 laboratory (addresses see **appendix G**). For asymptomatic contacts laboratory investigations for Ebola virus are not indicated.

For probable EVD cases, routine laboratory diagnostics (e.g. clinical chemistry) and specific laboratory tests for differential diagnosis (e.g. for malaria) should be performed accordingly in a special isolation unit (point-of-care diagnostics, "small series" of diagnostic tests).

If rarely diagnostics are necessary to be carried out for a patient outside of a special isolation unit, procedure should be agreed upon with the attending physician, the local health authorities and potentially with the Medical Competence and Treatment Center.

Emergency laboratory diagnostics (routine laboratory) for an isolated patient can also be carried out outside of the context of a special isolation unit as point-of-care diagnostics. In case the probable case is confirmed, the equipment used must be disinfected properly or, failing this, be disposed of accordingly. Personal protective equipment according to **chapter 7.2.3.2** has to be used.

5.3.1 Sample Taking

In order to confirm or rule out EVD in a probable case, or to document the recovery process, samples must be taken from the patient for laboratory investigation. During sample taking any risk to the personnel taking the sample is to be minimized. Based on the necessary protective measures, it is recommended to take samples primarily at Medical Competence and Treatment Centers.

Procedure

- Prior to shipping samples from a patient with probable EVD, the diagnostic laboratory (addresses of the laboratories see **appendix G**) is to be contacted regarding the types and number of samples needed and to consult about shipment details.
- Documentation by a complete protocol of specimen collection (including persons and times).
- Collection of patient samples in a case of probable or confirmed EVD must be performed wearing appropriate PPE (see **chapter 7.2.3.2**).
- Specific requirements of the sampling technique and of hygiene standards necessitate standard operating procedures and practical exercises by those physicians and nursing personnel taking the samples.
- When using pointed and sharp medical devices in sampling, tools provided with safety features ("safety tools" with automatic safety mechanism) must be used and be disposed of into a suitable container ("sharps container") (see **appendix H** section 4.2.5 paragraph 3 ff.).

- Sample materials: the preferred material for primary diagnostics is serum or EDTA whole blood (2 vials), to document recovery also urine, stools, sweat, swabs from conjunctiva or oral mucosa.
- Additionally a retained sample is to be taken.

5.3.2 Shipment and Transport of Samples

It must be ensured that the transport of samples runs smoothly and safely in order to reach a rapid clarification by laboratory diagnostics. At the same time, any hazard posed by improperly packaged sample material must be prevented.

Procedure (see also appendix G)

- Prior to shipping samples from a patient with a probable EVD, the diagnostic laboratory (addresses of the laboratories see **appendix G**) is to be contacted in order to announce samples and to consult about shipment details.
- A complete transport protocol (including persons, state of the samples and times) is to be kept.
- Shipment of diagnostic samples from a probable EVD case as UN 2814 (class 6.2 category A) according to ADR (European Agreement concerning the International Carriage of Dangerous Goods by Road); packing instruction P620 designated "Infectious substances affecting humans UN 2814".
- Attach the biohazard symbol required for dangerous goods class 6.2; in addition, the information "If packaging is damaged or contents released inform health authorities" can be placed.
- The submitter is the person responsible for announcing the shipment of the sample, its proper classification and adhering to the transportation directives; in case of doubt it is the head of the institution of the submitter.
- The laboratory acknowledges the arrival of the specimen by contacting the attending physician/medical officer and the submitter immediately after receipt of the specimen.
- Means of transportation and location of the diagnostic laboratory should be selected in such a way that the sample will arrive at the laboratory within six hours.
- Packaging (P620 for infectious substances according to UN 2814)
  - Triple packaging system, consisting of
    1. Leak-proof primary container,
    2. Leak-proof secondary packaging,
    3. Rigid outer shipping package.

    For liquid materials (e.g. blood) absorbent material in sufficient quantity to absorb the entire liquid, must be placed between the primary container(s) and the secondary packaging. If multiple primary containers are placed in one secondary container, they must be separated from each other so that they are not touching.
  - Certified packaging is available at specialist shops or is provided by the courier.
- The transport is carried out, for example, by the companies World Courier (Germany) GmbH, or CMK-Logistic Breisach, or other suppliers trained in ADR transportation. In case prompt transport cannot be guaranteed, it can be carried out potentially as an emergency transport, e.g. using emergency medical services, fire services or police (procedure is to be agreement in advance). Emergency transport intended to save human

lives or protect the environment is exempted from ADR regulations provided that all measures are taken to ensure that such transport is carried out in complete safety.

5.3.3 Laboratory Diagnostics of Ebola Viruses

Laboratory diagnostics for Ebola viruses in probable cases and confirmed cases of EVD should be performed in a BSL-4 laboratory (addresses of the laboratories see **appendix G**). Preliminary diagnostics for suspected cases of EVD (see below) can also be performed in an appropriate BSL-3 laboratory (TRBA 100 4.4.1 (4)).

Procedure

- Diagnostics usually consists of real-time PCR for the detection of virus genome in blood (serum or plasma) during the acute phase of the disease.
- Detection of specific antibodies (IgM, IgG) is possible using immunofluorescence, ELISA and neutralization tests, but results of these tests have no purpose as acute phase diagnostics.
- Confirmation diagnostics of a positive primary real-time PCR result is done through PCR amplification of an additional region on the virus genome with the same nucleic acid sample or by sequencing of the PCR product.
- For confirmation purposes it is not necessary to propagate the virus. This can only be done using non-inactivated patient material and therefore requires a BSL-4 (laboratories addresses of the laboratories see **appendix G**). Propagation of the virus can be attempted in order to characterize the virus further. In general, propagation of Ebola viruses plays only a minor role in primary diagnostics.
- If the confirmation test is negative, the analysis of an Ebola virus infection is repeated using a retained sample.
- Results can be expected within 6–8 hours after arrival of the sample at the diagnostic laboratory, provided that there are no unexpected technical problems.

Primary orientation diagnostics of an Ebola virus infection in an appropriate BSL-3 laboratory

In case orientation diagnostics are required outside of aBSL-4 laboratory, this should be arranged by consultation with the local health authority and, if necessary, a Medical Competence and Treatment Center.

Such primary diagnostic analysis using real-time PCR can be attributed to BSL-3 according to the Biological Agents Ordinance (BioStoffV) in conjunction with the TRBA 100 "Protective measures for activities involving biological agents in laboratories" (GMBl. number 51/52 from October 17., 2013, page 1010-1042; 1st amendments: GMBl. 2014 number 38 from June 30th, 2014, page 814):

"4.4.1 … (4) If an infection with a biological agent of risk group 4 is suspected, all indicative examinations of the primary sample with material that has not been inactivated must be conducted at least under the conditions of **protection level 3**."

*For further information see **appendix I**.*

Orientation diagnostics for probable cases of EVD in BSL-3 laboratories can be performed if for example the suspicion cannot be ruled out otherwise (addresses of the laboratories see **appendix G**).

Suitable laboratories are those that fulfil the following conditions:

- Operation of a virological BSL-3 laboratory ensuring the protection of the personnel,
- Experience in molecular diagnostics of viral diseases,
- Use of commercially available quality controlled kits for the detection of Ebola virus RNA, which contain an extraction and amplification control (e.g. from Altona Diagnostics, Roche Diagnostics etc.),
- Successful participation in external quality control trials regarding Ebola virus PCR diagnostics.

Simultaneously to the confirmation tests, in the case of a positive preliminary result, an aliquot of the retained sample is sent to the Consiliary Laboratory for Filoviruses, Institute of Virology, Philipps University Clinics, Marburg, or to the National Reference Centre for Tropical Infectious Agents, Bernhard Nocht Institute for Tropical Medicine, Hamburg.

5.3.4 Report on Diagnostic Findings / Assessment

Depending on the time of specimen taking from a suspected case, the following algorithms lead to these results:

1. The blood sample was taken > 48 hours after onset of symptoms consistent with EVD:

- Primary test and confirmation diagnostics are positive:
  → Confirmed case of EVD.
- Primary test is negative:
  → Ebola virus infection is not detected.

2. The blood sample was taken ≤ 48 hours after the onset of symptoms consistent with EVD:

- Primary test and confirmation diagnostics are positive:
  → Confirmed case of EVD.
- Primary test is negative and the patient continues to meet the criteria of a probable case:

  →Differential diagnostics should be performed.

  →Until 48 hours since symptom onset has passed, the patient continues to be isolated, but not necessarily in a special isolation unit (see **chapter 7.2.2** and **chapter 7.2.3**). (The first negative test result lowers the probability of the symptoms being those of EVD significantly, so that in certain cases (e.g. upon acute recovery from symptoms) patients can be isolated outside of the special isolation unit). For patient care the PPE listed in **chapter 7.2.3.2** has to be used.

  →Regardless of a laboratory confirmed differential diagnosis, an additional patient sample, taken at the earliest on the 3rd day (> 48 hours) after onset of symptoms consistent with EVD, should be tested for Ebola virus.

  Primary test of this sample is negative in the PCR:
  → Ebola virus infection is not detected.

  Primary test and confirmation diagnostics are positive:
  → Confirmed case of EVD.

