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DRAFT TANZANIA STANDARD

Biotechnology - Guidance for the handling, inactivating and testing of waste Part 2: Large-scale process and production

TANZANIA BUREAU OF STANDARDS

0 Foreword

This Tanzania standard supports industrial activities in the area of biotechnology covering operations both non-genetically and genetically modified microorganisms as well as both non-pathogenic and pathogenic microorganisms.

In the implementation of the draft Tanzania Standards, International, national rules, guidelines, safety regulations and instruction manuals for handling microorganisms in all steps of fermentation and downstream processes, as well as those used in environmental biotechnology, should be considered.

During the development of this draft Tanzania standard, assistance was derived from the following document:

- BS EN 12461:1998 *Biotechnology - Large-scale process and production - Guidance for the handling, inactivating and testing of waste*, published by British Standards Institute (BSI).

1 Scope

This Tanzania Standard provides guidance on the selection of procedures for the treatment of waste containing microorganisms, microbial toxins and other biological hazards from biotechnological plants, with the aim of ensuring the safety of both human and the environment.

This Tanzania Standard applies to wastes and effluents (solid, liquid and gaseous) emitted from biotechnological processes, including traditional processes such as brewing or food processing as well as modern processes like, fermentation for pharmaceutical and chemical products, and applications in environmental and agricultural sectors.

This Tanzania Standard for biotechnological processes applies only up to the point where gaseous, liquids and solids are ready for safe transfer to industrial or municipal waste handling units.

This Tanzania Standard is not applicable to the waste from hospitals, nor to the treatment of chemical and physical hazardous waste.

NOTE: Attention is drawn to relevant national regulations

2 Normative References

The following referenced documents are indispensable in the application of this Tanzania standard. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies:

No normative reference for this standards

3 Terms and definitions

For the purposes of this Tanzania standard, the following terms and definitions should apply:

3.1 biohazardous waste

biological waste which can cause a hazard

3.2 cell culture

in vitro growth of cells derived from multicellular organisms

3.3 disinfectant

chemical agent which is able to reduce the number of viable microorganisms

3.4 disinfection

process of reducing the number of viable microorganisms by various physical and chemical methods

3.5 hazard

intrinsic potential property or ability of something (e.g. any agent, equipment, material or process) to cause harm

NOTE Harm is an injury or damage to health of people and/or to the environment.

3.6 microorganism

Any microscopic biological entity, cellular or non-cellular, capable of independent replication or replication within host cell.

3.7 inactivation

partial or full destruction of a given activity up to destruction of the microbiological system **3.8 physical containment**

system for confining a microorganism or organism or other entity within a defined space

3.9 process microorganism

microorganism used for production purposes in a biotechnological process or constituting (part of) the product itself

3.10 sterile

state of being free from viable microorganisms

NOTE 1 In practice, no such absolute statement regarding the absence of viable microorganisms can be proven. However, sterile conditions can be regarded as established by using an accepted or recognized method of sterilization.

NOTE 2 The process of inactivation of viable microorganisms during a sterilization procedure is usually described by an empirical mathematical function, commonly an exponential function. By their mathematical nature, such functions can be reduced to very low numbers, but not to zero. However, these empirical functions can be applied to control or assess the process parameters of a sterilization procedure to realize a desired degree of inactivation of viable microorganisms.

3.11 sterilization

process used to reach a sterile state

3.12 validation

documented procedure for obtaining, recording and interpreting the results needed to show that a process will constantly yield a product complying with predetermined specifications

3.13 verification assay

assay used to determine whether material meets the intended specifications

3.14 waste

by-product arising from a process, or unwanted substance or article derived from any activity

NOTE Examples of waste are scrap material, effluent, unwanted residue or surplus arising from any process or activity, or any substance or article which is discarded or to be disposed of as being broken, contaminated, spoiled, or worn out

4 Waste management

4.1 The production of waste should be minimized and, if possible, the recovery of materials should be attempted. A documented waste management policy should be established, describing the measures for prevention, minimization, segregation, handling, storage, treatment, re-use, transportation and disposal of waste from a large-scale biotechnological process.

