Edition: March 2017
GMBl 2017, No. 10/11 of 31 March 2017
Amended on 3 July 2018, GMBl No. 30

Technical Rules for Biological Agents	**Guideline for Risk Assessment and for the Instruction of Employees regarding Activities involving Biological Agents**	**TRBA 400**

The Technical Rules for Biological Agents (TRBA) reflect the state of the art, the state of occupational medicine and occupational hygiene as well as other sound work-scientific knowledge relating to activities involving biological agents.

They are compiled and adapted by the **Committee for Biological Agents (ABAS)** and announced by the Federal Ministry of Labour and Social Affairs in the Joint Ministerial Gazette.

Within its scope of application, TRBA 400 “Guideline for Risk Assessment and for the Instruction of Employees regarding Activities involving Biological Agents” specifies the requirements of the *Biostoffverordnung* [German Ordinance on Biological Agents]. If the Technical Rules are adhered to, the employer can assume that the relevant requirements of the ordinances have been fulfilled. If the employer chooses a different solution, that solutions must achieve at least the same level of safety and health protection for employees.

Content

1. Scope of application and objective

(1) TRBA 400 is used for risk assessments in accordance with sections 4 to 7 of *Biostoffverordnung (BioStoffV)* [German Ordinance on Biological Agents] and for the instruction of employees. It describes the required process steps and the procedure and defines assessment criteria on the basis of which protective measures are to be derived.
(2) TRBA 400 is intended for employers and persons involved in the risk assessment as a superordinate aid for performing the risk assessment. If specific TRBA already exist for industries or activities, these TRBA have priority. An overview of the Technical Rules for Biological Agents can be found online at www.baua.de/trba.
(3) In addition, TRBA 400 serves as a basis for the compilation of industry-specific guidelines for risk assessments.
(4) Pursuant to section 4 of *BioStoffV*, the employer must gain activity-related insights into stress and exposure situations including psychological stress. TRBA 400 provides support in relation to the identification of psychological stress factors which can lead to an increase in the risk posed by biological agents (absorption) into the body and/or by influencing the immune system).

2. Definitions

2.1 Biological Agents

The term 'biological agents' is conclusively defined in section 2 of *BioStoffV*. In the broadest sense, the term refers to microorganisms which can cause sensitising or toxic effects or other health-damaging effects as a result of an infection.

2.2 Infectious effect of biological agents

Infectious biological agents can infest the surface of the body. They can also enter the body, propagate inside it and thereby cause an infection. If the body reacts to an infection by showing clinical symptoms, an infectious disease has developed. Infections can be caused e. g. by bacteria, fungi, parasites and viruses. For further information, please refer to appendix 1, part 1.

2.3 Sensitising effect of biological agents

A sensitisation is a hypersensitivity of the immune system to biological agents or their components. It can be caused by one time or repeated contact. A sensitisation caused by biological agents can lead to the development of an allergy. For further information, please refer to appendix 1, part 2.

2.4 Toxic effect of biological agents

A toxic effect of biological agents is an acute or chronic health damage which can be caused by metabolic products or cell components of biological agents. For further information, please refer to appendix 1, part 3.

2.5 Protective measures

Protective measures are the structural, technical, organisational and personal measures including hygiene measures which are to be defined based on the risk assessment for the protection of employees.

2.6 Activity

The term 'activity' is conclusively defined in section 2 of *BioStoffV*. For one thing, activity means using biological agents as is primarily the case with activities which have assigned protection levels. On the other hand, the activities also include occupational contact with humans, animals, plants, products, objects or materials, when biological agents occur or are released as a result of such work and employees can potentially come into contact with them.

2.7 Protection level activities

Protection level activities are activities involving biological agents which have to be assigned to a protection level according to section 5 of *BioStoffV*. This includes activities in laboratories, laboratory animal husbandry, biotechnology and healthcare facilities.

2.8 Non-protection level activities

Non-protection level activities are all activities involving biological agents which are not assigned to a protection level.

2.9 Professional expertise

The required professional expertise depends on the type of activity and the extent of the risk. Professional expertise basically includes a suitable professional training, relevant work experience and competence regarding occupational safety. Details on professional expertise are regulated by TRBA 200 “Requirements for professional expertise in accordance with the Biological Agents Ordinance”.

2.10 Exposure

Exposure means that employees come into contact with biological agents during their activities.

2.11 Psychological stress

“Psychological stress” refers to all measurable external influences on people which affect them psychologically[1].

[1] Definition of “psychological stress” according to DIN EN ISO 10075-1

2.12 Psychological strain

Psychological stress factors have different effects on everyone and depend on the individual personal preconditions (psychological strain)[2]. Individual coping strategies also play a role in this. The psychological strain of the same stress factors can therefore be very different for individuals.

In addition, certain psychological stress factors (e. g. intensification of working practices) usually have negative effects (impairments).

3. Basic principles for risk assessments

(1) Biological agents can have infectious, sensitising and toxic effects. These effects of biological agents may all occur at the same time. Other harmful effects can occur as a result of infections or toxic effects of biological agents. This refers to carcinogenic or teratogenic / reprotoxic effects. Further information on possible health risks is compiled in appendix 1.

(2) In the risk assessment, the risks of the activity involving biological agents are to be assessed. Pre-existing conditions or other individual predispositions which lead to an increased risk for the employees concerned when working with biological agents must be taken into account within the framework of occupational health prevention.

3.1 Responsibility and organisation

(1) According to section 5 of the German Occupational Safety and Health Act, the employer is obliged to assess the working conditions of their employees regarding risks to health or safety. The aim of this risk assessment is to determine which protective measures must be taken to prevent health risks from employees.

(2) At the workplace, various stress factors or risks may exist at the same time. First, they have to be identified and assessed separately. Subsequently, they have to be compiled in an overall risk assessment. The protective measures must be coordinated and must take all risks into account (see figure 1). The risk assessment process includes the following steps:

1. Compilation of work areas and activities.
2. Identification of the risks and exposures which exist at the workplace, e. g. by biological agents, genetically modified organisms, hazardous substances, noise, mechanical hazards, heat, cold or psychological stress.
3. Assessment of the identified exposures and risks.
4. Determination of the required protective measures and their implementation.
5. Regular checks of the effectiveness of the protective measures taken.
6. Documentation of the risk assessment.

[2] Definition of “psychological strain” according to DIN EN ISO 10075-1

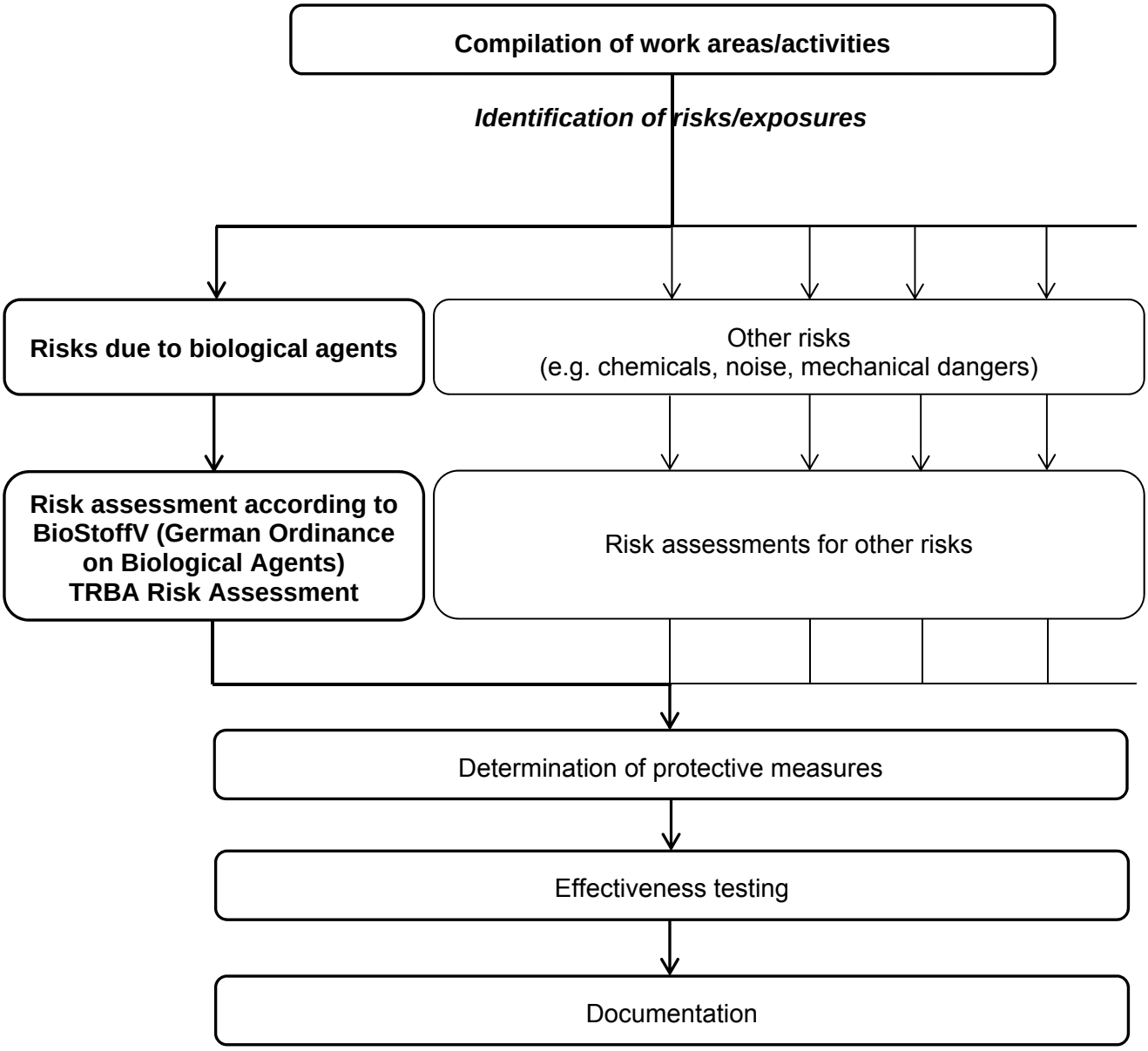

Figure 1: Risks posed by biological agents as part of the assessment of working conditions according to section 5 *ArbSchG*

(3) If employees of several employers work at a workplace or if certain activities in the company are contracted out to external companies, the corresponding employers are obliged to cooperate regarding safety and occupational health provisions according to section 8 *ArbSchG*. Mutual information on the work related risks concerning the safety and health of the employees is required. If applicable, the risk assessment is to be performed jointly and the implementation of protective measures is to be coordinated.

Depending on the type of activity, the employer must ensure that the employees of other employers have received appropriate instructions regarding the risks for their safety and health.

(4) If labour leasing is involved, the borrower is responsible for the provision of company-specific instructions. The experience and qualifications of the persons who were leased to perform work are to be taken into account.

3.2 Formal requirements

(1) According to the Biological Agents Ordinance, the risk assessment must be performed in a professional manner. If the employer does not have the required knowledge themselves, they shall seek expert advice. Regulations on the required professional expertise can be found in TRBA 200 “Requirements for professional expertise in accordance with the Biological Agents Ordinance”.

(2) According to section 4 paragraph 2 *BioStoffV*, the risk assessment must be reviewed at least once every two years, updated, if required, and the result must be documented. Reasons for updating:

1. major changes of the working conditions, e. g. use of new equipment or procedures, other biological agents or materials,
2. new information such as accident reports and results of accident investigations,
3. insights from preventive occupational healthcare,
4. insufficient efficiency of the determined protective measures.

(3) For comparable activities and exposure situations (e. g. several similar workplaces), the employer can perform a joint risk assessment. Activities with a high risk level such as activities of protection levels 3 and 4 should not be assessed together but separately. This also applies to activities which are not performed regularly, e. g. maintenance, repair or servicing work.

(4) As a precondition for a proper and complete assessment of the risks and for the determination of the required protective measures,

1. it must be determined whether activities are to be performed which are assigned to a protection level (protection level activities) or not (non-protection level activities),
2. information on biological agents is to be obtained,
3. information on the activities is to be obtained.