5.3.5 Reporting Results

Reporting of the laboratory results (negative and positive) must be done as soon as possible as they represent the foundation for potential further measures.

Procedure

- Immediate report of the laboratory results (negative and positive) to the sender/attending physician, because the results are relevant for further measures. They in turn notify the local health authorities according to § 6 paragraph 1 number 1g IfSG.
- Laboratories notify a positive result to the local health authorities according to § 7 paragraph 1 number 12 IfSG.

6. Assessment of Potential Further Spread

Should either cases of EVD appear in Germany or the situation change otherwise, the assessment of risk of spread is to be conducted by the local health authorities in cooperation with state and federal authorities, in order for appropriate infection control measures to be implemented. State health authorities transmit risk assessments and appropriate updates to the RKI.

Procedure

- Local health authority: Data entry and electronic transmission of probable and confirmed cases and possibly number of contacts daily via the state health authority to the RKI.
- On the basis of available data and information, RKI may compose a situation report to be distributed among appropriate state and federal authorities.

7. Management

7.1 Infection Control Measures

7.1.1 Notification / Transmission According to the IfSG and According to the Law on IHR Implementation (2005) (IGV-DG)

Only early recognition and notification of a case of EVD allow for timely implementation of comprehensive protective measures.

Procedure

- According to § 6 Nr. 1 IfSG, physicians have to notify by name any patient suspected or confirmed to suffer from a viral hemorrhagic fever, or to have died of one to the local health authority. Laboratories are similarly required according to § 7 Nr. 1 IfSG to notify by name any patient with direct or indirect diagnosis of acute Ebola virus infection. These notifications need to be received by the local health authority within 24 hours after the physician comes to raise the suspicion of EVD. According to § 11 and § 12 IfSG these notifications are then further transmitted electronically to the state health authorities and the RKI.
- According to the German Law on IHR Implementation (2005) Law (IGV-Durchführungsgesetz - IGV-DG) pilots in command of aircraft (§ 11 IGV-DG) and officers in command of ships (§ 16 IGV-DG) are also required to notify such cases. This is the case for any person aboard with signs of having an infectious disease posing a substantial threat to public health, or that there are other indications pointing towards a substantial threat to public health aboard.

- If a Public Health Emergency of International Concern, according to article 1 section 1 in appendix 2 of the International Health Regulations (IHR) of 23 May 2005 (officially published in Germany in BGBl. 2007 II p. 930) is on hand, according to § 12 IfSG the local health authority without undue delay transmits information about incident probable cases, measures taken around it, and any other information necessary to assess the situation (e.g. the number of contact persons) to the appropriate state health authority and on to the RKI. To avoid reception delays, the RKI recommends for the sender to announce any § 12 notification concurrently by telephone.
- Aside from laboratory confirmed cases or deaths, transmission according to § 12 IfSG specifically also includes probable cases without laboratory confirmation. The local health authority without undue delay informs the state health authority which in turn informs the RKI. The RKI evaluates the available information and further transmits it according to the IHR within 24 hours of evaluation via the German national IHR focal point (GMLZ) to the WHO. According to EU 1082/2013/EU the information is also passed to the European Commission and the other EU member states.

7.1.2 Measures Regarding Contacts

For targeted intervention, all contact persons of a confirmed case of EVD – and possibly even of any probable case of EVD – need to be ascertained. To comprehensively prevent spread of infection, contact persons must be ascertained without delay.

All persons shall be ascertained, who had direct contact with the EVD patient after onset of symptoms, and all those who may have come in contact with infectious materials from the case, including family members, medical staff, laboratory staff, flight passengers (those having sat one seat removed from the case in any direction including across the aisle as well as attending crew and anybody else with direct contact).

Especially body fluids and excretions (blood, urine, vomitus etc.) are highly contagious on direct contact. Contact persons ascertained through case questioning and other research are to be immediately informed of their contact status.

Procedure

- Local health authority: Query EVD patient regarding onset of symptoms and all of his/her contacts since symptom onset. Consider other sources of information on contacts.
- Local health authority: Query and class all contacts regarding their exposure risk category (see below "**Classification of persons according to their risk of exposure**") and list them (**appendices K and L**),
- Local health authority: Inform ascertained contacts about required rules of conduct:
  - Inform them about their risk of Ebola virus infection,
  - Advise them to self-monitor for any symptoms,
  - Explain, that until the maximum incubation period of 21 days after the last contact has passed, they will – depending on their risk exposure – either be daily questioned about the development of symptoms, especially fever, or asked to document their own health status and report to the local health authority accordingly.
- Local health authority: Consider infection control measures according to §§ 28-31 IfSG.

- States, RKI: Upon any state's request, an RKI team of intervention epidemiologists can assist state and local authorities (see Coordination Regulation / Koordinierungs-VWV according to § 5 IfSG).

Classification of persons according to their risk of exposure

High risk of exposure

Any person who during the past 21 days has had:

- A percutaneous or mucous membrane exposure to Ebola virus containing body fluids or tissue from a case of EVD or a person who died from EVD,
- Any unprotected direct contact with blood or other body fluids (including soiled clothing or fomites) of a case of EVD or a person who died from EVD,
- Any unprotected direct contact to any body of a dead person, e.g. during funeral rituals, or to fruit bats, other bats, non-human primates (e.g. bush meat) in an area with ongoing Ebola virus transmission (see **appendix A**).

Intermediate risk of exposure

Any person who during the past 21 days did not have a high risk exposure but without appropriate PPE:

- Treated, nursed or physically examined (e.g. measured temperature or blood pressure) any case of EVD who was so far only febrile (i.e. not yet very ill),
- Had contact (< 1m) with a case of EVD unaware of direct body contact or contact with body fluids (including household members, aircraft passengers/ attending crew[1]),
- Had contact to potentially Ebola virus containing clothing or fomites.

Very low risk of exposure (exposure only while wearing appropriate PPE)[2]

Persons who in the past 21 days were always following appropriate protective measures while having contact with:

- Cases of EVD, those suspected to have EVD or those having died of EVD,
- Body fluids of cases of EVD, those suspected to have EVD or those having died of EVD, or
- Ebola virus containing materials or infected animals.

No discernible risk of exposure

Examples of persons without discernible risk of exposure include:

- Those having had contact with an asymptomatic person, who is considered a contact to a case of EVD,
- Those who had contact to a case of EVD before this person developed symptoms,
- Those who have been to areas affected by an EVD outbreak but without any of the above mentioned risks of exposure,

[1] Air passengers having sat one seat removed from the case in any direction including across the aisle , those with other direct contact as well as crew members attending to the case.

[2] Since even under appropriate protective measures an unrecognized exposure cannot be completely excluded (e.g. due to procedural mistakes), a small risk of exposure remains. Thus this group of persons is included in this overview (not as contacts, but as persons which a potential very low risk of exposure).

- Those who left EVD outbreak affected areas more than 21 days ago,
- Those who have recently stayed in African countries unaffected by EVD outbreaks.

Recommendations regarding persons with an exposure risk

High risk of exposure

These persons have a high risk of having acquired infection. It is recommended to quarantine these persons for 21 days after their last exposure in an appropriate location selected by the local health authority conforming to § 30 IfSG. They should be queried daily by the local health authority regarding the development of any symptoms, especially fever (see **appendix L**).

Appropriate post-exposure prophylaxis can be considered. All approaches so far are experimental and ought to be considered on a case-by-case basis (see **chapter 7.2.5**.)

Intermediate risk of exposure

These persons should be monitored according to § 29 IfSG. The local health authority moreover assesses, whether measures according to § 28 IfSG are warranted. It may order these contacts to minimize their own respective contacts during the potential incubation period and to abstain from travel outside of Germany.
These persons should monitor themselves for any symptoms, especially fever, for 21 days after the last contact (see **appendix L**). The local health authority should contact them regularly to ask for the results of this self-monitoring according to § 29 section 2 IfSG (**appendix L**).

Very low risk of exposure (exposure only while wearing appropriate PPE)

Under actual working conditions, especially in patient care, risk of exposure is not zero due to potentially unrecognized mistakes committed while attempting to follow procedure, even with adequate training. Consequently, all persons who were only exposed while following adequate precautions are also recommended to self-monitor their health status, including twice-daily temperature taking and documentation of any arising symptoms (see **appendix M**).

The employer or deploying organization ought to guide and support self-monitoring through occupational health services. The latter is recommended to contact the local health authority to synchronize procedure. Returning persons who were involved in patient care or outbreak response during the current Ebola outbreak in West Africa are generally advised to contact their local health authority themselves and to plan reciprocal reachability.

Observation according to § 29 IfSG or quarantine according to § 30 IfSG is not recommended for this group. Under special circumstances, the local health authority may decide to vary from this recommendation. Work abstinence for 21 days after the last contact is not generally recommended on infection control grounds. However, on a case-by-case basis such work abstinence can be granted by the employer or deploying organization for other reasons (e.g. for rest, avoidance of harmless false alarm-generating infections), especially for medical personnel involved in direct patient care, when they return to Germany from very taxing missions in the African outbreak areas.

No discernible risk of exposure

No measures required.