4.2 The waste management system and the responsibilities and duties allocated to managers, supervisors and employees should be specified. The arrangements for effective control of biohazardous waste should be integrated with general management and supervisory organization within the production process.

4.3 Documented operational procedures, describing the methods used for effective waste management should be established. These documents should be reviewed at regular intervals and updated, if necessary.

4.4 A description should be given of the methods and procedures for handling, inactivating and treating waste for both normal conditions and deviations.

4.5 Comprehensive information should be provided on the risks to health and safety arising from waste which contains pathogenic microorganisms, together with details of its treatment and the prevention and control measures which are used in normal and emergency procedures. This information should be understandable to technical and non-technical personnel alike.

4.6 The waste management plan, together with the practical arrangements for the control, treatment and disposal for waste, should be subject to a quality assurance and control programme or equivalent systematic monitoring and auditing programme. The quality of the waste management system should be assured by periodic checks and inspections of the various arrangements and procedures. These include operating conditions and control devices of plant and equipment, the composition and characterization of the waste loads, and adherence to approved standard operating procedures. Test and inspection results should be documented, together with details of any action taken to correct deviations from the intended operating conditions. The results and documentation of quality assurance or audit programmes should be submitted to the internal supervising office.

5 Characterization of waste stream

5.1 The following are essential elements, which should be included and documented in a waste management plan:

i) definition of the physical and chemical parameters which can affect the choice of treatment and testing methods, such as the amount of suspended solids or pH;
ii) methods for the segregation of biohazardous waste from non-biohazardous waste at the point of origin, if possible;
iii) methods for the segregation of other categories of waste (such as hazardous chemical or radioactive products) which do not contain microorganisms when there is incompatibility with the biohazardous waste treatment methods.

5.2 A detailed statement should be given of the various activities, processes and the types of waste that are subject to the waste management plan

6 Establishment of waste treatment procedures

The procedures for appropriate treatment of waste steam should be developed. Figure 1 shows the main steps to be considered to guide the choice of waste treatment procedures.