(5) The obtained information on infection risks and the risks posed by sensitising or toxic effects are to be assessed independently. These individual assessments are to be compiled to form an overall risk assessment.

(6) For information procurement, the activity-related, in-house experiences including the employees’ knowledge and skills and relevant company documents are to be used, e. g. reports of meetings of the company committee for occupational safety, accident reports, insights regarding work-related illnesses and in-house documents on measurements, if available.

3.3 Activities assigned / not assigned to a protection level

(1) Activities involving biological agents are divided into activities with or without protection level assignment.

Activities involving biological agents in laboratories, laboratory animal husbandry, biotechnology and healthcare facilities are to be assigned to a protection level (in the following referred to as **protection level activities**). All other activities involving biological agents do not have to be assigned to a protection level (in the following referred to as **non-protection level activities**).

(2) With protection level activities, the occurring or used biological agents are usually known or at least sufficiently definable. For the most part, this is not the case with non-protection level activities; this is why extensive information procurement, in particular regarding the identity of biological agents, is not always possible, for example in sewage treatment plants and waste disposal. Due to these differences, a different risk assessment approach is used in each case. Protection level activities non-protection level activities are therefore regulated separately in this TRBA (see figure 2).

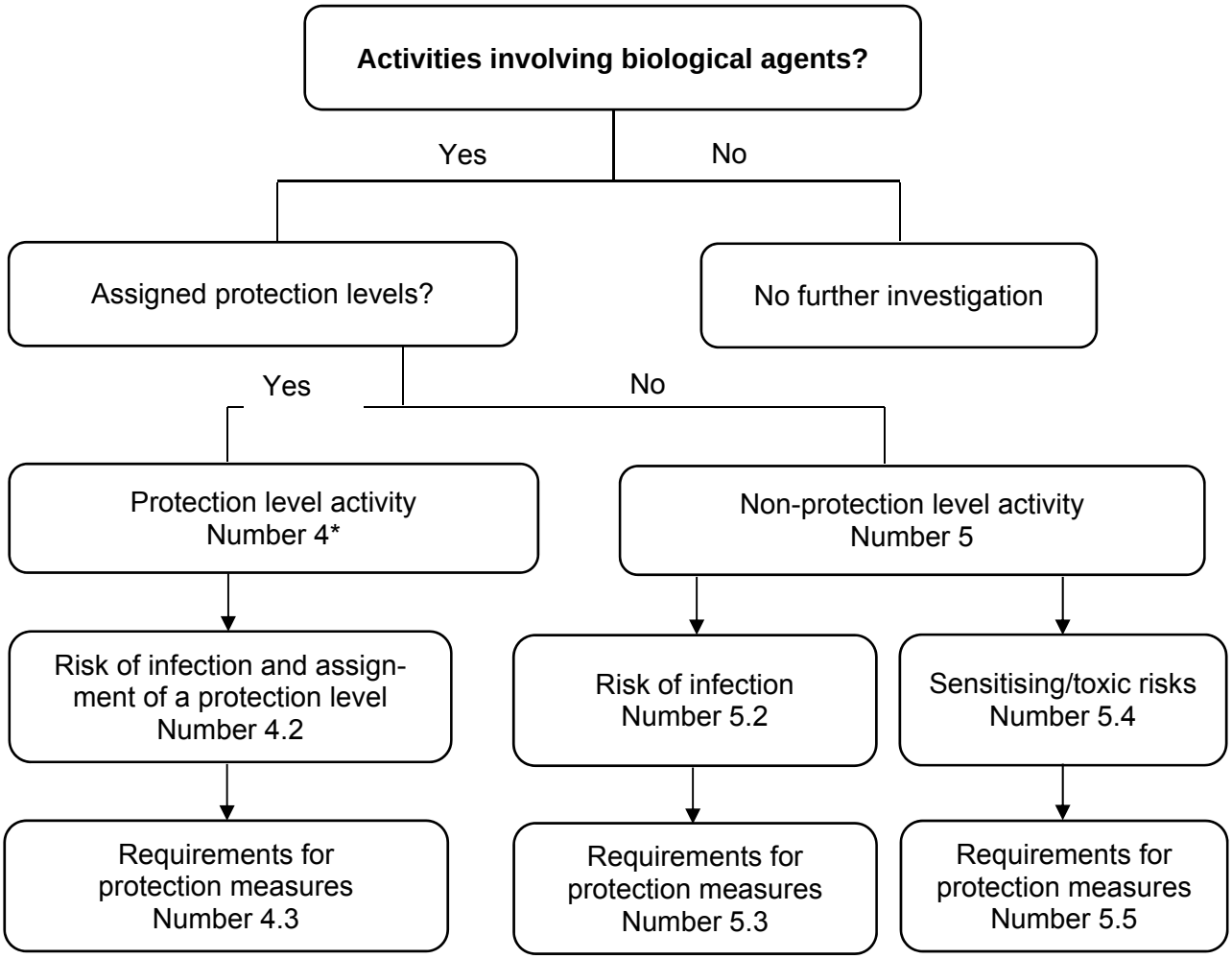

Figure 2: Process description of the risk assessment for activities assigned and not assigned to a protection level

* For sensitising/toxic risks, please refer to number 4 paragraph 3 and for requirements for protection measures, please refer to number 4.3 paragraph 3.

3.4 Derivation of protective measures

(1) The protective measures are to be determined and implemented based on the result of the risk assessment with the goal to prevent or, if this is not possible, minimise the exposure of employees. This is to be done with a focus on requirement, suitability and adequacy in the following order:

1. Substitution of biological agents

   Biological agents which are a health risk for employees are to be replaced by biological agents which are less risky for employees if this is reasonable and possible for the type of activity or according to the state-of-the-art (e. g. selection of suitable strains of risk group 1 for soil remediation or as feed supplements, selection of laboratory strains with a lower risk potential).

   Substitution of work methods and equipment

   If the risk cannot be minimised by a substitution of the biological agents, appropriate working methods and equipment must be designed or selected to ensure that biological agents are not released at the workplace.

2. Structural, technical and organisational protective measures

   The employer must define the structural, technical and organisational protective measures which are required to keep the exposure of employees at a minimum.

3. Personal protective equipment (PPE)

   Personal protective equipment such as respiratory protection is appropriate if the protection of employees is not sufficiently guaranteed even though the measures according to number 1 and 2 have been exhausted. Cumbersome personal protective equipment such as certain types of respiratory protection may not be a permanent measure.

(2) When specifying protective measures, the state-of-the-art as well as established work-scientific knowledge is to be observed.

(3) In general, hygiene measures in accordance with section 9 paragraph 1 or 2 of the Biological Agents Ordinance are to be specified and implemented for all activities involving biological agents. Activities involving biological agents of risk group 1 without sensitising, toxic or other harmful effects do not require any further measures.

(4) Existing protective measures must be checked regarding their compliance with the requirements which were determined in the risk assessment and adapted, if necessary. This also includes protective measures which were implemented due to other legal provisions (e. g. Hazardous Substances Ordinance), (see also figure 1).

(5) It shall be checked whether preventive occupational healthcare measures are to be taken.

(6) The required protective measures which were selected for the individual effect (infectious, sensitising, toxic) of a biological agent must be coordinated in an overall risk assessment (see number 7).

(7) Psychological stress can be connected to the risk potential of biological agents, e. g. with activities involving highly pathogenic agents. In addition, psychological stress may increase the risk of accidents such as needlestick injuries. Furthermore, psychological stress can have

an influence on the individual immune response. This is why this type of stress must be minimised as well.

4. Risk assessment for protection level activities (sec. 5 *BioStoffV*)

(1) The protection levels measure the level of the risk of infection of an activity and determine the extent of the required protective measures. They are based on the risk group of the corresponding biological agent. Based on the four risk groups, four protection levels (protection level 1 – 4) are differentiated.

(2) In sectors where protection level activities (number 3.3) are performed, activities involving biological agents with an infectious effect have priority.

(3) Sensitising and toxic effects of biological agents are not covered by the assignment to a protection level. However, sensitising and toxic properties of biological agents also determine the risk potential of the activities in case of protection level activities, e. g. if biological agents of risk group 1 with toxic and/or sensitising properties are used purposefully for research work.

(4) For the assignment to a protection level, the type of activity is relevant. The approach varies depending on whether the activities are specific or non-specific.

(5) With **specific activities,**

- the type (species) of the biological agent is known,
- the activities specifically involve the biological agent and
- the extent of exposure to the biological agent during normal operation is sufficiently known or can be assessed.

Examples for **specific activities**:
- cultivation and further processing of defined biological agents,
- use of reference strains for diagnostics,
- working with cell cultures,
- infecting laboratory animals with biological agents

(6) **Non-specific activities** are activities which do not meet at least one of the three criteria for a specific activity according to section 5.

Examples for **non-specific activities**:
- examination of human and animal sample materials (e. g. blood, urine, stool, tissue),
- examination, treatment and care of humans and animals,
- examination of environmental samples in the laboratory (e. g. soil, water, air),
- feeding of infected laboratory animals

4.1 Information gathering

4.1.1 Activity-related information

(1) Operating procedures, working methods and activities as well as working equipment are to be collected. It must be checked whether and to what extent employees are exposed to biological agents. The risks can differ significantly depending on the activity.

Example
Measuring the temperature of a patient who suffers from hepatitis B using an infrared thermometer is not a risky activity since the contact with hepatitis B viruses (HBV) is unlikely. Bandaging an open wound of the same patient on the other hand involves the risk of exposure to HBV through blood contact.

(2) With specific activities, the type, duration, level and frequency of exposure are usually known or at least sufficiently assessable. This may also apply to non-specific activities, e. g. feeding laboratory animals which were infected (on purpose) beforehand or the processing of samples with known infection status.

(3) Furthermore, it is to be determined whether any insights from comparable activities involving biological agents exist

- on risks and exposure situations including psychological stress,
- on activity-related diseases and countermeasures and
- from preventive occupational healthcare.

Note: *Information on comparable activities can e. g. be found in the bulletins of the German Federal States, the Bundesanstalt für Arbeitsschutz und Arbeitsmedizin [Federal Institute for Occupational Safety and Health] or the accident insurance institutions.*

4.1.2 Information relating to the biological agent

(1) For the risk assessment, the properties of known and possibly occurring biological agents are to be determined. This includes

- the risk group,
- the pathogen-specific transmission routes,
- if available – further specific information such as e. g. infection dose, infectious stages, etc. and
- possible sensitising or toxic effects.

Note: *For general information on the risk of infection and on transmission routes, please refer to appendix 1 part 1 and part 4. For information sources of further data relating to biological agents, please refer to number 11 “References”.*

4.2 Assessment of the risk of infection and assignment of a protection level

(1) Based on the collected information, the risk of infection is to be assessed and the activities are to be assigned to a protection level. The protection levels measure the level of the

risk of infection. For the assignment to a protection level, only the risk of infection is relevant and not the sensitising and toxic effects.

(2) The assignment of a protection level is performed as follows:

- With **specific activities**, the protection level corresponds directly to the risk group of the biological agents used. If e. g. activities involving biological agents of risk group 2 are performed, they are assigned to protection level 2. If various biological agents occur, the biological agent of the highest risk group determines the assigned protection level.
- With **non-specific activities**, the protection level does not necessarily depend on the biological agent with the highest risk group but on the risk of infection for the employees. The risk of infection is to be determined based on the following criteria:
  - probability of occurrence of biological agents taking into account their corresponding risk group;
  - specific properties of the biological agent (e. g. survival capability under the conditions at the workplace, stage-specific infectiousness, dependence on vectors);
  - type of activity (e. g. manual work steps or automated processes, risks of injury, aerosol formation);
  - type, duration, level and frequency of the determined exposure.

(3) The assigned protection level cannot be higher than the one determined by the biological agent with the highest risk group.

4.3 Requirements for protective measures

(1) The protection level is decisive for the determination of the required protective measures. These measures are to be determined and implemented in accordance with the basic principles specified in number 3.4. For activities with protection level 1, hygiene measures in accordance with section 9 paragraph 1 and 2 *BioStoffV* or TRBA 500 are sufficient. For the rest, the protective measures must be appropriate with

- activities of protection level 2 to minimise the exposure of employees,
- activities of protection level 3 to prevent the exposure of employees,
- activities of protection level 4 to safely prevent the exposure of employees.