Procedure, should a contact person become symptomatic

Persons with **intermediate or high risk of exposure** developing any symptoms compatible with EVD within the 21 days maximum incubation period should be considered probable cases of EVD unless such an infection can be ruled out by laboratory diagnostics (for measures, see **chapter 5.1**).

These persons are to be instructed beforehand to isolate themselves from others within the context of their then current location, unless they are already quarantined according to § 30 IfSG. They are to immediately inform the local health authority. Suspicion of EVD should be defined in a sensitive way in symptomatic persons with known contacts, including the presence of just an elevated temperature in conjunction with other symptoms typical for early EVD.

The local health authority should contact the proper Medical Competence and Treatment Center and the appropriate state health authority without delay, to coordinate any further actions (e.g. patient transport and hospitalization, laboratory diagnostics).

Symptomatic persons, who had contact to probable or confirmed cases of EVD, or those having died of EVD, **only while wearing appropriate personal protective equipment** do not automatically constitute probable cases. Nevertheless, for any symptoms compatible with EVD developing within the 21 days maximum incubation period they are to self-isolate and immediately inform the local health authority by phone. Case specifics and an extensive patient history are essential for the risk assessment. The local health authority decides whether to consider the case probable and to trigger appropriate measures (see **appendix M**).

Advice

Should it be necessary to call emergency services, the patient or any person assisting (e.g. a family member) need to alert the emergency services operator at the earliest opportunity of the status of that patient as a contact to a case of EVD.

7.1.3 Screening

Entry screening for fever and questioning of travelers at points of entry are theoretically possible. However, the benefit of entry screening is judged to be very limited (see assessment of the European Center for Disease Prevention and Control, published 13 October 2014: http://www.ecdc.europa.eu/en/publications/Publications/Ebola-outbreak-technicalreport-exit-entry-screening-13Oct2014.pdf).

7.1.4 Preventive Measures

To prevent introduction of Ebola virus, regulations regarding import of animals and animal products are to be followed: (http://www.zoll.de/DE/Unternehmen/Warenverkehr/Einfuhr-aus-einem-Nicht-EU-Staat/Einschraenkungen/Waren/Tiere-und-Produkte-daraus/tiere-und-produkte-daraus_node.html).

It is possible, that infected dead animals or their meat ("bush meat") are illegally imported into Germany. This process conveys risk of infection for custom officers and others supervising import and transit of animal products at international transitions points (airports, ports). Altogether the risk for Germany is considered to be small. However, this risk is thought to be minimal for Germany.

For further information see **appendix N**.

7.2 Patient Care

7.2.1 Patient Transport

Procedure

- Transport of patients (confirmed and probable cases) is conducted under guidance and in close consultation/agreement with local health authorities and possibly state health authorities and Medical Competence and Treatment Centers.

- The selected facility (special treatment center or under rare circumstances also regular hospitals) must be informed immediately. Due to localization of the seven special treatment centers across Germany patient transport to a special isolation unit should not take longer than four to five hours.
- An ambulance suitable for transporting highly infectious patients should be requested. Request can be made through local emergency services switchboard or the Medical Competence and Treatment Centers.
- Should such a special ambulance vehicle not be available (e.g. because of urgent hospital administration), a regular ambulance that is cored can be utilized. The windows separating cockpit and patient area need to be kept closed.
- Transfer of patient is best done accompanied by a team of the designated Medical Competence and Treatment Center.
- Treatment of patient during transport should only be performed by experienced personnel that is equipped with adequate PPE (see **chapter 7.2.3.2**)
- During transport the patient is provided with a mask covering mouth and nose (as long as this is tolerable for the patient), hood and protective gown, in order to minimize environmental contamination of the vehicle.
- After patient transport all surfaces of ambulance must be wiped with disinfectant which has been proven to be effective with regard to category AB (see. http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittellist/Desinfektionsmittelliste_node.html); if appropriate further measures lie within the decision of local health authority (see § 18 IfSG).
- For disinfection procedure and donning and doffing of PPE see **chapter 7.2.3** and **chapter 7.2.4**.
- Confirmed EVD cases and probable cases shall not be transported within the same vehicle at the same time or sequentially without in-between disinfection. This also applies to the transport of multiple probable cases. However, the probability of multiple probable or confirmed cases arising simultaneously at the same place is considered very low.
- As helicopters cannot be disinfected without compromising on-board electronic systems and patient access in them is limited, EVD patient transport by helicopter at this time is not advisable and should be avoided.

7.2.2 Treatment Unit Requirements

Treatment of probable cases and confirmed cases should be primarily carried out within the dedicated Medical Competence and Treatment Centers in special isolation units. The requirements of the Technical Rules for Biological Agents are to be fulfilled (see **appendix H**).

Probable cases or already confirmed cases (the latter only under the rare circumstances that they are not transport competent, or where other unforeseen factors prevent transport) who need to be treated elsewhere than special isolation units, still need to be spatially isolated ("barrier nursing": contact and aerosol isolation comparable to that applied to patients with open TB, even though in contrast to Mycobacterium tuberculosis Ebola virus is not transmitted by aerosols).

The decision which institution can be considered for temporary treatment of non-transferable EVD patients is taken by the local health authorities or on the state level.

The following minimum standards are mandatory:

- The patient room has vestibule or another designated entry area separating clean from unclean areas.
- This includes realization of:
  - appropriate means for desinfection,
  - possibilities to safely don and doff PPE, and
  - options for safe collection and subsequent disposal of used PPE.
- For all actions in the treatment area standard operating procedures need to be provided. This specifically pertains to the donning and doffing procedures for PPE, PPE decontamination including that for reusable PPE items such as boots, necessary disinfection and decontamination procedures, waste management, and accident emergency measures.
- Staff needs to be instructed and trained in safe donning and doffing of PPE (regarding PPE see **chapter 7.2.3.3**).
- Staff needs to be willing to examine and nurse EVD patients. A sufficient number of staff members needs to be available.
- Point of care diagnostics (small diagnostic series) for infectious samples should be available within the isolation unit (standard diagnostics for clinical chemistry with hematology and hemostaseology, blood group serology (ABO and D) with cross-matching as well as basic microbiology).

Appropriate waste management procedures (waste key 180103*) needs to be in place (see **chapter 7.2.4.6**).

7.2.3 Staff Personal Protective Measures and Equipment

Basic remarks

Care of EVD patients (probable and confirmed cases) must be performed only by instructed and trained personnel. Such treatment should strive to minimize contact. Invasive procedures, especially outside of special isolation units, must be reduced to the absolute minimum required. Basic protective procedures such as complying with hygienic standards and safe waste management (including solid and liquid waste) are mandatory for treatment of all patients.

If sampling from or treatment of patients requires the use of pointed and sharp instruments, tools provided with safety features ("safety tools" with automatic safety mechanism) must be used and be disposed of into a suitable container ("sharps container") (see **appendix H** section 4.2.5 paragraph 3 ff.).

General notice

Comply with hygienic standards and minimize contact.

Special notice

In case of close contact (physical exam, medical treatment, patient transport) with probable and confirmed cases, the following rules and procedures of occupational health and safety need to be obeyed. These rules and procedures are based on TRBA 250. The measures outlined hereafter have been agreed with the coordination unit and the ad-hoc Ebola working group of the Committee for Biological Agents in the workspace (ABAS).

Depending on the situation, the following three concepts are specified:

1. Patient care in special isolation units,
2. Temporary isolation of patients outside of special isolation units, and
3. Patient care outside of special isolation units (when patient transport is not an option).

7.2.3.1 Patient Care in Special Isolation Units

Protective measures as indicated in appendix 1, part 1 of TRBA 250 (see **appendix H**).

7.2.3.2 Temporary Isolation of Patients Outside of Special Isolation Units

A probable case newly detected is at first to remain in his or her current locale. It is assumed that the time in this locale will be short and only the most necessary procedures involving direct contact with the patient are to be conducted prior to transfer to a special isolation unit.

The designated personal protective equipment shall ensure that skin and mucous membranes are protected against pathogen contact. All skin and mucous membranes ought to be covered. The material properties of the personal protective equipment should allow for the reduction of visible contamination with patient body fluids by wipe disinfection. Additional measures regarding hygiene and waste management are addressed separately (see **chapter 7.2.7**).