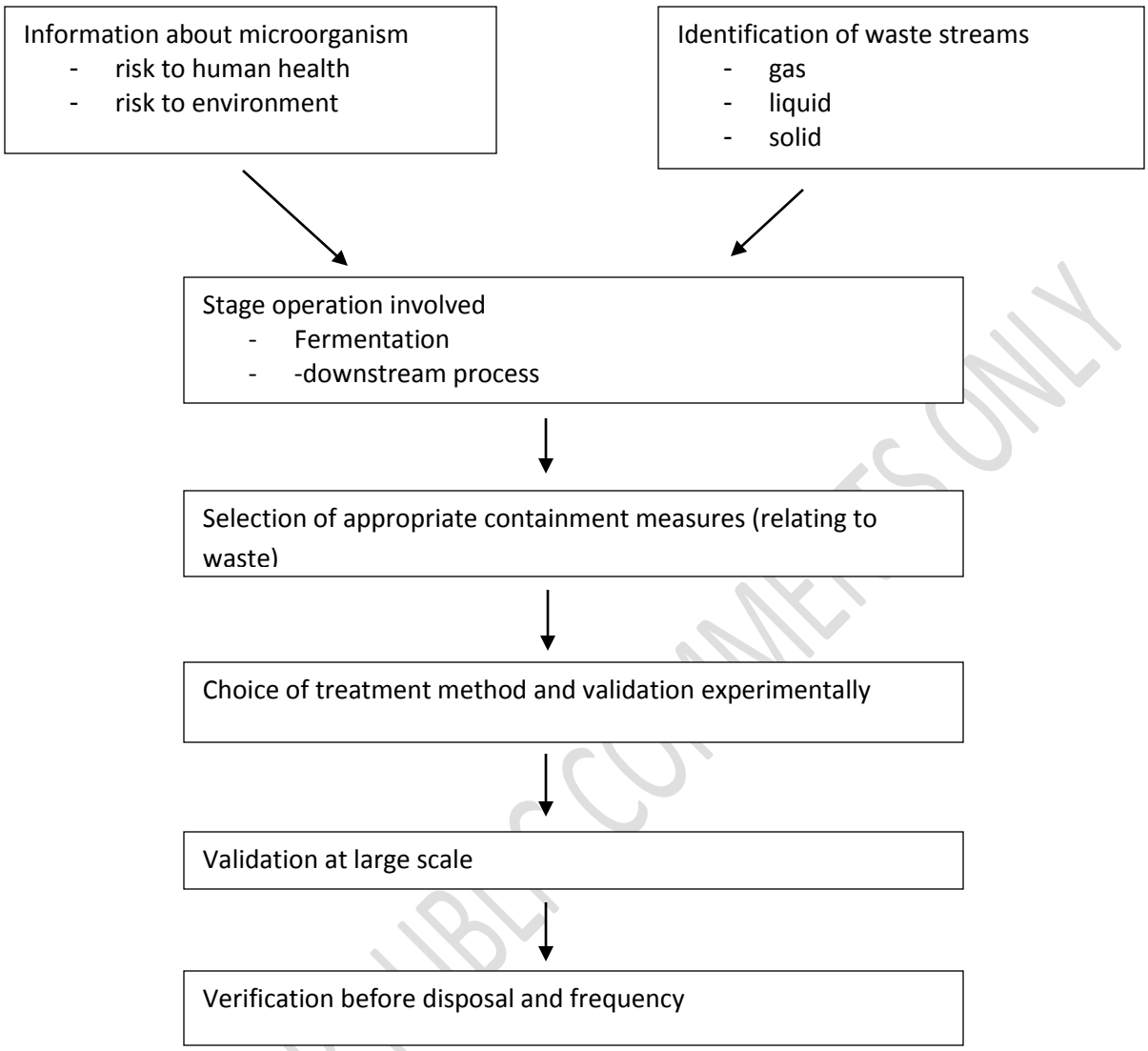

Figure 1: Establishment of procedures

7 Waste treatment methods

7.1 General

7.1.1 The choice of methods should take into account the category of microorganism or biological entity, determined in accordance with national, or international classification rules, the objectives of the treatment (minimize or prevent) and the following criteria:

i) efficiency of the method;
ii) process-specific operation conditions;
iii) interference with other process parameters;
iv) maintenance conditions.

7.1.2 Different methods can be used. The inactivation process, which can combine different methods of treatment, should be validated and documented. Any change relevant to safety in the process should be reviewed, validated as necessary and documented (see Table 1).

Table 1 - Example of waste treatment methods related to the type of waste

Treatment	Type of waste		
	Gas	**Liquid**	**Solid**
Thermal	X[1)]	XXX[3)]	XXX
Chemical	XX[2)]	XX	XX
Irradiation	X	X	X
Incineration	XX	X	XXX
Filtration	XXX	X	N/A[4)]
Biological	X	XX	X

[1)] X possible
[2)] XX appropriate
[3)] XXX recommended
[4)] N/A not applicable

7.2 Thermal treatment

The combination of temperature and time is critical for the effectiveness of the thermal treatment. A number of factors also influence the success of thermal treatment, such as the number and type of microorganisms present, the composition of the liquid and solid phases, the pH value and water activity.

NOTE: Some examples are given as follows:

i) for the majority of non-sporulating process microorganisms, temperatures from 60°C to 70 °C for 10 min to 20 min are usually sufficient;
ii) for most thermo resistant microorganisms in wet conditions (for example sporulating microorganisms), batch procedure at 121°C for 20 min or continuous flow at 140°C for 30 s to 60 s are typical (see annex A);
iii) for gaseous effluent, heated gas mantle is possible.

7.3 Chemical treatment

There is a considerable diversity in the formulation and handling of chemical disinfectants. It is therefore essential to follow the recommendations of the manufacturer.

Examples of disinfectants are sulfuric acid, peracetic acid, sodium hydroxide solution, hypochlorite, formaldehyde, glutaraldehyde and alcohols (e.g. isopropanol, ethanol).

NOTE: Examples of application are given in Table B. of Annex B.

7.4 Irradiation

In special cases, the use of irradiation (e.g. UV radiation) is possible. Combination of time and energy should be considered.