(2) The applicable TRBA for activities with assigned protection level are to be observed. The Technical Rules TRBA 100 “Protective measures for activities involving biological agents in laboratories” and TRBA 120 “*Versuchstierhaltung*” [Laboratory animal husbandry] provide guidelines for the risk assessment in laboratories and in laboratory animal husbandry respectively. They include examples for protection level assignments, among other things for typical non-specific activities in these work areas. TRBA 250 “Biological agents in health care and welfare facilities” provides guidelines for the risk assessment in health care and welfare facilities. It specifies the criteria for protection levels 1 – 4 of the corresponding activities (all non-specific) and supports them with examples.

(3) Sensitising and toxic effects are to be assessed separately. It is to be checked whether the protective measures which have been determined based on the protection level are sufficient. If this is not the case, further measures are required.

Note: *If activities are assigned to protection level 1, individual measures of protection level 2 (e. g. working under a biological safety cabinet) may provide sufficient protection against sensitising and toxic effects. At higher protection levels, it can generally be assumed that the protective measures which are to be taken are sufficient.*

5. Risk assessment for non-protection level activities (sec. 6 *BioStoffV*)

Non-protection level activities are all activities involving biological agents which are **not** performed in laboratories, in laboratory animal husbandry, biotechnology or healthcare facilities (see number 3.3). Such activities are for example performed in agriculture and forestry, veterinary medicine, outpatient care, waste and waste water management, slaughtering businesses, pet shops, for work on existing sanitary installations, cleaning and remediation work or in biogas plants.

5.1 Information gathering for non-protection level activities

5.1.1 Activity-related information

(1) Operating procedures and work methods are to be recorded so that the individual activities can be checked regarding

1. the possibility of the release of biological agents and of the exposure of employees,
2. the type of exposure and
3. the level, duration and frequency of exposure, in particular regarding biological agents with sensitising or toxic effects.

(2) Exposure means that employees come into contact with biological agents during their activities. The type and the extent of exposure in combination with the properties of the biological agent are the decisive factors for the degree of endangerment. With infectious biological agents, various transmission routes are relevant for the occurrence of infection depending on the pathogen (for transmission routes, see appendix 1 part 1 and part 4).

Example

Legionella have to enter the respiratory tract to lead to an infection whereas with tetanus, a skin injury is the precondition for an infection.

(3) The sensitising or toxic effects of biological agents occur e. g. when air which is contaminated with mould or endotoxins enters the respiratory tract.

(4) The type of exposure is of central importance for the selection of suitable protective measures with the goal to interrupt possible transmission routes and/or absorption paths of biological agents.

(5) To determine the type, frequency and level of exposure, operating procedures, work methods, equipment and activities must be checked to determine whether and in which way biological agents are released. Regarding the level of exposure, for example, the amount and nature of the materials used and the intensity of their mechanical processing are important.

Example

The dust formation is higher during the processing of dry natural raw materials such as hay, straw, crop or onions than during comparable activities using wet material. The degree of processing may also have an influence on the exposure level. With activities involving raw cotton, the exposure is usually higher than with activities involving the finished fabric. With activities involving liquids, aerosols may form depending on the work process (e. g. activities involving high-pressure cleaners, grinding processes, milling). The conditions at the work-place, e. g. unfavourable ventilation conditions, may also influence the exposure level.

(6) It is to be checked whether conditions exist which facilitate e. g. the infestation of materials with biological agents and/or the propagation of existing biological agents. Factors which may play a role in this are e. g. high air humidity, heat, insufficient ventilation or poor cleaning and hygiene as dust and other dirt accumulations may serve as a nutrition base for biological agents.

(7) Experiences and insights from comparable activities, also from other industries, if applicable, are to be observed, e. g.

- regarding exposure, if available also data from measurements, and
- regarding activity-related illnesses.

If applicable, corresponding information may be obtained from the prevention departments of accident insurance institutions, the occupational health and safety authorities of the German Federal States or may be found in accident reports or preventive occupational healthcare.

5.1.2 Information relating to the biological agents

(1) It is usually not possible to determine the occurring biological agents comprehensively and in detail since the time and place of their occurrence may vary depending on the activity and work material and may also depend on external influences (e. g. temperature, humidity). This is why during information gathering, those biological agents must be taken into account which according to experience will probably occur during the activity which is to be assessed. In number 11 “References” corresponding information sources are listed.

(2) For the identified biological agents, it is to be determined, where possible,

1. which harmful properties they possess (infectious, sensitising, toxic), which risk group they are assigned to and
2. via which transmission routes and/or absorption paths they enter the body.

(3) The information gathering includes checks whether

- the biological agents are only likely to occur,
- an exposure to biological agents, in particular those of risk group 3, is likely,
- it is a known fact that biological agents of risk group 3 exist.

(4) If sensitising and toxic biological agents occur, no differentiation has to be made between the individual types. Here, the information that mould regularly occurs during the sorting of waste is, for example, sufficient.

(5) When determining the information, it must also be checked whether, due to special situations, biological substances that do not normally occur have to be taken into account. This is the case, for example, in the keeping of farm animals, when a particular animal epidemic has broken out, or in parks which are used by the drug scene where discarded used syringes are likely to be found. The presence of animals which transfer or discharge infectious agents must be taken into account as well, e. g. rats during sewer cleaning.

(6) Regional or seasonal differences are to be observed. Specific pathogens which can be transferred via vectors, for example, only play a role in certain regions.

Examples for vectors are ticks and mosquitos. Rodents, dogs, cats or bats, however, may also transfer pathogens as vectors.

(7) Regarding a possible risk of infection, usually at least the occurrence of biological agents of risk group 1 and 2 are to be expected in work areas of activities not assigned to a protection level. For some work areas, the possible or definite occurrence of biological agents of risk group 3 is decisive for the assessment of the risk of infection. For an overview, see appendix 3.

(8) Regarding possible sensitising or toxic effects, usually a mixed exposure to sensitising and toxic biological agents is to be expected in work areas of non-protection level activities.

Note: *For general information on the possible effects of biological agents and transmission routes, see appendix 1.*

5.2 Convention for the assessment of the risk of infection

(1) For the assessment of the risk of infection, the following risk categories are defined by convention.

- ***No or negligible risk of infection:***
  - Only biological agents of risk groups 1 and 2 occur and an exposure is unlikely or marginal.
  - Only biological agents of risk groups 1 and 2 occur and employees are exposed to these biological agents. There is, however, no evidence of the occurrence of occupational infectious diseases in these or comparable activities or working conditions.
- ***Existing risk of infection:***
  - Biological agents of risk groups 1 and 2 occur and employees are exposed to these biological agents. There is evidence of the occurrence of occupational infectious diseases in these or comparable activities or working conditions.
  - If an exposure to biological agents of risk group 3 is to be expected, it must always be assumed that there is a risk of infection.

(2) See appendix 3 for an exemplary compilation of industry-specific activities, the occurring infectious biological agents including their transmission routes and the corresponding risk categories.

5.3 Requirements for protective measures against the risk of infection

(1) Protective measures are to be determined and taken in accordance with the basic principles specified in number 3.4. The requirements increase with the degree of endangerment.

- For activities without or with a negligible risk of infection, the general hygiene measures according to section 9 paragraph 1 of the Biological Agents Ordinance are usually sufficient.
- For activities with an existing risk of infection, the protective measures must be suitable to minimise the exposure of the employees.

(2) In special cases, such as the outbreak of an animal epidemic caused by biological agents of risk group 3 or remediation work at old tanneries with viable anthrax spores, the protective measures must be suitable to safely prevent any exposure of the employees.

(3) For activities which are comparable to those with assigned protection level, e. g. in outpatient care or veterinary medicine, suitable protective measures can be selected from the protection levels (see number 4.3).

5.4 Convention for the assessment of risks due to airborne sensitising and toxic biological agents

For the assessment of risks caused by the sensitising and toxic effect of biological agents, the level, duration and frequency of exposure are particularly important. To assess the exposure, three exposure levels are defined by convention. Based on the duration and frequency of exposure, the risk levels “increased”, “high”, “very high” are assigned on the basis of which the requirements for protective measures are defined. These conventions are to be used for the risk assessment in particular in industries and for activities which are not covered by a specific TRBA.

5.4.1 Exposure levels for airborne biological agents

(1) The concept of exposure levels is based on the assumption that the risk increases with the level of exposure. The exposure levels are defined by convention.

(2) At the workplace, in particular airborne sensitising biological agents can lead to sensitisation or even allergic respiratory diseases when inhaled at high concentrations over a long period of time and repeatedly. For the assessment of the sensitising potential, neither occupational exposure limits nor dose-response relationships are available.

(3) Toxic biological agents can have systemic or local effects (e. g. respiratory tract, eye mucosae). For the toxic effect of fungi or bacteria, no dose-response relationships and therefore also no health-based limits are available.

(4) The exposure to sensitising or toxic biological agents in the air at the workplace is assigned to the following exposure levels based on conventions:

- Exposure level “increased”
- Exposure level “high”
- Exposure level “very high”

(5) For the assignment to exposure levels, there are two possibilities:

a) based on measured values,

b) based on material properties, activity and workplace characteristics.

a) Assignment of activities based on measured values

Even if the Biological Agents Ordinance does not require mandatory measurements, workplace measurements or the use of existing measured values, if applicable from comparable activities, can be helpful for the risk assessment. Only measured values are suitable which are based on a standardised measurement method and for which representative background levels are available (see appendix 2). If measured values for various biological agents are available for an activity, the ones with the highest assigned exposure level are decisive.

Mould fungi

The exposure levels for airborne mould fungi are assigned as follows:

- **Exposure level “increased”**

  10,000 (10^4) to 100,000 (10^5) cfu*/m³; at this level, the workplace concentration is increased.

- **Exposure level “high”**

  100,000 (10^5) to 1,000,000 (10^6) cfu/m³; at this level, the workplace concentration is high.

- **Exposure level “very high”**

  over 10^6 cfu/m³; at this level, the workplace concentration is very high.

* cfu stands for colony-forming units

Endotoxins

The exposure levels for airborne endotoxins are assigned as follows:

- **Exposure level “increased”**

  100 (10^2) to 1,000 (10^3) EU*/m³; at this level, the workplace concentration is increased.

- **Exposure level “high”**

  1,000 (10^3) to 10,000 (10^4) EU/m³; at this level, the workplace concentration is high.

- **Exposure level “very high”**

  over 10^4 EU/m³; at this level, the workplace concentration is very high.

* EU stands for endotoxin units

The exposure levels are not health-based. They are based on the natural background concentration of biological agents in the ambient air (see appendix 2).

b) Assignment of activities based on material properties, activity and workplace characteristics

If no values are available from workplace measurements, material properties, activity and workplace characteristics may be used as a guideline.

For activities involving materials which contain biological agents, are contaminated or colonised with biological agents, e. g. untreated natural materials or waste, the release of biological agents into the breathing air and an increased exposure is to be expected unless the release is ruled out. This also applies to activities involving animals, animal materials such as animal hair or animal excretions. Activities with a minor extent, in particular regarding the handled amount, usually do not have an “increased” exposure level, e. g. the filling of fruit and vegetable displays in the retail sector.

Whether activities are to be assigned to a “high” or “very high” exposure level depends on various factors. These include:

Material properties

- untreated natural products, e. g. jute, hops, reeds,
- visible mould infestation, e. g. restoration of archive material,
- high specific surface, e. g. wood chips, herbs and spices,
- tendency to release dust, e. g. hay, crops,
- level or processing, e. g. with cotton or flax.

Activity-related factors

- intensity of the movement or the machining and processing of materials, e. g. vibration sieves, open transfer points of conveyor belts,
- direct contact with contaminated materials,
- amount of the handled materials, e. g. at a wholesale scale,
- duration and frequency of the activity to be assessed,
- activities involving aerosol formation, e. g. the use of high-pressure cleaners, milling or grinding.