For primary care of patients in hospitals, especially in emergency departments, at doctors' surgeries, with rescue services, and on local health authority premises the following minimum protective equipment ought to be available:

- Respiratory protection
  FFP3-half-mask according to EN 149:2001, preferably additionally according to EN 14683:2005 oder EN 14683:2014 (splash guard IIR)
  Technical justification of the ABAS for the application/use of FFP3-half-masks: Although it is assumed that the Ebola virus is not aerogenic (non- transmissible as aerosol by particles < 5 µm), infectious particles might originate upon release of body fluids by the patient (e.g. in consequence of vomiting or medical measures) that could lead to infection if medical staff is in close contact to the patient. Therefore, from a preventive perspective, respiratory protection is necessary. Surgical masks (e.g. mouth/nose protection) are not respiratory protective equipment; neither filter performance nor the fit on the face provide sufficient protection.
- Eye and face protection
  Protective goggles (anti-fog, with side shields, CE Kat. II, EN 166:2002) as used in endoscopic practices and a face shield (preferably according to EN 166:2002).
- Hand protection
  In order to protect the hands, two pairs of liquid-proof gloves with protection against mechanical and biological risks (CE Cat. III, e.g. according to DIN EN 420, 388, 374, AQL ≤ 1.5) are mandatory. Gloves should have cuffs to ensure a sufficient overlap to the clothing mentioned below.
- Body protection
  Protective equipment has to consist of liquid-tight material allowing for safe doffing. Disposable suits Category III, Type 3B, are recommended in combination with a disposable plastic apron. If they are not available, the institution is obliged to provide the same safety level using other means, e.g. with floor-length long-sleeved gowns with back lock made of liquid-tight material (e.g. according to EN 13795 High Performance) in

combination with a disposable plastic apron as additional splash protection. Disposable suits ought to have a hood. Hoodless suits are to be complemented with separate shoulder length head hood.

- Foot protection
  Disposable over boots of liquid-proof material or rubber boots.

All staff members must be familiar with the proper use of protective clothing.

Notice

Probable EVD cases or already confirmed cases should be transferred as soon as possible to a special isolation unit for further treatment.

7.2.3.3 Patient Care Outside of Special Isolation Units (when patient transport is not an option)

When a confirmed EVD patient must be treated outside a specialized isolation unit for a longer period of time (e.g. when the patient is too sick to be transported) fan-supported breathing protection (TH 3P, if disinfectants are used, with appropriate particle filter A, B, E or K) is recommended in terms of respiratory protection.

Alternatively, full face masks (P3, if disinfectants are used additionally with appropriate particle filter A, B, E or K; see **appendix H**, Appendix 1, 1.4.1) can be used. Advantages are the lack of fan noise; a disadvantage is the reduced working time allowance. In any case appropriate physical fitness and minimally a 2-day practical and theoretical training is required.

7.2.3.4 Donning and Doffing of Personal Protective Equipment

Protection against infections by personal protective equipment (PPE) is only guaranteed if it is correctly applied, worn, decontaminated, doffed and discarded. For this reason, regular exercises for the usage of PPE are necessary in order to avoid mistakes and resulting infection (see **Appendix D**).

Procedure

- Before PPE doffing, PPE disinfection is required.
- In the context of confirmed cases of EVD full body decontamination must be performed. Donning and doffing of protective clothing and decontamination must be performed with the help of a second person (so called "buddy-system").
- In the context of probable cases of EVD after careful assessment full body decontamination may be considered unnecessary. In this case the PPE should be wipe-disinfected with a sponge and appropriate disinfectants before doffing – especially areas of visible contamination (see **appendix D**).

Decontamination (full body decontamination and decontamination of selected areas, see appendix O)

- Application of an at least limited virucidal disinfectant while maintaining specified exposure times.
- The disinfectant should be collected – either with sufficient absorbent towels or in a pan – and should be disposed of appropriately (see **chapter 7.2.4.8**).

- Regarding the disinfection of PPE specific details are provided in the appendix of the RKI list regarding certified means and procedures for disinfection "surface disinfection" (in German).
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf
- After disinfection, protective clothing must be taken off in a way that the outside of the clothing does not contaminate the skin of the person ("peeling off"), meaning that the inside of the protective clothing is supposed to be outside after doffing.
- Gloves have to be doffed/disposed of after touching the mask. Then hands must be disinfected and washed, and the gloves must be replaced.
- When leaving the contaminated room protective clothing must be taken off and prepared for disposal in the vestibule. Either the protective clothing is autoclaved in appropriate bags according EAK 180103 or supplied as infectious waste in appropriate packing after (thermal) waste disinfection to waste management/disposal (see **chapter 7.2.4.6**).
- Before doffing, gloves should be disinfected with a hand disinfectant with at least limited virucidal efficacy.
- After doffing of gloves, hands should be disinfected with a hand disinfectant with at least limited virucidal efficacy.
- All potentially contaminated surfaces, e.g. in the vestibule, must be disinfected by a careful wipe disinfection (limited virucidal or virucidal efficacy).

*For further information see **appendix D**.*

7.2.4 Required Disinfection Measures / Waste Management

Procedure (see appendix O)

The procedures in the special isolation unit are governed by **TRBA 250** (see **appendix H**) and other regulations, e.g. for protection against infection. The following remarks mainly refer to the procedure outside the special isolation unit (see **appendix O**).

- All measures must be carried out in accordance with the local health authority and if applicable with the Medical Competence and Treatment Center for patients with highly contagious infections.
- The environment in which the potentially contagious patient has stayed (e.g. apartment, car, doctor's office) and where a direct contact with body fluids or with the patient's skin occurred or could have occurred, should pending receipt of the secured diagnosis be blocked and controlled.
- If this is not possible or a case of EVD is confirmed, the decontamination should be carried out using disinfection measures as described below.
- In this context the access to the respective area is to be blocked and the number of persons in this area must be restricted to the smallest necessary number.
- Appropriate opportunities for decontamination of each other and for changing PPE need to be set up at the entrance to the area.
- Wipe disinfection of the contaminated areas listed above and of the PPE is the measure of choice. Only in exceptional circumstances, where not all contaminated areas can be disinfected by a surface disinfection, additional room disinfection by evaporation of formaldehyde or hydrogen peroxide should be taken into consideration.

- Contaminated objects, where disinfection cannot be assured entirely are to be discarded together with used and decontaminated PPE, according to waste code number 180103*.
- Disinfectants with proven, at least limited virucidal effectiveness (active against enveloped viruses; see document "Testing and Labeling of Disinfectant Activity against Viruses") are sufficient for disinfection of contamination with Ebola virus. Disinfectants with virucidal effectiveness, i.e. agents that are also active against non-enveloped viruses, can also be used.
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Viruzid.pdf3
- Disinfectants of type AB from the list of RKI tested and approved disinfectants and disinfection methods (short "RKI list") or the disinfectant list of the Association for Applied Hygiene (short "VAH list") with limited (or full) virucidal activity are appropriate in this instance. If the local health authority officially orders disinfection, it is mandatory to use the RKI list.
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf
  - http://www.vah-online.de/index.php?page=desinfektionsmittel-liste-2
- Regarding disinfection of personal protective equipment specific information is also referenced in the appendix of the list of RKI tested and approved disinfectants and disinfection methods.
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf
- Staff engaged in disinfection activities must wear personal protective equipment according to a situational risk assessment. In case of a high risk potential, e.g. due to massive contamination with bodily fluids or for confirmed Ebola virus infection, personal protective equipment as specified in **chapter 7.2.3.2** must be used. Personnel must be specially instructed and trained in donning and doffing procedures of personal protective equipment.

7.2.4.1 Hand Disinfection, Skin Disinfection, Mucous Membrane Disinfection

Procedure (see appendix O)

- While caring for a probable or confirmed case of Ebola virus infection, personal protective equipment including gloves must be worn. After doffing of gloves or after any contamination, hands are to be disinfected with a hand disinfectant with proven at least limited virucidal effectiveness (virucidal disinfectants can also be used). For practical reasons, these disinfectants can also be used for disinfection of other accidently contaminated areas of the skin.
  - Further information about this is available in the RKI list, section 2.3, and the VAH list as well as in the recommendations of the "Commission for Hospital Hygiene and Infectious Disease Prevention at the Robert Koch Institute - Hand Hygiene". http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf
  - http://www.vah-online.de/index.php?page=desinfektionsmittel-liste-2
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/Haendehyg_Rili.pdf

- For disinfection of mucous membranes octenidine dihydrochloride /phenoxyethanol- or chlorhexidine-containing drugs or povidone-iodine complexes (7.5%) can be used, according to their certified areas of application e.g. Octenisept, Skinsept mucosa, Braunol. For the application on eyes 5% povidone-iodine complex is suitable.

7.2.4.2 Disinfection of Surfaces

Procedure (see appendix O)

- All surfaces clearly or potentially contaminated with body fluids, as well as skin contact areas are to be disinfected by thorough wiping with approved disinfectants according to the RKI list, section 2.2 or the VAH list (see above).
- For conducting surface disinfection, reference is made to the recommendation of the Commission of Hospital Hygiene and Infection Prevention on "Hygiene requirements for surface cleaning and disinfection".
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/Flaeche_Rili.html
- Wearing the required protective clothing, visible contamination (e.g. with blood, vomitus) has to be absorbed into a single-use cloth drenched with surface disinfectant and discarded as infectious waste according to waste code number 180103* These areas should be wiped twice with disinfectants prior to an overall surface disinfection (see document Decontamination/disinfection in biological threat situations):
  - http://www.rki.de/DE/Content/Infekt/Biosicherheit/Dekontamination/Dekontamination_node.html
- Immediately after discharge or death of a patient a final disinfection has to be performed by abrasive wipe disinfection of all accessible surfaces and objects (incl. bed frames and mattresses with the use of protective covers, otherwise thermal disinfection).