Workplace-related factors

- working in closed rooms with insufficient ventilation, e. g. halls without transverse ventilation,
- storage conditions which enable the propagation of biological agents, e. g. outdoor storage with weather exposure,
- failure of technical facilities, e. g. ventilation, drying processes.

It can be assumed that the exposure level increases with the number of applicable factors.

In case of doubts regarding the exposure level, workplace measurements in accordance with TRBA 405 “*Anwendung von Messverfahren und technischen Kontrollwerten für luftgetragene Biologische Arbeitsstoffe*” [Application of measurement methods and technical control values for airborne biological agents] can be helpful.

The table in appendix 4 lists exemplary activities and the exposure level which is usually connected to them.

5.4.2 Assessment of the exposure duration and frequency

It is generally assumed that with sensitising and toxic biological agents, the risk also increases with the duration and frequency of exposure and/or is lower for short-term and rare activities than for regular and long-term activities.

For the further assessment steps, the exposure duration and frequency are summarised under exposure time (see table 1).

Table 1: Convention for the assessment of the exposure time

Exposure duration / Exposure frequency	up to two hours per working day	longer than two hours per working day
Less than 30 working days per year	**short**	**medium**
30 and more working days per year	**medium**	**long**

With activities at varying workplaces (e. g. mould remediation in buildings), the frequency of exposure cannot always be reasonably applied as a criterion. In these cases, the risk is to be derived based on the exposure level and exposure duration.

5.4.3 Convention for the summarising assessment of risks caused by sensitising and toxic biological agents

For the risk assessment, the exposure parameters of level, duration and frequency have to be brought together.

By combining exposure level and time, a grading of the risk posed by sensitising and toxic biological agents can be derived which is the basis for the requirements for protective measures (see table 2).

Table 2: Derivation of risk levels for activities involving sensitising and toxic biological agents

Exposure level / Exposure time	increased	high	very high
Short	Increased risk	Increased risk	High risk
Medium	Increased risk	High risk	High risk
Long	Increased risk	High risk	Very high risk

5.5 Requirements for measures for the protection against risks posed by sensitising and toxic biological agents

(1) The basic aim of the protective measures is to minimise the exposure of employees to sensitising and toxic biological agents. Independent of the risk levels, the general hygiene measures in accordance with section 9 paragraph 1 of the Biological Agents Ordinance must be observed. Further protective measures, e. g. as per section 9 paragraph 3 of the Biological Agents Ordinance, are to be applied depending on the risk assessment:

a) **Increased** risk by sensitising and toxic biological agents

- In addition to the hygiene measures in accordance with section 9 paragraph 1 *BioStoffV*, the required organisational measures are to be selected and taken to ensure that the exposure of employees is minimised.
- It is to be checked, whether apart from point 1 technical or structural measures have to be taken as well, if these measures can be implemented with reasonable effort.
- If the above-mentioned measures are not sufficient, personal protective equipment (PPE) may also be necessary.

b) **High** risk by sensitising and toxic biological agents

- In addition to the general hygiene measures in accordance with section 9 paragraph 1 *BioStoffV*, structural, technical or organisational measures are to be selected and taken to ensure that an exposure is prevented or at least reduced by one risk level. This can be achieved, for example, by reducing the duration and frequency of the activities or by changing the work procedure.
- If the exposure cannot be reduced by one risk level despite the exhaustive use of technical, structural or organisational measures, the employees must be provided with suitable PPE. The PPE must be worn.

c) **Very high** risk by sensitising and toxic biological agents

- In addition to the general hygiene measures in accordance with section 9 paragraph 1 *BioStoffV*, structural, technical or organisational measures are to be selected and taken to ensure that an exposure is prevented or at least reduced by two risk levels.
- If the exposure can only be reduced by one risk level despite exhaustive use of technical, structural or organisational measures, the employees must be provided with suitable PPE. The PPE must be worn.

Notes: *In individual cases, e. g. if an employee has an allergy which is relevant at the workplace, even a complete prevention of the exposure may be required.*

Criteria for the selection of personal protective equipment can be found in the ABAS statement “Kriterien zur Auswahl der PSA bei Gefährdungen durch biologische Arbeitsstoffe” [PPE selection criteria for risks posed by biological agents] [1]. Cumbersome personal protective equipment is to be limited to the absolutely required minimum for each employee.

(2) It is to be checked whether preventive occupational healthcare measures are required.

6. Psychological stress of activities involving biological agents

6.1 Consequences of psychological stress

Psychological stress can have a negative impact on employees with acute or long-term consequences which may increase the risk of infections or allergic or toxic reactions with certain activities involving biological agents.

(1) Acute consequences may include unsafe behaviour and an increasing risk of accidents. The reasons for this are in particular

- decreasing alertness, concentration,
- information loss due to easy distractibility from work,

- longer reaction times,
- delayed or missing realisation of own mistakes,
- tendency to work reactively instead of proactively,
- fear.

(2) Long-term consequences may include a changed immune system so that

- viral and bacterial processes may be activated,
- wound healing is delayed which can cause passages for infectious agents,
- the sensitivity to allergens increases,
- the expression of symptoms of autoimmune diseases may be increased,
- the immune response is suppressed,
- less antibodies form after vaccinations and the vaccination may be unsuccessful.

Due to immunological processes, diseases may also occur with a time delay after exposure, e. g. on holiday.

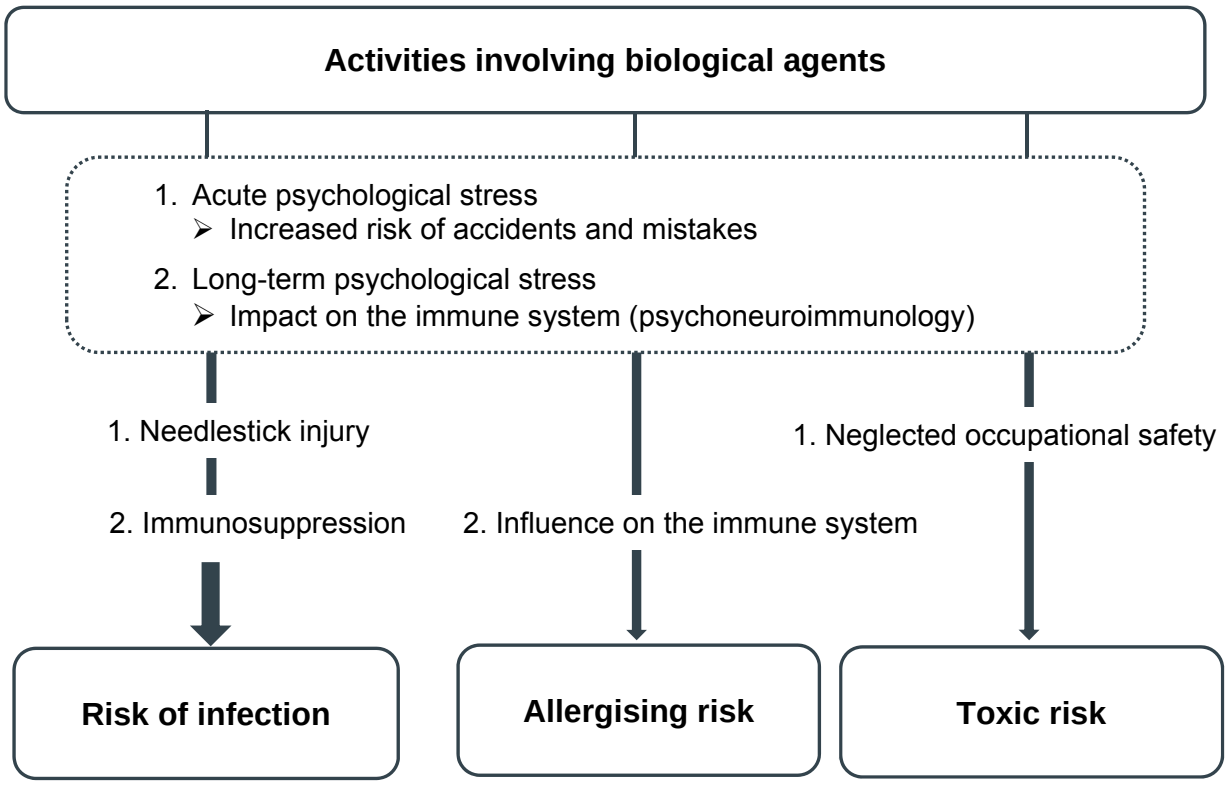

Figure 3: Risks posed by biological agents under the influence of psychological stress

Acute psychological stress may cause symptoms such as fatigue, decreased alertness and mental exhaustion. These symptoms may lead to accidents such as needlestick injuries or neglected occupational safety, e. g. not wearing respiratory protection. The risk of infection and the toxic risk are increased.

Long-term psychological stress can change the immune system. The resulting immunosuppression increases the risk of infection.

In addition, the change of the immune system may increase the sensitivity to allergens and the severity of allergic symptoms may increase.

6.2 Determining psychological stress factors

The psychological stress factors which are relevant for the risk assessment according to *BioStoffV* may occur in connection with work organisation, work environment including work equipment, work task and professional social relations.

To determine the psychological stress factors, observation and interviews, employee surveys and moderated analysis workshops are possible methods. In addition, the analysis of near misses, sick leave, analyses by accident insurance institutions and insights from preventive occupational healthcare may be used (see appendix 6).

7. Summarising assessment as a basis for protective measures

(1) When protective measures are determined, all existing risks posed by biological agents including the psychological stress factors of activities involving biological agents must be taken into account. The individual required protective measures must be brought together in an overall concept. The measures regarding psychological stress may affect work organisation, work environment, work task and social interactions.

(2) The summarising assessment is to be performed at the protective measure level. If there are higher requirements for protective measures due to the infection risk than due to the sensitising/toxic effect, for example, the requirements based on the higher risk are applicable.

(3) The protective measures taken due to different risks must not limit or impede each other in their effectiveness.

8. Effectiveness testing

(1) The testing of the effectiveness of the implemented protective measures is an integral part of the risk assessment. In addition to the inspection of structural and technical protective measures, it also includes the inspection of organisational and personal protective measures.

(2) It is to be determined how and at what intervals the effectiveness testing of the protective measures will be performed. With technical protective measures, the function is to be checked regularly and the effectiveness at least once every two years according to section 8 paragraph 6 *BioStoffV*. The result and the date of the effectiveness testing are to be documented.

(3) A review of the protective measures will be required if there is evidence for a lack of effectiveness. Evidence includes for example accidents, the occurrence of diseases or cross contaminations (e. g. in laboratories) or is based on indications of non-compliance with organisational or personal protective measures.

(4) The effectiveness testing must be in line with the aim of the protective measures. Examples are the intended reduction respectively minimisation of injuries through the use of safe work equipment, the minimisation of exposure to airborne biological agents, the compliance with hygiene provisions or the correct use of personal protective equipment.

(5) An effective minimisation of the exposure can be assumed if “high” risk levels are reduced by at least one level or a “very high” risk level is reduced by at least two levels according to number 5.4.2 (see also number 5.5).

(6) If a Technical Control Value (TCV) was specified for certain work areas, work methods or systems in accordance with TRBA 405 “*Anwendung von Messverfahren und technischen Kontrollwerten für luftgetragene Biologische Arbeitsstoffe*” [Application of measurement methods and technical control values for airborne biological agents], this value is to be used for the effectiveness testing of the corresponding technical protective measures.

(7) If no TCV has been specified, the effectiveness of the technical protective measures is to be tested by checking the target parameters which were used as a reference. In the case of ventilation systems, these parameters include

- incoming flow velocity,
- detection speed,
- detection air flow.

Information which can be used for effectiveness testing can be found in the manufacturers’ specifications for the correct operation of systems or equipment or can be obtained from the manufacturers.

(8) Whether protective measures are effective can also be checked by measuring relevant parameters. Depending on the work area, these parameters may include the concentrations of relevant biological agents or defined indicators in the air which can be detected using standardised measurement procedures.

(9) In addition to the correct selection, the effectiveness of personal protective equipment also depends on the correct use.

9. Documentation

(1) According to section 8 *BioStoffV* in conjunction with section 6 paragraph 1 of the German Occupational Safety and Health Act, the employer has to document the risk assessment and submit it to the competent authority on request.

(2) The assessment must be performed and documented in a way that ensures that the decisions made are comprehensible.

(3) The documents must a least show:

- time and persons who participated in the risk assessment,
- verification of the professional expertise in accordance with TRBA 200,
- for which concrete activities the risk assessment was performed,
- the underlying information on the frequency of activities, the duration and level of exposure and, if applicable, additional stress factors (e. g. heavy physical work, high microbial contamination of the material),
- issues on which no sufficient information could be determined,
- the result of the risk assessment,

- the defined protective measures and, if applicable, the preventive occupational healthcare measures,
- explanations, if there are deviations from the Technical Rules,
- explanations why there are deviations from the order of the protective measures,
- the result and date of the effectiveness testing of the protective measures,
- the result of the regular and, if applicable, event-based repetition of the risk assessment.

(4) The documents also include the list of biological agents in accordance with section 7 paragraph 2 *BioStoffV*. For specific activities, the biological agents used are to be listed. For non-specific activities and non-protection level activities, the list must at least contain the biological agents or groups of biological agents (e. g. mould fungi) which are likely to occur and which significantly determine the risk of the activity (see example).

List of biological agents (example from forestry)					
Serial no.	Biological agent	Risk group	Transmission route Absorption path* * if known	Type of effect i=infectious s=sensitising t=toxic	Material
	Bacteria:				
	Borrelia burgdorferi	2	parenteral	i	Ticks
	Chlamydophila psittaci	3	airborne	i	Bird droppings
	Clostridium tetani	2	parenteral	i	Soil
	Sporothrix schenkii	2	parenteral	i	Wood splinters, plant thorns
	Viruses:				
	Central European tick-borne encephalitis (TBE-Eu)	3(**)	parenteral	i	Ticks
	Hantaviruses	2/3	airborne	i	Rodent droppings
	Lyssaviruses (rabies)	3(**)	parenteral / airborne	i	Infected animals
	Fungi:				
	Mould fungi	1 (2)	inhalative	s, t	Soil, plant material
	Parasites:				
	Echinococcus multilocularis	3(**)	oral	i	Contaminated berries and mushrooms

(5) For activities of protection level 3 or 4, the employer also has to keep a list of the employees who perform these activities. The list has to include the type of activities, the occurring or handled biological agents as well as accidents and operational disruptions. In relation to persons, this list has to be stored for at least 10 years after completion of the activity according to section 7 paragraph 3 *BioStoffV*. The employees are to be informed about the information which concerns them, and the protection of personal data must be ensured. If the employment relationship ends, the employee will receive a copy of the data concerning them.

The verification of the submission of this copy is to be filed by the employer like personnel documents.

(6) The form of documentation can be determined by the employer. Industry-specific guidelines or checklists may also be used as a basis.

(7) If only activities involving biological agents of risk group 1 without sensitising or toxic effects are performed, the following may be omitted in the documentation:

- the result of the substitution check (section 4 paragraph 3 number 4 *BioStoffV*) and
- the explanation if there are deviations from the state of the art or the insights published by the Committee for Biological Agents (*ABAS*) (section 19 paragraph 4 number 1 BioStoffV).

10. Operating instructions, briefing and general occupational health counselling

(1) For activities involving biological agents of risk groups 2 to 4, the employer has to issue written operating instructions based on the risk assessment prior to the start of the activity according to section 4 *BioStoffV*. Operating instructions are also required for activities involving biological agents of risk group 1 with sensitising or toxic effect. The main contents of the operating instructions are described in section 14 paragraph 1 *BioStoffV*. If the risk assessment needs to be updated, the operating instructions have to be amended accordingly.

Note: *For sample operating instructions, refer to DGUV Information 213-016 [2].*

(2) Based on the respective current version of the operating instructions, the employer has to inform the employees orally and in relation to their specific workplace about the risks occurring and the applicable protective measures before the start of employment and then at least once a year. Content and time of the instruction are to be documented in writing and have to be confirmed by the signature of the instructed employees.

(3) If employees of other employers (third-party companies) work at the company, it must be ensured that these employees are also instructed regarding possible risks and required protective measures. This must be ensured based on the duty of cooperation of several employers (see number 3.1 paragraph 3).

Note: *Often, the commissioned third-party company performs the general instruction of their employees while the specific instruction on the conditions on site is performed by the persons responsible of the ordering company. The corresponding employers must coordinate the content of the instructions.*

(4) The instruction is to be performed so that the employees develop awareness for safety. In addition to conveying know-how on work procedures, risks and protective measures in the instruction (knowledge) and conveying adequate skills and protective measures (competence), an awareness for the safety of employees is to be developed (motivation). They have to be motivated to always work safely. This can be achieved e. g. by involving them in the preparation of risk assessments or actively involving them during instructions and tutorials.
In this way, occupational health and safety play an important role in the company culture. Here, the documented and communicated objectives, such as written rules and organisa-

tional structure, as well as clear standards and values are important basic factors. They must be comprehensible for the employees.
The value concept is only as good as its implementation and the compliance with it. Only if superiors implement and live these defined values and measures every day, can they serve as a role model for their employees.
To the same extent, deviations from this behaviour not only have to be defined but also communicated. Employees have to be informed about consequences and their implementation, i. e. sanctions or rewards. This is possible in a trusting communication in which deviations can be discussed openly.

(5) As part of the instruction, a general occupational health counselling has to be performed including information on any specific risks, e. g. in case of reduced immune response. By improving the employees’ knowledge regarding possible health effects of their activities, the reasonable use of the instrument of preventive occupational healthcare is supported.

Employees must be informed in particular about

- their right to preventive occupational healthcare and/or its type and extent (mandatory, optional and elective healthcare) including possible vaccinations,
- possible activity-related health risks due to handled and/or occurring biological agents, in particular regarding
  - transmission routes and/or absorption paths,
  - possible disorders and symptoms,
  - medical factors which may lead to an increased risk (e. g. reduced immune response) and
- first aid measures and, if necessary, post-exposure prophylaxis,
- early symptoms of infections and allergic and/or toxic diseases relating to the workplace,
- activity-related information which should be provided to the attending physician in case of symptoms – even if these symptoms occur with delay after completion of the activity (e. g. extrinsic allergic alveolitis).

The physician who has been commissioned with the preventive occupational healthcare has to participate in the occupational health counselling. “Participate” does not necessarily mean that the physician personally provides the entire counselling. The requirement to involve the physician may also be fulfilled by training persons to perform the instruction or by participating in the preparation of suitable instruction material.

11. References

[1] *Kriterien zur Auswahl der PSA bei Gefährdungen durch biologische Arbeitsstoffe* [PPE selection criteria for risks posed by biological agents]. Resolution 45/2011 of ABAS dated 05/12/2011 (www.baua.de/abas)

[2] DGUV Information 213-016 – *Betriebsanweisungen nach der Biostoffverordnung* [Operating instructions according to the Biological Agents Ordinance]

[3] *Irritativ-toxische Wirkung von luftgetragenen biologischen Arbeitsstoffen am Beispiel der Endotoxine* [Irritative-toxic effect of airborne biological agents using endotoxins as an example]. BAuA report, 6/2005

[4] *Bedeutung von Mykotoxinen im Rahmen der arbeitsplatzbezogenen Gefährdungsbeurteilung* [Importance of mycotoxins for the workplace-related risk assessment]. BAuA assessment report, 6/2007

[5] *Verfahren zur Bestimmung der Schimmelpilzkonzentration in der Luft am Arbeitsplatz (Kennzahl 9420)* [Methods to determine the concentration of mould fungi in the workplace air (number 9420)]. In: *IFA-Arbeitsmappe Messung von Gefahrstoffen* [IFA work folder on the measurement of hazardous substances]. 30st edition IV/03. Published by: Deutsche Gesetzliche Unfallversicherung (DGUV), Berlin. Berlin: Erich Schmidt 1989 – loose-leaf edition www.ifa-arbeitsmappedigital.de/9420

[6] *Verfahren zur Bestimmung der Bakterienkonzentration in der Luft am Arbeitsplatz (Kennzahl 9430)* [Methods to determine the concentration of bacteria in the workplace air (number 9430)]. In: *IFA-Arbeitsmappe Messung von Gefahrstoffen* [IFA work folder on the measurement of hazardous substances]. 32nd edition IV/04. Published by: Deutsche Gesetzliche Unfallversicherung (DGUV), Berlin. Berlin: Erich Schmidt 1989 – loose-leaf edition www.ifa-arbeitsmappedigital.de/9430

[7] *Verfahren zur Bestimmung der Endotoxinkonzentration in der Luft am Arbeitsplatz (Kennzahl 9450)* [Method to determine the concentration of endotoxins in the workplace air (number 9450)]. In: *IFA-Arbeitsmappe Messung von Gefahrstoffen* [IFA work folder on the measurement of hazardous substances]. 28. edition IV/02. Published by: Deutsche Gesetzliche Unfallversicherung (DGUV), Berlin. Berlin: Erich Schmidt 1989 – loose-leaf edition www.ifa-arbeitsmappedigital.de/9450

[8] Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. J Psychosom Res 2002; 53: 865–871

[9] Cole SW, Sood AK. Molecular pathways: beta-adrenergic signaling in cancer. Clin Cancer Res 2012; 18: 1201−1206

[10] Dhabhar FS. Effects of stress on immune function: the good, the bad, and the beautiful. Immunol Res 2014; 58: 193−210

[11] Tracey KJ. The inflammatory reflex. Nature 2002; 420: 853−859

[12] Schubert, C. . *Psychoneuroimmunologie und Psychotherapie* [Psychoneuroimmunology and psychotherapy]. Schattauer Verlag, 2015, ISBN 978-3-7945-3046-5.

[13] Nicolaides NC, Kyratzi E, Lamprokostopoulou A et al. Stress, the stress system and the role of glucocorticoids. Neuroimmunomodulation 2015; 22: 6-19

[14] Van Houdenhove B, Van Den Eede F, Luyten P. Does hypothalamic-pituitary-adrenal axis hypo-function in chronic fatigue syndrome reflect a „crash“ in the stress system? Med Hypotheses 2009; 72: 701-705

[15] Cohen S, Janicki-Deverts D, Doyle WJ et al. Chronic stress, glucocorticoid receptor resistance, inflammation, and disease risk. Proc Natl Acad Sci USA2012; 109: 5995−5999

[16] Morag, M.; Morag, A.; Reichenberg, A.; Lerer, B.; Yirmiya. R. (1999) Psychological variables as predictors of rubella antibody titers and fatigue - a prospective, double blind study. In: J Psychiatr Res. 33, S. 389–395.

[17] Miyazaki, T.; Ishilkawa, S.; Natata, A. et al. (2005) Association between perceived social support and Th1 dominance. In: Biol Psychology. 70, S. 30–37.

[18] iga Report 31 – *Risikobereiche für psychische Belastungen* [Risk areas for psychological stress]

[19] Praxis zkm 2013 – *Psychoneuroimmunologie und Infektanfälligkeit* [Psychoneuroimmunology and susceptibility to infection]

[20] UGBforum 6/14 – *Kein Körper ohne Seele* [No body without soul]

As a further source of information, the following can be used:

- Technical Rules for Biological Agents
  (see www.baua.de/trba)
- branch- or activity-specific guidelines (e. g. rules and information by the German Federal States or accident insurance institutions)
- GESTIS biological agent database
  (see www.dguv.de/ifa/gestis-biostoffe)

Information on pathogens causing infectious diseases at a national level is provided by

- Robert Koch-Institute (RKI) and
- Friedrich-Loeffler-Institute (FLI).

The risk of infection may differ depending on the region. Current information on the epidemiological situation of individual pathogens is also provided online, in particular on the homepages of Robert Koch-Institute and Friedrich-Loeffler-Institute.

For many work areas in which activities involving biological agents are performed, experiences and branch-specific guidelines already exist and can be used for a risk assessment. Cross-company information sources are available in addition to the sources of information described in paragraph 1, for example

- information provided by associations, chambers, etc., and
- other freely accessible, specialised literature.