7.2.4.3 Disinfection of Medical Devices (Instruments and Equipment)

Procedure (see appendix O)

- All instruments and technical equipment contaminated or potentially contaminated with body fluids from patients with EVD are to be disinfected individually and specifically. Depending on the reprocessing instruction of the respective instrument or equipment, a surface disinfection (by wiping) or an instrument disinfection (by dunking) needs to be performed. Contaminated devices which cannot be fully disinfected are to be discarded according to waste code number 180103*.
- Advice on the reprocessing of medical devices can be found in the recommendations of the Commission for Hospital Hygiene and Infectious Disease Prevention at the Robert Koch Institute and the Federal Institute for Drugs and Medical Devices on "Hygiene Requirements for Reprocessing of Medical Devices".
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Aufb_MedProd/Aufb_MedProd_node.html
- Disinfection of large equipment has to be individually planned. It depends on the estimated degree of contamination and should be performed in accordance with the general rules for disinfection and the manufacturer's specifications. In addition, fumigation with formaldehyde or hydrogen peroxide is possible. If applicable, special precaution needs to be provided for tubing and liquid systems that will be a) emptied and b) disinfected. In case equipment must be transported before decontamination, e.g. to the

autoclave room, liquid systems must be emptied in advance, disinfected and emptied again.

- An individual approach is also necessary for analytical equipment (e.g. in vitro diagnostics). A wipe or spray disinfection is NOT sufficient, as liquids can reach inaccessible areas (corners, gaps, joints) in the equipment. A fumigation procedure is more appropriate and needs to be validated for the individual type of device.
- For equipment and machines that are used for primary diagnosis and sample preparation under BSL-3 conditions, the conditions mentioned in the first paragraph of this section apply. Patient samples which, after proper treatment with virus lysis buffer (AVL buffer + EtOH) are e.g. subjected to PCR analysis and are subsequently controlled and transferred to BSL-2 in new sample tubes, do not pose risk of contamination for the analysis instrument (PCR analyzer). These are to be treated according to the usual disinfection instructions and the manufacturer's instructions.

7.2.4.4 Room Disinfection

Procedure (see appendix O)

- In the exceptional case that it is not possible to clean all contaminated areas by surface disinfection, a room disinfection using formaldehyde or hydrogen peroxide vapors (RKI list, section 3.3) can be considered in addition to the surface disinfection.

7.2.4.5 Laundry Disinfection

Procedure (see appendix O)

- During the care for probable and confirmed cases of Ebola virus infection, single-use bed linens should be used and subsequently discarded. Potentially contaminated clothing and other potentially contaminated laundry needs to be discarded using appropriate packing procedures and materials.

7.2.4.6 Waste Disposal[3]

For information and training material on waste management see www.rki.de/ebola-desinfektion.

Measures and recommendations for institutions of the health service

- The waste, produced during the care for a probable or confirmed case of EVD should if possible be inactivated in close proximity to the place where the waste was generated, according to the Biological Agents Ordinance (BioStoffV).
- Currently, medical facilities are only in individual cases equipped with autoclaves. For planned refurnishing or re-fitting, disinfection systems must fulfill certain requirements, as specified in the Federal/State Waste Committee (LAGA) execution guidelines (see **appendix P**). As stated in the guidelines "the disinfection systems are to be used according to the operating parameters specified for the disinfection of waste. This mode of operation is to be documented. The operation is only permissible, if the operator can provide proof that the system is in constructional and functional accordance with DIN 58949 or other specifications, as determined for the implementation into the RKI list

[3] Developed by a working group with experts from RKI, Federal Institute for Materials Research and Testing (BAM), Federal Environment Agency (UBA), Federal Institute for Occupational Safety and Health (BAuA), DFV, Association of the Chemical Industry e. V. (VCI) and additional experts (last updated November 2014).

according to § 18 IfSG and that the system is tested and operated according to these rules."

- Additional information on methods of disinfection can be found in the list of RKI tested and approved disinfectants and disinfection methods, section 3.4
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf?__blob=publicationFile
- In special isolation units double-door autoclaves should preferably be present in order to allow on-site disinfection of waste generated by patient care (see also **appendix H**, attachment 1, section 1.2.6).
- If necessary, when using stationary autoclaves, rules for the transport of infectious waste within the facility need be taken into consideration.
- An alternative to stationary autoclaves can be mobile disinfection units installed on vehicles, which fulfill the respective specifications. Concepts for these have already existed for a while; however, these would need to be verified by potential supplier with regard to feasibility and would need to be implemented. Mobile disinfection units could be used e.g. on airports and treatment facilities, which are rarely confronted with the corresponding requirements of disposal.
- In case the on-site inactivation of infectious waste is not possible due to technical or logistical reasons, the waste needs to be disposed in an appropriate manner outside of the place where it was generated. In this instance, the waste needs be burned in a special waste incineration plant that is approved for waste with waste code number 180103*.
- For transportation to the special waste incineration plant, the waste has to be packed in accordance to ADR and packing instruction P620 with the label UN2814. For small amounts of materials, appropriate containers are approved by BAM.
  - http://www.tes.bam.de/de/service/aktuelles/Ebola_Verpackungen.pdf
- It has, however, become apparent, that for larger quantities of infectious waste there are currently no sufficiently large containers available in Germany and other countries of the European Union, which are in compliance with packing instruction P620. For this reason, on 27.11.2014, Germany signed and enacted the multilateral agreement M281 of member states of the European Union (see **appendix Q**). This agreement is limited until 31.12.2016 and provides an exemption for the packaging for shipment of waste that may be contaminated with Ebola viruses. The safety is ensured according to the packing instruction P620 by the application of a high-quality triple packaging. Generally, the packaging is comprised of:
  - Primary receptacle: 1H2/Y plastic drum with removable head hat meets the requirements of 4.1.1 and 4.1.3 ADR, internal volume up to 60 liters available for this purpose, opening diameter approx. 400 mm , leak-proof, lid preferably with adhesive seal, single-use closure (not to reopen),
  - Secondary packaging: PE bag with a material thickness of preferably 100 µm, but at least 75 µm,
  - Outer packaging: 1H2/X plastic drum with removable head and clamping ring closure, external dimensions approx. 500 mm diameter, 800 mm height.

  *An exemplary instruction can be found in **appendix R.***
- According to dangerous goods officer regulations (GBV), the sender (the hospital or medical facility) must appoint a dangerous goods officer before the first shipment. This

can be a demonstrably trained and certified internal employee, as well as an external dangerous goods officer with valid training certificate as a consultant. The dangerous goods officer shall assign all procedures described, instruct the involved parties and finally carefully monitor each operation

- The sender of the infectious waste is also required to create a transport document for the carrier. *An example can be found in* ***appendix S****.*
- In health care facilities that take care of patients with EVD, a safety plan for the management of infectious waste containing with a high probability hemorrhagic fever viruses (such as Ebola virus) must be created. *An example can be found in* ***appendix T****.*

Measures and recommendations on the transport of infectious waste

- The transport of infectious substances is mainly regulated by ADR. The transport of non-inactivated waste from confirmed hemorrhagic fever cases (such as EVD) is carried out as Class 6.2, Category A under UN number 2814. Additional safety requirements in relation to ebola virus containing waste can be found in the above mentioned exemption agreement M281.
- In Germany, appropriate companies, that can carry out the proper and safe transport of infectious waste, are available and are usually already part of the waste management in the clinical practice. Prior to the transport of waste, appropriate arrangements for receiving must be made with a suitable special waste incineration plant.

Measures and recommendations on the incineration of infectious waste

- For the special waste incineration plants, which are approved for waste with waste code number 180103*, it can be assumed that the constructional and technical requirements for proper incineration are guaranteed. As an additional organizational measure a clear work instruction has to be established in the special waste incineration plants for a prompt and proper handling of hazardous waste with the identification UN 2814. It has to be taken into account:
  - That the sender uses multi-layer packaging that is safe and approved for the intended use, including a high resistance against mechanical strains.
  - That a timely incineration of these packages is performed.
  - That only barrel lifts or similar feeder equipment are used, which do not damage the waste containers.
  - That in the unlikely event of breakage or leakage of waste containers or other disorders, the affected area must be shut off and further measures must be established with the responsible local health authority.
- The waste code number 180103* also includes waste potentially contaminated with pathogens causing viral hemorrhagic fever (including Ebola virus). From existing contracts or tender agreements with this waste code number, an obligation of disposal derives for the operator of the special waste incineration plant. The detailed description of the waste code number is regulated in the LAGA execution guideline M18, which is implemented in the majority of the federal states by decree (see **appendix P**).
- For the incineration of waste from health institutions that is contaminated with risk group 4 pathogens (such as Ebola virus), no special regulations in the special waste incineration plants are necessary in addition to those mentioned above.

7.2.4.7 Waste Water Disposal

Additional information can be found in ***appendix O.***

Procedure for probable cases

In the early stages of the disease only low levels of virus are shedded and furthermore a high dilution effect can be expected. Thus, waste water including feces and urine, which is generated during initial care for a probable EVD case, can be discarded outside the special isolation unit via a separately used toilet into the normal wastewater system.