For a summary of relevant questions on information search, see appendix 5.

- information on the consideration of psychological stress: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (ed.) (2014) *Gefährdungsbeurteilung psychischer Belastung, Erfahrungen und Empfehlungen* [Risk assessment of psychological stress, experiences and recommendations], 1st edition, Erich Schmidt Verlag, ISBN 978-3-503-15439-5.
- *Empfehlungen zur Umsetzung der Gefährdungsbeurteilung psychischer Belastung* [Recommendations on performing a risk assessment of psychological stress], version

from 27/06/2014 and 2nd amended edition, published by Leitung des GDA-Arbeitsprogramms Psyche c/o Bundesministerium für Arbeit und Soziales

- *Konzept zur Ermittlung psychischer Fehlbelastungen am Arbeitsplatz und zu Möglichkeiten der Prävention* [Concept for determining psychological stress at the workplace and possibilities for prevention], LV 28, 10/06/2002, published by: Länderausschuss für Arbeitsschutz und Sicherheitstechnik
- Schedlowski, M.; Tewes, U.: *Psychoneuroimmunologie* [Psychoneuroimmunology], 1996, Spektrum Akademischer Verlag 1996, ISBN 3-86025-228-3.
- *Psychische und psychosomatische Gesundheit in der Arbeit* [Psychological and psychosomatic health at work], 2014, published by: Angerer, Glaser, Gündel, Henningsen, Lahmann, Letzel, Nowak
- *Psychosoziale Gesundheit* [Psychosocial health at work], 2007 1st edition, published by: Prof. Dr. med. habil. Andreas Weber and Prof. Dr. med. Dr. phil. Dr. rer. soc. Dipl. Psych. Georg Hörmann
- The immune system as the sixth sense, 2005, J. E. Blalock

Appendix 1: General information on biological agents and their risks

Part 1: Information on the risks of infection

(1) Biological agents are classified into risk groups 1 – 4 according to the risk of infection they pose where among other things their pathogenicity, the severity of the disease and the prevention and/or treatment options are important criteria (see also TRBA 450). The classification of biological agents in risk groups is solely derived from their effect on a healthy human being. Only few mould fungi have an infectious potential which mainly affects immunocompromised employees. Sensitising and toxic effects are not taken into account for the classification.

(2) Depending on the entry passage, the following transmission routes for infectious agents are differentiated

- **airborne** (transmitted through the air): by inhaling air which contains pathogens or contact of airborne pathogens with the mucous membranes of the upper respiratory tract;
- **percutaneous** (via the skin): through direct or indirect contact with injured or intact skin or mucous membrane;
- **oral** (via the mouth): by ingestion;
- **parenteral** (via injuries): e. g. through needlestick injuries and cuts or bites, scratches, insect bites.

If applicable, several transmission routes may apply (see appendix 1 part 4).

(3) In addition to EU legal classifications, the Technical Rules for Biological Agents TRBA 460 – 466 contain additional national classifications of biological agents into risk groups, among other things classifications into risk group 1 as well as additional information, e. g. on the zoonotic potential or on sensitising and toxic properties:

- TRBA 460 “*Einstufung von Pilzen in Risikogruppen*” [Classification of fungi into risk groups]
- TRBA 462 “*Einstufung von Viren in Risikogruppen*” [Classification of viruses into risk groups]
- TRBA 464 “*Einstufung von Parasiten in Risikogruppen*” [Classification of parasites into risk groups]
- TRBA 466 *“Einstufung von Prokaryonten (Bacteria und Archaea) in Risikogruppen”* [Classification of prokaryotes (bacteria and archaea) into risk groups]

Note: *TRBA 468 “Liste der Zelllinien und Tätigkeiten mit Zellkulturen“ [List of cell lines and activities involving cell cultures] provides a classification of cell cultures.*

(4) Information on the occurrence of infectious agents can be found in the Technical Rules for Biological Agents and specific documents by the German Federal States or accident insurance institutions (see appendix 1 part 4). For a non-exhaustive list with information on the occurrence of infectious agents in various industries and various activities, see appendix 3.

(5) It can be assumed that the risk of infection always increases with the extent (duration, frequency and level) of exposure. It must be noted, however, that a one-time contact may be sufficient to cause an infection. The occurrence of infectious biological agents, however, does not necessarily mean that an infectious disease will occur. Even a colonisation of the

body does not necessarily lead to an infection. The interaction of many factors is required, for example infection potential, transmission route, concentration and physical condition of the persons exposed (e. g. immunity due to vaccinations).

(6) In the environment, e. g. in the air, the soil and in the water, biological agents of risk groups 1 and 2 naturally occur. For healthy persons, contact with these biological agents usually does not pose a risk of infection; if the immune response is reduced, however, or in case of injuries, infections may occur.

Part 2: Information on the sensitising effect

(1) Sensitisation means the increase in the sensitivity of the immune system to an exogenous substance (allergen). If the allergen contact is repeated, an allergic disease may occur.

(2) Biological agents with sensitising effect are mainly fungi (pritargemarily mould fungi) as well as some parasites. For bacteria, except thermophilic actinomycetes, information on a sensitising potential is only available for a few species and is primarily based on individual case descriptions or low case numbers. Even non-viable bacteria, mould fungi (dead cells, parts of spores) and parasites or their components (e. g. proteins) may lead to sensitisations or allergic respiratory diseases. Regarding the sensitising potential, the risk assessment does not need to differentiate between the individual species. Viruses do not have a known sensitising potential. The sensitising effect is independent of the classification into risk groups.

(3) Experience shows that only a long-term exposure to respiratory tract sensitising biological agents at high concentrations leads to a sensitisation or even severe allergic diseases.

(4) An exposure to airborne mould fungi is unlikely to cause an allergic skin reaction.

(5) In aqueous media, the growth of mould fungi is limited; a possible sensitisation therefore does only play a minor role or no role at all.

(6) For additional information on the sensitising potential of biological agents, refer to TRBA 460 “*Einstufung von Pilzen in Risikogruppen*” [Classification of fungi into risk groups] and TRBA 464 “*Einstufung von Parasiten in Risikogruppen*” [Classification of parasites into risk groups]. Further information can be found in TRBA/TRGS 406 “*Sensibilisierende Stoffe für die Atemwege”* [Respiratory tract sensitising agents].

Part 3: Information on the toxic effect of biological agents

(1) Toxic effects may be caused by cell wall components and metabolic products of bacteria and fungi. They can, for example, be absorbed via the respiratory tract bonded to airborne particles and have acute as well as chronic effects.

(2) Examples for toxic cell wall components are endotoxins or beta-1,3-D-glucans which are cell wall components of gram-negative bacteria or fungi and can cause inflammation of the mucous membranes, fever, toxic pneumonitis and chronic bronchitis. Cell wall components are released especially during the decay of dead bacteria and fungi.

(3) Examples for toxic metabolic products are mould fungi toxins, so-called mycotoxins. Mycotoxins are released by numerous types of mould fungi as secondary metabolic products depending on the habitat conditions.

(4) For detailed information on endotoxins and mycotoxins, please refer to the ABAS assessment reports [3, 4].

Part 4: Overview of transmission routes and absorption paths

Transmission route	Examples	Risks		
		infectious	toxic	sensitising
via the air	Absorption of bioaerosols by inhalation	+[1]	+	+
	Absorption of bioaerosols via the mucous membrane of mouth, pharynx, nose or the conjunctiva of the eye or injured skin, e. g. eczema, attrition dermatosis, neurodermatitis	+	+[2]	-
via the mouth	Touching the mouth with dirty hands/gloves, objects	+	-	-
	Ingestion; also of nose/pharyngeal secretion	+	-	-
via direct contact with skin or mucous membrane	Splashes, contact with mucous membrane of mouth, pharynx, nose, the conjunctiva of the eye or contact with injured skin, e. g. eczema, attrition dermatosis, neurodermatitis	+	+	-
through injuries	Absorption via cuts, needlestick injuries/stings (e. g. insect bites) or bite wounds	+	+	-

+ Relevant for occupational health and safety

- Not relevant for occupational health and safety

[1] Infections caused by fungi only in case of a severely weakened immune system (e. g. chemotherapy); usually not relevant for occupational health and safety.

[2] An exposure to airborne endotoxins may lead to toxic effects on the mucous membranes. A toxic effect on intact or injured skin is not known.

Appendix 2: The exposure level concept

For the assessment of the exposure to airborne biological agents, no health-based limit values exist. To be able to assess the level of airborne exposure anyway, the workplace concentrations are compared to the average concentrations in the ambient air. For mould fungi, the annual average background concentration in the ambient air is around 1,500 cfu (colony-forming units)/m³ [5]. At workplaces, mould fungi concentrations of $>10^9$ cfu/m³ may occur depending on the activity.

For endotoxins, the annual average ambient air concentration is 7 EU (endotoxin units)/m³ [6]. Depending on the activity, endotoxin concentrations up to 10^5 EU/m³ may occur.

Based on the comparison with the ambient air concentration, it can be determined whether the concentration at the workplace is increased, high or very high in relation to the ambient air. A health-based statement cannot be derived.

The concentrations of biological agents at the workplace and in the natural ambient air are subject to fluctuations. According to the convention, a significant difference is only assumed if two measured values differ by one power. This means that the lowest exposure level starts only at a concentration which after rounding up is one power above the natural ambient air concentration.

Applicability of the exposure level concept to other sensitising or toxic biological agents

The concept of exposure levels for assessing the level of a sensitising and toxic exposure on the basis of measured data can be applied to other biological agents than mould fungi and endotoxins with the following preconditions:

- The measured data are collected using generally accepted and standardised measurement methods (e. g. published in the IFA work folder).
- The measured data are to be collected using typical activity and workplace conditions. This refers to factors which have an influence on the release of biological agents into the air (see number 5.4.1, letter b).
- To assess the measured data and answer the question whether the concentration is to be classified as increased, high or very high compared to the natural background concentration, the median of the average natural background concentration is used, which is measured over at least a year, taking different seasons into account.

The “increased” exposure level is defined as being at least one decimal power higher than the median of the ambient air concentration. The “high” and “very high” exposure levels are defined in steps of at least one more decimal power in each case.

Appendix 3: Possible occurrence of infectious agents during activities without assigned protection level (not exhaustive)

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
<u>Gardening / forestry</u> - Activities with soil contact (outdoors) - Earthworks raising dust - Contact with wild animals and, if applicable, their excretions (the latter occurs in particular while handling soil) - Activities in low vegetation (risk of tick bites)	Occurring everywhere in soil / forests:				Depending on the type / scope of activity
	Clostridium tetani	2	Tetanus	Percutaneous (contact with injured skin, also with micro lesions)	➤**Existing risk of infection**
	Borrelia burgdorferi	2	Lyme disease	Parenteral (bite of the castor bean tick)	➤**Existing risk of infection**
	Endemic areas: Rabies virus (RABV) / Europ. bat lyssavirus (EBLV)	3 (**) 3 (**)	Rabies Rabies	Parenteral (bite), percutaneous (contact of injured skin / mucous membrane with the saliva of infected animals)	➤**Existing risk of infection** **See TRBA 230**
	Hantaviruses (depending on habitat of infected rodents)	2/3	Various types of diseases, e. g. haemorrhagic fever with renal syndrome	Airborne (inhalation of dusts), parenteral (bites) if applicable	
	Central European tick-borne encephalitis (TBE-Eu)	3 (**)	ESME (early summer meningoencephalitis)	Parenteral (bite of the castor bean tick)	

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
	Echinococcus multilocularis *Echinococcus granulosus*	3 (**) 3 (**)	Echinococcosis	Oral (ingestion with contaminated food, smear infection by close contact with infected animals)	
Waste disposal - Waste collection - Manual sorting	Bacteria, viruses which occur in any kind of waste	RG 1 (RG 2)	--		**➤Negligible risk of infection**
	Possible in waste from households, doctor’s offices, missorting:				With activities involving this kind of waste.
	Faecal germs (e. g. *Escherichia coli* and noroviruses)	2	Diarrhoea	Oral (smear infection)	**➤Existing risk of infection**
	Hepatitis B virus (HBV) or hepatitis C virus (HCV)	3 (**)	Hepatitis B or C	Parenteral (bite or cut injury), percutaneous (contact with injured skin / mucous membrane)	**See TRBA 213, 214**
Outpatient care - Basic care (washing, dental care, support when going to the toilet, etc.)	Faecal germs (e. g. *Escherichia coli* and noroviruses)	2	Diarrhoea	Oral (smear infection)	**➤Existing risk of infection**