In case a bedside commode or bedpan must be used due to limited mobility of the patient, this should preferably be performed with disposable equipment. The content can – using adequate personal protective equipment – be disposed of using the separately used (personalized) toilet. If no disposable equipment is available, the used material, after emptying via the toilet, is to be disinfected directly in the room using an appropriate container with disinfectant of type AB from the RKI list. The contaminated sanitary equipment is to be carefully disinfected.

Procedure for confirmed cases

Temporary isolation outside special isolation units

Waste water including feces and urine, which is generated during care for a confirmed case of EVD, has to be collected in suitable containers and a disinfectant of at least limited virucidal effectiveness, suitable for disinfection of excretions, has to be added in an effective concentration (primarily limewater according to the specifications of the RKI list of tested and approved disinfectants and disinfection methods; disinfectant type AB (RKI list, section 2.2)). Subsequently (after the end of the required soaking time) it can be discarded via a separately used fecal drain, if thermal inactivation is not possible.

Feces and other body fluids which could not be collected, have first to be covered with a cloth or cellulose that are drenched in disinfectants and then safely absorbed and removed.

Alternatively, excretions can be collected in containers containing suitable absorbent material (e.g. incontinence aids). The thus absorbed liquids are subsequently disposed of as infectious waste (waste code number 180103*) (see chapter **waste disposal** above).

In case sanitary facilities have already been used by the patients or if circumstances do not allow for another possibility, contaminated sanitary facilities need to be carefully disinfected.

Special isolation units

Waste water disposal in special isolation units is performed after appropriate inactivation and is regulated in TRBA 250, appendix 1.

7.2.4.8 Disposal of Used Disinfectant

Procedure

- In case the used disinfectant was not diluted by during use and after a holding time that at least corresponds to the required soaking time for (limited) virucidal effectiveness, it can be assumed that no relevant pathogen concentrations remain.
- Solid components (environmental dirt, organic material, especially patient excretions etc.) can affect the effectiveness of the disinfectant in the disinfectant- containing liquid after

decontamination. Therefore, these residues should, if possible, be disposed in the same way as patient excretions in compliance with the appropriate protective measures.

- The disposal of the used disinfectant is generally to be carried out in accordance with local official regulations according to the safety data sheet. Preferably, procedures are to be used, for which the used disinfectant can be disposed of via the drain / toilet (connected to the public sewage).

7.2.5 Post-Exposure Prophylaxis (PEP)

Local measures

- If possible, contaminated areas are to be disinfected immediately using a disinfectant with proven at least limited virucidal effectiveness.
- Hands are to be disinfected with a hand disinfectant with proven at least limited virucidal effectiveness (virucidal disinfectants can also be used). For practical reasons, these disinfectants can also be used for disinfection of other accidently contaminated areas of the skin.
- Further information about this is available in the RKI list, section 2.3, and the VAH list as well as in the recommendations of the "Commission for Hospital Hygiene and Infectious Disease Prevention at the Robert Koch Institute - Hand Hygiene":
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Desinfektionsmittel/Desinfektionsmittelliste.pdf
  - http://www.vah-online.de/index.php?page=desinfektionsmittel-liste-2
  - http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/Haendehyg_Rili.pdf
- For disinfection of mucous membranes octenidine dihydrochloride /phenoxyethanol- or chlorhexidine-containing drugs or povidone-iodine complexes (7.5%) can be used, according to their certified areas of application e.g. Octenisept, Skinsept mucosa, Braunol. For the application on eyes 5% povidone-iodine complex is suitable.

Post-exposure vaccination

- Approaches for vaccines (e.g. administration of VSV-EBOV) are experimental. Their application needs to be assessed on a case-by-case basis (see also **chapter 7.2.6**).

Post-exposure antiviral prophylaxis

- Ribavirin is frequently used against other viral hemorrhagic fevers, but is NOT effective against Filoviruses.
- The treatment with T-705 (Favipiravir) or other substances are purely experimental measures. These substances are not approved as medication in Germany. However, their administration can be offered to patients in individual cases. Precondition is written documentation and education about the individual treatment attempt using an unlicensed medication.

7.2.6 Pre-Exposure Immunization

Currently, several vaccines against Ebola virus infections are at different stages of development. The two most important vaccines are ChAd3-Ebola and VSV-ZEBOV.

Clinical studies are currently being conducted in West Africa, their results will indicate which doses generate optimal immunogenicity and whether the administration of these doses results in specific intolerances.

Phase-III and Phase III clinical studies are currently being conducted in West Africa for Ch-Ad3-Ebola. In January 2015, preliminary data on the safety profile of Ch-Ad3-Ebola were published (Rampling et al. 2015).

Concerning VSV-ZEBOV, preliminary results of a Phase III-study were published describing an efficacy of 100%: In contacts and contacts of contacts immediately vaccinated after exposure, Ebola Virus Disease did not occur ≥ ten days after immunization (Henao-Restrepo et al. 2015).

7.2.7 Therapy[4]

EVD patients are medically treated and isolated. Since there is currently no causal therapy available, patients suffering from EVD are mainly treated for their symptoms, especially considering homeostasis of fluids, electrolytes, and glucose.

Supportive, and if required, intensive medical care

Among others, the following measures are available:

- Supportive and, if required, intensive medical care (intensive medical measures according to capacity, severity, and prognosis),
- Diagnostics and anti-microbial therapy of co-infections,
- Depending on the clinical condition (objectivized by suitable intensive care score) administration of intensive therapeutical measures at early stages, including:
  - Cardiovascular support;
  - Respiratory support;
  - Organ replacement therapy (kidney, liver);
  - Blood component therapy;
  - Appropriate monitoring;
- Hydration of the patient should be performed under cardiovascular and clinical-chemical monitoring.

Specific therapy options

- Ribavirin is used against other viral hemorrhagic fevers, but is not effective against Filoviruses.
- The few specific treatment approaches are experimental. An overview is available in the following two documents:
  - WHO document "Potential Ebola therapies and vaccines" http://apps.who.int/iris/bitstream/10665/137590/1/WHO_EVD_HIS_EMP_14.1_eng.pdf?ua=1;

[4] A working group on the therapy of EVD was established, consisting of members of STAKOB, medical professional societies, PEI, BfArM and RKI.

- EMA document "Interim assessment report. Medicinal products under development for the treatment of Ebola" http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/12/WC500179062.pdf.

- According to media reports, first preliminary results of a trial with Favipiravir in Guinea are promising (http://www.nytimes.com/2015/02/05/science/ebola-drug-has-encouraging-early-results-and-questions-follow.html?smid=tw-share&_r=2). Patients with a low viral load might benefit better from a treatment with Favipiravir (Sissoko et al. 2015). Administration of this drug for post-exposure prophylaxis is being discussed, too (van Herp, 2015).
- A study on ZMAPP which started in Liberia is currently being conducted in Sierra Leone.
- The development of Brincidofovir for the therapy of EVD has been ended by the manufacturer (http://ir.chimerix.com/releasedetail.cfm?releaseid=893927).
- A study on TKM-Ebola has been ended in Guinea because no therapeutic benefit could be identified (www.nytimes.com/2015/06/20/health/clinical-trial-of-experimental-ebola-drug-is-halted.html).

Therapeutic candidates that can be considered for a therapy of EVD

In Germany, so far no medication is licensed for the treatment of EVD. The administration of the following therapeutics can be offered to patients on a case-by-case basis. Precondition is written documentation and education about the individual treatment attempt using an unlicensed drug.

In general – if available – the following candidates can be considered for the treatment of EVD in Germany:

- ZMapp, respectively the analogue MIL-77, – Mixture of monoclonal antibodies (therapeutic approach, virus reduction),
- Favipiravir – RNA polymerase inhibitor (virus-static),
- FX06 – Peptide (capillary leak syndrome-inhibitor),
- Convalescence serum – A national concept for the production and therapy is in preparation; possibilities for cooperation on the European level are being evaluated.

A position paper regarding the requirements of clinical evaluations for potential medical therapies of EVD patients is currently being prepared by the working group on therapy of EVD (see footnote 4 on page 34).

The STAKOB treatment centers are connected with each other and with the WHO for the exchange of expertise.

7.2.8 Criteria for the Release of EVD Patients from Hospital

Before an EVD patient, who is recovering from the disease, can be released from the special isolation unit, certain criteria have to be fulfilled so that the release does not put other people in danger of infection.

Recommendation

1. Transfer of the patient to a regular infectious disease unit (conditions similar to the treatment of patients with e.g. open lung tuberculosis - even though Ebola viruses, in contrast to mycobacteria, are not transmitted by aerosols - that is vestibule, protective clothing), if all four of the following conditions are fulfilled:

- Clinical symptoms have subsided,
- Patient must be able to comply to rules (stable mental condition),
- Continence in urine and stool, solid stool (after transfer, usage of bedside commode and professional disposal of stool and urine),
- Negative PCR result in blood (in 2 independently taken samples at least 24h apart from each other).

2. The patient can be fully released from the hospital, if all three of the following conditions are fulfilled:
   - All conditions listed under 1,
   - No infectious virus in cell culture (in 2 independently taken samples at least 24h apart from each other), testing urine, stool, sweat, conjunctival swab and mouth-swab,
   - Education on potential sexual transmission of the infection even after full recovery, since Ebola viruses can be detected for up to six months after onset of symptoms in seminal fluid.