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
- Treatment care (bandage changes, injections, catheter insertion, etc.)	Hepatitis B virus (HBV) or hepatitis C virus (HCV)	3 (**)	Hepatitis B or C	Parenteral (needlestick or cut injury), percutaneous (contact with injured skin / mucous membrane)	**See TRBA 250**
- Intensive care (port care, ventilation therapy, etc.)	Human immunodeficiency virus (HIV)	3 (**)	Immunodeficiency (AIDS)	Parenteral (needlestick or cut injury), percutaneous (mucous membrane contact)	
Preschool child care - Changing nappies, accompanying and supporting children when going to the toilet - Managing small wounds, close body contact during care	e. g. - Measles virus - Mumps virus - Rubella virus - Human cytomegalovirus - Varicella zoster virus - Faecal germs - *Bordetella pertussis*	 2 2 2 2 2 2 2	 Measles Mumps Rubella Cytomegaly Chicken pox Diarrhoea Pertussis	 Airborne (droplets) Airborne (droplets) Airborne (droplets), Oral (smear infection), percutaneous Airborne (droplets), smear infection Oral (smear infection) Airborne (droplets)	➤**Existing risk of infection** (depending on diseases occurring at the facility)
Activities involving contact with waste water (e. g. purification of household waste	*Escherichia coli* Enteritis salmonellae	2 2	Diarrhoea Diarrhoea	Oral (smear infection) Oral (smear infection)	➤**Existing risk of infection**

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
water)	Hepatitis A virus (HAV)	2	Hepatitis A	Oral (smear infection)	**See TRBA 220**
	Rotaviruses	2	Diarrhoea	Oral (smear infection)	
	Noroviruses	2	Diarrhoea	Oral (smear infection)	
	Hepatitis B virus (HBV) (*little relevance*)	3 (**)	Hepatitis B	Parenteral (needlestick or cut injury), percutaneous (contact with injured skin / mucous membrane)	
	Adenoviruses	2	Diseases of the respiratory system, conjunctivitis, diarrhoea	Airborne	
	Giardia lamblia	2	Diarrhoea	Oral (smear infection, ingestion with food)	
	Entamoeba histolytica	2	Amoebic dysentery	Oral (smear infection, ingestion with food)	
	Ascaris lumbricoides (roundworm)	2	Roundworm infection	Oral (smear infection, ingestion with food)	
<u>Removal of pigeon droppings</u>	*Chlamydophila psittaci*	3	Ornithosis	Airborne and percutaneous (direct contact with feathers, droppings and respiratory secretions)	➢**Existing risk of infection** **See “*Gesundheitsgefähr-***

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
	Campylobacter spp.	2	Campylobacteriosis (diarrhoea)	Oral (contact with faeces, smear infection, ingestion with food)	***dungen durch Taubenkot* [Health risks caused by pigeon droppings]” – Instruction manual for risk assessments by BG BAU**
	Salmonella spp.	2	Diarrhoea	Percutaneous (smear infection)	
	Yersinia spp.	2	Diarrhoea	Percutaneous (smear infection)	
	Mycobacterium avium	2	Pneumonia	Airborne	
	Cryptococcus neoformans	2	Cryptococcosis (pulmonary mycosis)	Airborne	
<u>Animal keeping</u> - Cleaning work (in particular with aerosol formation)	*Chlamydophila psittaci* (poultry)	3	Ornithosis	Airborne, percutaneous (direct contact with feathers, droppings and respiratory secretions)	**➢Existing risk of infection**
- Caging up / capturing animals	*Coxiella burnetii* (sheep, goats)	3	Q fever	Airborne, oral, parenteral (tick bite)	**See TRBA 230**
- Inspection rounds	*Trichophyton* spp. (horses, sheep, cattle)	2	Dermatophyte	Percutaneous	
- Examination / Treatment of sick animals	*Escherichia coli*	2	Diarrhoea	Oral (smear infection, ingestion with food)	**➢Particular risk of infection** (e. g. during a bird flu outbreak caused by H5N1 in poultry keeping)
	Salmonella spp.	2	Diarrhoea	Oral (smear infection, ingestion	

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
				with food)	
	Brucella spp. (rare)	3	Brucellosis	Airborne, oral	**See ABAS resolution 608**
	Leptospira spp. (rare)	2	Leptospirosis	Percutaneous (contact with injured skin / mucous membrane), air-borne, oral	
	Other zoonosis pathogens depending on the epidemiological situation				
<u>Recovery of dead wild birds</u> with suspected bird flu infection - Capturing and culling animals with suspected infection in poultry keeping (high aerosol development during herding up, capturing and killing) - Subsequent cleaning work	Highly pathogenic avian influenza virus A, subtypes H5 and H7	3	Bird flu	Airborne, oral (smear infection)	➢**Particular risk of infection** **See ABAS resolution 608**

Work area / Activity	Infectious agent	Risk group	Disease	Transmission routes	Assessment
Tannery with suspected occurrence of anthrax spores: - Sampling: contact with contaminated soil - Remediation work, if necessary	*Bacillus anthracis*	3	Splenic fever (skin, lungs, bowel)	Airborne, oral (smear infection), percutaneous (mucous membrane contacts)	➤**Particular risk of infection** **See “*Gefährdungsbeurteilung nach BioStoffV - Tätigkeiten mit Boden sowie bei Grundwasser- und Bodensanierungsarbeiten“* [Risk assessment according to BioStoffV - Activities involving soil as in ground water and soil remediation work] by BG BAU**

Appendix 4: Exposure levels for mould fungi and endotoxins in various work areas

The table is based on an analysis of the MEGA exposure database (measured values on the exposure to hazardous substances at the workplace) by the *Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (DGUV)* and data by the *Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA)*. The data are based on standardised measurement methods and comparable measurement and analysis procedures.

The exposure level (EL) specifications indicate the percentage of analysis values which is within the mentioned exposure level or below the “increased” exposure level.

MOULD FUNGI in industries and work areas	Number of analyses	EL “very high”	EL “high”	EL “increased”	< EL “increased”
	[n]			[%]	
Building restoration					
Sawing, dry	11	100	0	0	0
Waste incineration					
Crane station in waste bunker, general	12	17	83	0	0
Waste bunker, hopper level, general	17	18	82	0	0
Supervisory personnel, managers	13	0	23	77	0
Waste bunker, hopper level, cleaning using brooms	14	29	64	0	7
Waste disposal					
Control room, control centre	10	0	0	100	0

MOULD FUNGI in operating units and work areas (> 30 data sets/operating unit)	Number of analyses	EL “very high”	EL “high”	EL “increased”	< EL “increased”
	[n]			[%]	
Waste collection					
Pressing, general	9	0	0	100	0
Conveying, mechanically, in containers, general	57	0	11	88	2
Disposal	42	0	17	83	0
Composting facilities					
Delivery, picking of foreign material	27	0	22	78	0
Delivery, auger, conveyor belt	9	33	67	0	0
Material processing, general	14	0	7	71	21
Material processing, cabins and control stands	14	0	0	79	21
Recycling					
Packaging material, pressing, general	17	0	82	18	0
Automatic sorting, general	18	0	28	72	0
Cleaning of the material, general	18	17	17	67	0
Bulk goods, open (e. g. bunker)	21	14	14	71	0
Bag opener, automatic	21	10	67	19	5
Paper recycling, manual sorting cabin, central sorting conveyor	18	11	6	83	0
Conveying, automatically, open (e. g. belt, chute), general	24	0	33	63	4
Repair and maintenance, general	18	0	0	89	11
Processing, dry, sorting, manual	34	9	18	65	9
Quality control	36	0	6	69	25
Waste disposal					
Waste loading work	76	11	64	25	0

MOULD FUNGI in operating units and work areas (> 30 data sets/operating unit)	Number of analyses	EL “very high”	EL “high”	EL “increased”	< EL “increased”
	[n]			[%]	
Sorting system					
Processing, dry, classification, general	211	8	11	60	20
Storage activities, manual, open goods	63	5	5	62	29
Pressing, room	54	6	13	65	17
Agriculture					
Cattle farming	68	0	10	6	52
Hollow glassware, production and processing					
Storage, sorting, final check, sorting	15	0	40	60	0
Plastic and plastic foam, processing					
Storage activities, manual, open goods	9	100	0	0	0
Wholesale of textiles					
Conveying, automatically, open, transfer	21	0	0	71	29

Endotoxins in industries and work areas	Number of analyses	EL “very high”	EL “high”	EL “increased”	< EL “increased”
	[n]			[%]	
Spinning and weaving					
Bast fibre spinning, bast fibre cards	21	0	71	29	0
Air-conditioning system (supply air), above breathing height	25	16	12	72	0
Cotton spinning, rotor spinning machine	24	0	17	63	20
Spinning materials, e. g. raw cotton (except asbestos), processing					
Carding, room	11	0	73	27	0
Agriculture					
Cattle farming	48	6	13	57	24
Pig farming	258	22	61	14	3
Wholesale of crops, seeds, feedstuff, fertiliser, milling products					
Storage activities, general	16	25	75	0	0
Silo (bunker), room	15	20	67	13	0
Bulk goods, enclosed (silo)	9	33	67	0	0

Appendix 5: Synopsis of relevant questions for information gathering

To determine	Comments
Which activities are performed?	The activities have to be described in concrete terms. Are manual activities performed? (risk of injury, direct contact, do dusts/aerosols occur?)
Do employees come into contact with biological agents or can biological agents be transferred?	Transmission routes are described in appendix 1, table 1. Several transmission routes and absorption paths may apply.
Which micro-organisms occur and/or are important regarding the risk?	For information, see e. g. TRBA, branch-specific guidelines or other references.
To which risk group are the biological agents assigned?	Assignment to a risk group only if the biological agents are known and significant for the risk. TRBA 460, 462, 464, 466, BGI 631 to BGI 636.
Are there any known sensitising or toxic effects?	Annex III of directive 2000/54/EC and its amending directives, TRBA/TRGS 406.
Where do biological agents occur?	Are the work steps performed inside devices (enclosed, open, air routing ...)?
Are the materials or products which are handled contaminated with microbes?	Natural raw materials such as crops, spices, straw, etc. have a natural colonisation which is not visible to the eye.
Are there any special regional or epidemiological situations involving the occurrence of specific biological agents?	Examples are the regionally limited occurrence of early summer meningoencephalitis or animal epidemics.
Which activities involve an exposure and/or is the contact with biological agents possible?	Contact includes, for example, direct skin contact or dust deposits on the mucous membranes of the eyes.
Are there any conditions which support the propagation of biological agents?	This particularly includes high humidity.
Is there any contact with animals?	Animals can transfer pathogens, e. g. through bites or scratches. The contact to animal droppings may also be relevant.
How long and frequent is the exposure?	Is there only a rare short-time contact with aerosols when opening a container?
Is any information available regarding the exposure level?	This may include: industry-specific or activity-related analyses (assessments, measurements).
What are the experiences from comparable activities?	Have risk assessments already been performed for comparable activities? Are any industry-specific guidelines by expert committees available?
Have rarely performed activities also been taken into account?	This includes, for example, maintenance, repair and servicing work.
Have any diseases already occurred in connection with the activity in question?	If applicable, contact the competent accident insurance institutions.
Are there any insights from preventive occupational healthcare?	Involve the company physician.
Are any minors, pregnant women or nursing mothers employed?	This group of people may be particularly endangered. (*JArbSchG* [German youth employment protection act], *MuSchG* [German maternity protection act])

Appendix 6: Further information on the consideration of possible effects of psychological stress for the risk assessment of activities involving biological agents

Part 1: Interrelation between psyche and immune system

Acute and chronic stress leaves “biochemical traces” in the immune system. For this purpose, stress can be defined as the adaptation of the human organism to internal and external changes to maintain its biological equilibrium [8].