7.2.9 Handling of Deceased

Post-mortem care

- Direct handling of patients deceased of EVD should be reduced to a minimum.
- Manipulations of the deceased body (e.g. embalming) are prohibited.
- Internal post-mortem examination (necropsy) of the body should not take place. After the post-mortem examination and possible additional necessary medical examinations (collection of tissue samples or blood samples) the body should immediately be fully covered with special absorbent powder. This material can bind body fluids and additionally functions as a disinfectant.
- Then the body is to be covered in two formalin-drenched sheets (10% solution). Subsequently, the body must be placed in two tightly sealable, leak-proof plastic body bags (e.g. inside silver-grey, outside white). The closures of the bags should be taped with leak-proof tape, such that they are sealed. The whole surface of the body bags has to be disinfected from the outside with a pathogen-adequate disinfectant (RKI list). After the appropriate required soaking time, the body can leave isolation and be placed in the casket.
- The body bags are (according to VDI guideline 3891) biologically degradable after burial and burn without residue during cremation. Cremations are preferred over burial. For the preferably immediate cremation a wooden casket should be used. The casket floor should be covered with a sufficiently high (minimum 5 cm) layer of absorbent material (e.g. sawdust, wood shavings, mat of fibers).
- For the mortician that will receive the human remains accordingly to the measures described, no additional protective measures are necessary.
- The casket must be tightly locked and a biohazard sign (“highly contagious”) must be visibly displayed on the outside. Until cremation, the casket has to be placed in a definitely secure, if possible separate, and cold area.

- For the transportation of the casket to the closest cremation unit, trained personnel are required. The transport has to be supervised by the authorities.

For further information see Eisenmenger et al. 2007.

8. Communication

A massive demand for information and communication is to be expected, should EVD occur in Germany. Subsequently, different entities will be in charge depending on respective target groups. Appropriate coordination of contents and time points will be essential to avoid public unrest and panic.

8.1 Information for the Expert Audience

Physicians and members of police, fire departments and aid organizations are essential addressees due to their exposed position as primary aid and care providers and as multipliers. These target groups (e.g. employees of the public health service, physicians, aid workers) must be promptly and comprehensively informed about new developments of the situation, the assessment, as well as risks and protective measures in order to guarantee and support their operational capabilities. The communication of the public health service (ÖGD) with physicians as well as hospital staff should preferentially be performed through the State Chambers of Physicians, the Association of Statutory Health Insurance Physicians and the regional hospital associations.

Procedure

- Target groups will be provided with information adapted to the current situation, e.g. information relevant for specific occupational groups on pathogens, protective measures and hazard assessment, as well as on intervention measures and ongoing operations. Information should be available according to the different tasks and circumstances on federal, state and communal level.
- Generally, doctors should first directly contact their responsible local health authority. The local public health authorities are then to contact the state authorities in charge, which in turn should communicate with federal authorities such as the RKI.

8.2 Information for the Population and the Media

Based on recent experience, feelings of insecurity in the population are to be expected, should EVD occur in Germany. Factual and objective information must be used to counteract this development as much as possible. In addition, the population must be informed about measures to be followed.

Procedure

- The manner in which public authorities communicate outbreaks of contagious diseases substantially influences the way in which the public deals with these crisis situations. The aims of the communication include minimizing the number of infections in Germany while avoiding overreactions which could lead to unnecessary limitations of the medical care available to the population. Useful and effective preventive measures based on expert knowledge and adapted to the specific situation should be communicated to the public. This requires flexible means and paths of communication tailored to the specific epidemiological situation. Whether or not the population will successfully implement the recommended preventive measures greatly depends on how the target audience views the source of information and whether it rates the sender of the information message as trustworthy. It is therefore important to address existing fears and not to withhold

uncertainties. It might be necessary to address especially audiences that are of high risk or are hard to reach through target group specific communication strategies. Experts and the media act as multipliers for communication with the public.

- Inconsistent or contradictory communication by different institutional players must be avoided. The coordination between the authorities and institutions is stated in§10 of the general administrative regulation for the coordination of infection protection in epidemically significant cases as follows:

  "(1) A substantial part of coping with an epidemically significant situation is the external communication of the authorities with

  1. the demographic groups whose health is affected,
  2. the medical expert audience,
  3. additional affected players,
  4. the general public and
  5. the media.

  (2) Authorities in charge must ensure that communication with the groups named in paragraph 1 is uniform as far as possible and corresponds to those groups' informational needs. Authorities are to communicate the situation, its assessment, the investigations as well as the respective actions, including recommendations for conduct, the manner in which those recommendations were devised and their reasons continually, comprehensively and promptly. The extent of this communication should match the extent of the risk situation as well as the degree of interest to be expected by the general public and the media."
  (https://www.bundesgesundheitsministerium.de/fileadmin/dateien/Downloads/Gesetze_und_Verordnungen/GuV/I/Verwaltungsvorschrift-IfSG-Koordinierung-IfSGKoordinierungs-VwV.pdf)

8.3 International Cooperation

International cooperation is necessitated due to the lack of facilities (isolation wards, BSL4-laboratories, special isolation transportation/repatriation) in other countries afflicted by infection events. It is within the interest of the individual countries to supporting the containment of hazards abroad in order not to impede or endanger domestic control efforts by importing or reimporting cases.

Procedure

- Mutual information (International Health Regulations (IHR), Global Health Security Initiative (GHSI), Early Warning and Response System (EWRS)).
- Active participation in international workgroups to generate joint strategies.
- Exchange and harmonization of recommendations and strategic papers with other countries.
- Identification of necessary / feasible assistance (e.g. medical resources, experts etc.).

9. Evaluation

Subsequent to an extraordinary biological risk situation, the evaluation of the structure, process, and results of all levels involved is necessary. Important in this process is primarily the experience exchange between all stakeholders involved, horizontally and vertically. The goal is to learn from the event to improve the reaction in crisis for the future.

Procedure

Possible methods are:

- Workshops/ focus-groups presenting a report of the results,
- Final report (using the example of infection epidemiology) after an outbreak ended:
  - Epidemiological background,
  - Description of the case/ description of the outbreak,
  - List of people with disease as well as identified contacts (e.g. from transmission software) containing information regarding the gender, date of birth, appearance of disease, vaccine status, laboratory results, clinical course/complications,
  - Critical evaluation of the case and outbreak management,
  - Description of performed procedures and evaluation of their effectiveness,
  - Critical evaluation of the framework/ existing emergency epidemic plans,
  - If applicable, calculation of costs (costs for intensive surveillance, laboratory, communication, training, transport, etc.).
- Scientific review / publications.

List of Abbreviations

ABAS	Committee for Biological Agents
ADR	European Agreement concerning the International Carriage of Dangerous Goods by Road
AS	Waste key
BMG	Federal Ministry of Health
BNITM	Bernhard Nocht Institute for Tropical Medicine
BSL	Biosafety level
BZgA	Federal Center for Health Education
CDC	Centers for Disease Control and Prevention
DG SANCO	European Commission Health and Consumer Protection Directorate General
EAK	European Waste Catalogue
ECDC	European Centre for Disease Prevention and Control
EDV	Data processing
ELISA	Enzyme Linked Immunosorbent Assay
EpiLag	Weekly epidemiological telephone conference
EU	European Union
EVD	Ebola virus disease
EWRS	EU Early Warning and Response System
FFP3	particle filtering respirator mask
GHSI	Global Health Security Initiative
GIS	Geographic Information System
GMLZ	German Joint Information and Situation Center
HEPA	High Efficiency Particulate Air
HIV	Human Immundeficiency Virus
IF	Immunfluorescence
IfSG	Protection Against Infection Law
IgG/M	Immunoglobuline G/M
IHR	International Health Regulations
IGV-DG	German IHR-Implementation Law (2005)
IRTW	Ambulance especially equiped for the transport of infectious patients
IT	Information technology
LAGA	States‘ Working Group on Waste
NT	Neutralization assay
ÖGD	Public Health Service
PCR	Polymerase Chain Reaction
PEP	Post-exposure prophylaxis
PPE	Personal Protective Equipment
RKI	Robert Koch Institute
STAKOB	Permanent Working Group of Medical Competence and Treatment Centers for highly contagious, life-threatening diseases

TRBA	Technical Rules for Biological Agents
VHF	Viral hemorrhagic fever
VAH	(German) Association for Applied Hygiene
VwV	German administrative regulation
WHO	World Health Organization

Further literature

1. Baggi FM, Taybi A, Kurth A, et al.: Management of pregnant women infected with Ebola virus in a treatment centre in Guinea, June 2014. Eurosurveillance 2014; 19(49).

2. Baron RC, McCormick MJ, Zubeir OA: Ebola virus disease in southern Sudan: hospital dissemination and intrafamiliar spread. Bull WHO 1983;61:997-1003.

3. Bausch DG, Towner JS, Dowell SF, et al.: Assessment of the risk of Ebola virus transmission from bodily fluids and fomites. J Infect Dis. 2007; 196 (Supplement 2): S142-S147.

4. Calisher H, Childs JE, Fields HE, et al.: Bats: Important reservoir hosts of emerging viruses. Clinical Microbiology Reviews, July 2006, p. 531–545 Vol. 19, No. 3.

5. Centers for Disease Control and Prevention: Case Definition for Ebola Virus Disease EVD), updated August 7, 2014. http://www.cdc.gov/vhf/ebola/hcp/case-definition.html.

6. Centers for Disease Control and Prevention: Interim Guidance for Managing Patients with Suspected Viral Hemorrhagic Fever in U.S. Hospitals. 2005.

7. Chertow DS, Kleine C, Edwards JK, et al.: Ebola virus disease in West Africa - Clinical manifestations and management. N Engl J Med. 2014 November 5.

8. Drosten, C, Kümmerer BM, Schmitz H, et al.: Molecular diagnostics of viral hemorrhagic fevers. Antiviral Research 2003; 57:61–87.

9. Eisenmenger W, Gillich R, Graf P, et al.: Maßnahmen bei Todesfall an gemeingefährlichen Infektionserregern. Handbuch Biologische Gefahren I 2007. Hrg.: BBK und RKI. 509–517.

10. European Centre for Disease Prevention and Control: Risk assessment guidelines for diseases transmitted on aircraft. 2nd ed. Stockholm: ECDC; 2010. http://www.ecdc.europa.eu/en/publications/publications/1012_gui_ragida_2.pdf.

11. Falldefinitionen des Robert Koch-Instituts zur Übermittlung von Erkrankungs- oder Todesfällen und Nachweisen von Krankheitserregern http://www.rki.de/DE/Content/Infekt/IfSG/Falldefinition/falldefinition_node.html.

12. Fisher-Hoch SP, Platt GS, Neild GH, et al.: Pathophysiology of shock and hemorrhage in a fulminating viral infection (Ebola). J Infect Dis 1985; 152(5):887-94.

13. Fock R, Koch U, Finke EJ, et al.: Schutz vor lebensbedrohenden importierten Infektionskrankheiten. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 2000; 43: 891–899.

14. Fock R, Koch U, Wirtz A, et al.: Erste medizinische und antiepidemische Maßnahmen bei Verdacht auf virales hämorrhagisches Fieber. Med Welt 2001; 52:126–132.

15. Fock R, Wirtz A, Peters M, et al.: Management und Kontrolle lebensbedrohender hochkontagiöser Infektionskrankheiten. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 1999; 42: 389–401.

16. Hayman DT, Yu M, Crameri G, et al.: Ebola virus antibodies in fruit bats, Ghana, West Africa. Emerg Infect Dis. 2012 Jul;18(7):1207-9.

17. Henao-Restrepo AM, Longini IM, Egger M, et al.: Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial, Lancet 2015 August 3 (online), http://dx.doi.org/10.1016/S0140-6736(15)61117-5.

18. Kreuels B, Wichmann D, Emmerich P, et al.: A case of severe Ebola virus infection complicated by gram-negative septicemia. N Engl J Med. 2014 December 18; 371:2394-2401.

19. Moreau M, Spencer C, Gozalbes JG, et al.: Lactating mothers infected with Ebola virus: EBOV RT-PCR of blood only may be insufficient. Euro Surveill. 22 January 2015;20(3):pii=21017.

20. Piercy TJ, Smither SJ, Steward JA, et al.: The survival of filoviruses in liquids, on solid substrates and in a dynamic aerosol. J Appl Microbiol. 2010 Nov;109(5):1531-9.

21. Prescott J, Bushmaker T, Fischer R, et al.: Postmortem stability of Ebola virus. Emerg Infect Dis 2015. Vol. 21 No. 5 (May 2015). http://dx.doi.org/10.3201/eid2105.150041.

22. Rampling T, Ewer K, Bowyer G, et al.: A monovalent chimpanzee Adenovirus Ebola vaccine - Preliminary report. N Engl J Med. 2015 January 28.

23. Rodriguez LL, De Roo A, Guimard Y, et al.: Persistence and genetic stability of Ebola virus during the outbreak in Kikwit, Democratic Republic of the Congo, 1995. J Infect Dis 1999; 179(Suppl 1):S170–6.

24. Schieffelin JS, Shaffer JG, Goba A, et al.: Clinical illness and outcomes in patients with Ebola in Sierra Leone. N Engl J Med. 2014 October 29.

25. Sissoko D, Folkesson E, Abdoul M, et al.: Favipiravir in patients with Ebola virus disease: Early results of the JIKI trial. CROI 2015, abstract no. 103-ALB , http://www.croiconference.org/sessions/favipiravir-patients-ebola-virus-disease-early-results-jiki-trial-guinea.

26. van Herp M, Declerck H, Decroo T: Favipiravir–a prophylactic treatment for Ebola contacts? Lancet 2015 June 13 (correspondence), http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736%2815%2961095-9.pdf.

27. Varkey JB, Shantha JG, Crozier I, et al.: Persistence of Ebola virus in ocular fluid during convalescence. N Engl J Med. 2015 June 18; 372:2423-2427.

28. WHO Media Centre Fact Sheet Ebola Haemorrhagic Fever, http://www.who.int/mediacentre/factsheets/fs103/en/.

29. WHO Statement on the Meeting of the International Health Regulations Emergency Committee Regarding the 2014 Ebola Outbreak in West Africa, 8 August 2014. http://www.who.int/mediacentre/news/statements/2014/ebola-20140808/en/.

30. Wolf T, Kann G, Becker S, et al.: Severe Ebola virus disease with vascular leakage and multiorgan failure: Treatment of a patient in intensive care. Lancet 2015 April 11, 385:1428-35.

31. Wood JL, Leach M, Waldman L, et al.: A framework for the study of zoonotic disease emergence and its drivers: Spillover of bat pathogens as a case study. Philos Trans R Soc Lond B Biol Sci. 2012 Oct 19;367(1604):2881-92.

Appendices

Appendix A – List of areas in Africa currently potentially affected by EVD [in German]
www.rki.de/ebolagebiete

Appendix B – Flowchart: Initial suspicion of Ebola virus disease (EVD) – Advice for physicians in Germany to help recognize probable cases of EVD (German case definition)
www.rki.de/ebola-flussschema

Appendix C – List of Medical Competence and Treatment Centers for highly contagious, life-threatening diseases and their catchment areas [in German]
www.stakob.rki.de

Appendix D – Advice on PPE [in German]
www.abig.rki.de/abig/ebola-psa

Appendix E – Measures regarding a probable case of Ebola virus disease in Germany – Orientation for Health Care Professionals –
www.rki.de/ebola-massnahmen

Appendix F – Malaria testing for patients with suspected Ebola virus disease (EVD) not yet hospitalized in a special care unit
www.rki.de/ebola-malariadiagnostik

Appendix G – Details regarding laboratory diagnostics for suspected cases of Ebola virus disease
www.rki.de/ebola-labordiagnostik

Appendix H – Biologische Arbeitsstoffe im Gesundheitswesen und in der Wohlfahrtspflege (TRBA 250) [in German]
http://www.baua.de/de/Themen-von-A-Z/Biologische-Arbeitsstoffe/TRBA/TRBA-250.html

Appendix I – Protective measures for activities involving biological agents in laboratories (TRBA 100)
http://www.baua.de/en/Topics-from-A-to-Z/Biological-Agents/TRBA/TRBA-100.html

Appendix K – Proposed table for a contact person line listing [in German]
www.rki.de/ebola-kontaktpersonen-liste

Appendix L – Proposed differentiation of contact persons and symptom diary to be kept during incubation period [in German]
www.rki.de/ebola-kontaktpersonen-tagebuch

Appendix M – Recommended measures for medical and other staff who were involved in patient care or outbreak response during the Ebola outbreak in West Africa
www.rki.de/hilfskraefte

Appendix N – Advice on customs' handling of packages and freight from EVD endemic areas [in German]
www.rki.de/ebola-zollbehoerden

Appendix O –Measures regarding disinfection and waste management as pertaining to an at least probable case of Ebola virus infection in Germany
www.rki.de/ebola-desinfektion

Appendix P – Execution guidelines for disposal of waste generated by health institutions (States' Working Group on Waste (LAGA)) [in German]

http://www.rki.de/DE/Content/Infekt/Krankenhaushygiene/Kommission/Downloads/LAGA-Rili.pdf

Appendix Q – Multilateral Agreement M281 under paragraph 1.5.1 of Annex A of ADR, concerning the carriage of waste contaminated with viruses causing haemorrhagic fever
http://www.unece.org/fileadmin/DAM/trans/danger/multi/agree.wpf/M281.pdf

Appendix R – Proposed guideline for packaging according to MV281 with additional options / Handing over of potentially infectious waste for transport according to UN2814 (Ebola) [in German]
www.rki.de/ebola-verpackungsanleitung

Appendix S – Proposed carriage log for transport according to paragraph 1.5.1 of ADR (M281) [in German]
www.rki.de/ebola-musterbefoerderungspapier

Appendix T – Proposed security plan for UN 2814. Measures to secure dangerous goods and prevent risks according to 1.10.3.2 ADR / RID [in German]
www.rki.de/ebola-mustersicherungsplan