Acute stress

In the case of an acute physical or psychological stress stimulus which lasts for minutes or hours, the body’s own systems are activated in order to mobilise and enable the organism to adapt to dangers as quickly as possible (fight-or-flight response). This becomes evident, e. g., by an increased respiratory and heart rate, an increased muscle tone and a reduced digestion activity. In addition, the sympathicus (an area of the nervous system) activates the immune reactions via the messengers adrenalin and noradrenalin [9]. In the immune system, a functional adaptation occurs, i. e. a short-term inflammatory reaction, so that it can quickly and effectively react to possible stress-related injuries. This is a protective function of the organism which is essential for survival [8, 10].

Regulation of the immune system

To counteract a permanent increase in the activity of the immune system, which would be dangerous for the organism, the inflammation activity is regulated to a lower level again. This is achieved via feedback loops in the brain (hypothalamic-pituitary-adrenal axis) and the vagus nerve [11]. The cellular activity of the immune system which was briefly out of balance is balanced out again.

Chronic stress

If the described regulation mechanism of the stress system is excessively activated by repeated biological and psycho-social stress situations, increased cortisol levels (hypercortisolism), a permanent reduction of the cellular TH1 immunity and a long-term increase of the humoral TH2 immunity will result [12].

It is a known fact that hypercortisolism and the related TH1/TH2 shift has a damaging effect on the body tissue and is therefore associated with health risks such as increased susceptibility to infection, impaired wound healing, depression, allergies and the development of cancer [8, 12, 13]. The immune function is thus reduced in the long term.

The overstraining of the systems leads to a type of collapse (“crash” [14]) of the functions. As a result, the required amount of cortisol can no longer be provided (hypocortisolism) in case of renewed functional strain, e. g. in a psychological stress situation, or the glucocorticoid receptors no longer appropriately react to cortisol (glucocorticoid resistance [15]). A system which works insufficiently like this is no longer able to efficiently regulate the stress-related increase in inflammations. Permanently increased inflammation parameters (“silent inflammation”) form the basis for increased susceptibility to infections, accelerated ageing and health impairments such as autoimmune diseases (e. g. rheumatism, diabetes), cardiovascular diseases, cancer, depression or asthma [8, 12, 13].

Positive psychological influences on the immune response
Personality traits which lead to a positive attitude towards life correlate with an improved functionality of the immune system.

Self-esteem
A study found that after a rubella infection, the number of antibodies correlates with a higher self-esteem of the patients [16].

Self-efficacy
Self-efficacy means the belief in one’s own ability to successfully perform desired actions based on one’s aptitude. There are similarities to optimism which is the general belief in a good outcome of all things. With self-efficacy, however, the focus is on the belief in one’s own ability to achieve the good outcome.
Studies on this subject are available from the area of HIV research. It was proven that patients with high self-efficacy have a lower concentration of viruses in the blood, a less frequent manifestation of AIDS symptoms and a lower mortality rate.

Social relations
Attachment theory assumes that humans have an innate need to build close relationships to fellow humans which are characterised by intense feelings. Experiencing social support provides respect, personal identity, belonging and security.
Several studies have shown that social support correlates with a high number of natural killer cells (NK cells) and a good equilibrium of various cells which are part of the immune system. In psychologically stressful situations, reliable social relations have a stimulating effect on the immune response [17].

Part 2: Harmful coping strategy

Psychological stress which lasts for an extended period may lead to coping strategies which are harmful to health. Examples include increased nicotine, alcohol and drug use, insufficient sleep hygiene and an unhealthy eating behaviour. Effects and side effects of drugs or medicine may directly lead to deficits in concentration and awareness. The same is true for excessive alcohol intake, insufficient sleep or fluctuating blood sugar. This may result in an increased risk of accidents and mistakes with the consequence of an infection.

Part 3: Health problems without immediate connection to biological agents

There is evidence that stress constellations such as high work intensity with little freedom of action, overtime and shift work can lead to cardiovascular diseases and/or type 2 diabetes. Role stress, insecurity and long working hours can cause depression. Musculoskeletal diseases and reproductive disorders may be the result of work-related psychological stress [18].

Part 4: Methods to determine psychological stress factors

To determine psychological stress factors, three main methodological approaches may be applied. It is to be ensured that the determination of these factors is performed in a professional manner.

1. Observation/Observational interview

Trained persons assess the psychological stress based on observations which are usually supplemented by short interviews with the employees. The questions the employees are asked directly relate to their experience.

2. Standardised written employee surveys
   Assessments by employees are obtained using a standardised questionnaire. The questionnaires include questions regarding the existence, frequency and intensity of the perceived psychological stress factors.
3. Moderated analysis workshops
   The psychological stress factors are determined in a moderated discussion and communication process. The knowledge which is based on the experience of employees and managers as well as the knowledge of the experts is used.

The selection of the applied method depends on the operational conditions. If required, several methods are to be combined.

Part 5: Psychological stress factors

1. Psychological stress factors due to work organisation

Stress factors due to work organisation include in particular

- working hours which are not adapted to the stress level and dependency on cycle times (changing and long working hours, no limitation of particularly stressful activities which may lead to fatigue and reduced alertness),
- inappropriately organised shift work,
- night work,
- no sufficient and timely compensatory time off,
- inappropriate or missing break organisation,
- no separation of work and leisure time (constant availability),
- time, performance and deadline pressure,
- multitasking,
- insufficient number of employees.

Further stress factors are in particular missing or insufficient

- communication (no sharing of experiences with colleagues and superiors, e. g. feedback processes for clarification of responsibilities or timely provision of information),
- Introduction of new work equipment or work methods.

Example: Time pressure as a psychological stress factor in the emergency service

Working in the emergency service involves a number of psychological stress factors even if the work procedures are well organised and a sufficient number of qualified personnel is available.
Punctures for blood samples, the insertion of ports and reanimation with potential exposure to biological agents count among the routine tasks in the rescue service. Unforeseeable and uncontrollable workload peaks which require quick reactions as well as high emotional strain

are normal. This can lead e. g. to fatigue or negligence of protective measures. Under these conditions, the risk of injury when handling pointed or sharp instruments increases. Protective measures include among other things shift planning with sufficient personnel and spare personnel for work peaks, if required, as well as regular training.

Example: Shift work as a psychological stress factor in the healthcare service

There are personal services which have to be provided 24/7. This also includes work areas in which activities involving biological agents are performed. In particular, this concerns the healthcare service. For example, employees in hospitals, paramedics and emergency physicians are affected. Shift work and/or night work as well as on-call duty are the rule, but also excessive working hours frequently occur. In emergencies and when patients require supervision around the clock, blood samples have to be taken and/or therapeutic interventions are required again and again. It is a known fact that the ability of persons to concentrate is significantly reduced at night and in irregular shifts due to the circadian rhythm. The likelihood of errors increases. At the same time, it can be observed that this performance reduction is not sufficiently taken into account for work organisation which means that there may well be a higher workload at the end of the shift prior to the handover. In particular in the area of emergency care and emergency physicians, there is also the risk of traumatising events which leads to a significant increase of the psychological stress and the negligence of hygiene and safety standards with the risk of increased exposure/infection.
Protective measures include among other things shift planning which takes into account the recommendations of occupational research, prevents excessive working hours and ensures sufficient breaks.

2. Psychological stress caused by work content/task

Stress factors are in particular missing and/or insufficient

- qualification for the task (missing and/or insufficient instruction of new, temporary or marginally employed persons, training and briefing),
- information on the biological agents relevant for the task (transmission routes, possible diseases, therapy, protective measures),
- knowledge and training regarding the use of personal protective equipment,
- preparation for dangerous situations,
- varying workload (e. g. unforeseen peak workloads, seasonal peak workload),
- variable work content,
- overstimulation.

Example: Dangerous situations or unusual operational circumstances as a psychological stress factor during activities in a laboratory of protection level 4

In a laboratory of protection level 4, biological agents of risk group 4 are handled. The rooms are entered via a lock system. In addition, externally ventilated personal protective equipment (PPE, here protective coverall) must be worn. Despite intensive training in which unusual operating conditions or dangerous situations are also practised, situations occur in which the employee is exposed to a high level of psychological stress. In case of accidents,

there is always a risk for the employee to be exposed to the biological agent. This may cause fear that such an incident might occur or that a potential exposure might lead to infection. Further stress situations may be due to the fact that if unusual operating conditions occur (e. g. failure of the external breathing air supply), the employee gets the feeling that they will not be able to leave the laboratory in time or will not have the time for decontamination. The unavoidable duty to wear PPE may increase the feeling of working at a high risk and cause fear. Fear and insecurity increase the stress level, can be a permanent psychological stress factor and thereby increase the risk of accidents.

Example: Insufficient communication and information regarding activities involving mouldy objects, e. g. archive material

In archives, mould contamination may occur due to water damage or unsuitable conditions for file/book storage. The knowledge of possible health risks due to mould fungi may be influenced by unprofessional reporting. So-called qualified statements that some types of mould fungi spores can be deadly for humans lead to fear and negative expectations of the affected employees. These negative expectations may cause employees to feel symptoms which were mentioned in the reports. The consequences of negative expectations are referred to as nocebo effects.
Objective information on possible health risks in case of exposure to contaminated archive material and the corresponding protective measures prevent nocebo effects. Effective protective measures protect the employees adequately.

Emotional stress is the experience of very emotional events which cause emotional dissonance (permanently showing the required emotions independent of own feelings) or fear, e. g. as a result of:

- threats of violence by persons (e. g. threats of violence towards employees in law enforcement, social work with drug addicts),
- psychological stress due to known accidents and possible infections,
- colonisation with problematic biological agents (e. g. MRSA in animal keeping, agriculture or the medical area),
- exposure to new, unknown or harmful biological agents,
- planned screenings of employees to search for sources or hygiene errors in outbreak situations.

Example: Emotional dissonance (permanently showing required emotions independent of own feelings)

At a children’s ward, where young children with infectious diseases are treated, children are visited by their relatives. The employees have to instruct the visitors again and again regarding the required hygiene measures for the interaction with their own and the other children. E. g. eating and drinking from the same dishes is as problematic as using the same tissues. The employees are obliged to inform the visitors regarding hygiene. The ignorance of various visitors leads to disappointment, anger and resentment. The permanent requirement to act friendly towards visitors when employees actually feel resentment, anger and disappointment leads to the phenomenon of emotional dissonance. This psychological stress factor can be addressed by training, concretely instructing, briefing and guiding the employees.

Example: Insecurities regarding activities involving a potential Ebola danger in a hospital

At a large outpatient clinic, employees work according to a shift plan which is often drawn up last-minute due to the shortage of personnel.
Some employees work part-time and are not sufficiently qualified and trained. When during recent shifts patients from Africa came to the clinic with unclear fever symptoms, fear of an Ebola infection was spread. This was particularly due to the fact that the instructions in different clinics deviate, sometimes mouth and nose protection and sometimes a closed mask (FFP 2/3) is recommended. Press reporting increases the feeling of insecurity so that some employees fear that the virus is transferred via the air. The specialised press also spreads differing information. Some pictures show employees in protective coveralls. There are press releases which doubt the safety of these protective coveralls. Employees fear that they will get infected by the patients who are infected with the virus, will get sick and might even die. Some employees are not willing to care for the patients. This situation can only be overcome constructively with regular instructions and training. Only if the fears are addressed and a safe routine is in place for putting protective clothing on and taking it off, will a professional and safe management be ensured. It is absolutely necessary that the activities are performed voluntarily.

3. Psychological stress caused by an unsuitable work environment

Stress factors include in particular

- noise,
- straining climate (e. g. greenhouses, agriculture),
- insufficient lighting (e. g. emergency rescue),
- odours of microbial origin (MVOC, e. g. waste management, sewage system),
- personal protective equipment (e. g. protective coveralls, wearing FFP 2/3 masks for an extended period),
- unsuitable work rooms, confined space, interior rooms with locks.

4. Psychological stress due to unfavourable professional social relations

Stress factors include in particular

- lack of leadership,
- missing social support by employers, managers and colleagues,
- social pressure situations,
- conflicts.