7.5 Incineration

Incineration can be used as a method of waste treatment.

NOTE: Incineration can be heating to more than 600°C or direct burning.

7.6 Filtration

To remove microorganisms from gaseous effluent, filtration is appropriate and can also be used for liquid effluent.

NOTE: The filter will have to be treated to inactivate microorganisms.

7.7 Biological treatment

Biological treatment can be used to minimize the number of process microorganisms in waste from containment level 1 facilities. For higher containment levels, only physical and chemical treatments are recommended.

NOTE: Biological methods can be an anaerobic or aerobic treatment.

8 Risk management

8.1 Risk assessment

Microorganisms are classified with respect to human health and safety, and to hazard to the environment, according to the national, or international classification rules.

A documented risk assessment should be made for the microorganisms and waste treatment process with regard to the general hazards identified. This should be reviewed and revised, if necessary, at the different stages of process design, process implementation and significant process change, and at periodic intervals.

In the case of activities involving exposure to several categories of microorganism, the hazard to environment and human health presented by each microorganism should be considered in preparing the assessment.

8.2 Selection of containment measures

8.2.1 General

Assessment of the microorganism and characterization of the waste stream should allow the appropriate containment measures to be applied (see Table 2). Attention is drawn to relevant national and international regulations.

Table 2 - Physical containment levels for waste from biotechnological processes

Requirements[1)]	Physical containment level			
	1	2	3	4
Treatment of exhaust gases from closed	No[2)]	Minimize release	Prevent release	Prevent release
Containment of spillage with the entire contents of the largest vessel	No	Optional[3)]	Yes[4)]	Yes
Effluent from sinks and showers collected and inactivated before	No	No	Optional	Yes
Treatment of contaminated and/or aborted culture and	No	Minimize release	Prevent release	Prevent release
Treatment of effluent before final discharge	No	Minimize release, case-by-case	Prevent release by inactivation by validated means	Prevent release by inactivation by validated means

1) When using this table, attention is drawn to existing national regulations concerning the requirements area.
2) No: No special requirement for safety.
3) Optional: The extent to which these measures are to be applied should be decided on a case-by-case assessment.
4) Yes: Requirement

8.2.2 Containment level 1

For waste issued from facilities of containment level 1, the principles of good occupational safety and hygiene should be observed. There are no special requirements for dealing with microorganisms at this level.

NOTE 1: Inactivation can be necessary and carried out for purposes other than human health or environment protection; for example, patent confidentiality or quality assurance.

NOTE 2: Waste can be recovered and used as a new product.

8.2.3 Containment level 2

Waste, gaseous, liquid and solid, from facilities of containment level 2 should be treated so as to minimize the release of viable microorganisms. Other national health regulations and environmental protection rules should also be followed.

8.2.4 Containment level 3

8.2.4.1 Waste from facilities of containment of level 3 (including fermentation broth, spillage, waste basins, steam condensate, exhaust gas and biomass) should be treated so as to prevent the release of any viable microorganism.

8.2.4.2 Effluents from sinks and showers should be inactivated before release if appropriate.

8.2.5 Containment level 4

There is currently little experience of procedures performed at this level. Special safety measures should be set case-by-case.

8.3 Verification assays of the treatment

8.3.1 Verification assays should be carried out to ensure that the number of viable microorganisms in a treated waste stream does not exceed specified acceptable levels established by the environmental risk assessment. Appropriate statistical methods should be used to make inferences from these tests, because it is impossible to verify the complete absence of microorganisms. For containment levels 3 and 4, when it is necessary to ensure absence of process microorganisms in the waste stream, this cannot be proven by testing of samples. Instead, validation is crucial.

8.3.2 Validation of any waste treatment process can also involve the periodic checking by verification test for the presence of viable microorganisms in the waste. Where the characteristics of a waste stream can vary, the treatment method should be validated for effectiveness under "worst case" load conditions. The method chosen should indicate the concentration of viable microorganisms remaining in the waste stream after treatment.

NOTE: Different complementary testing methods are available, including the following:

i) growth-related methods:
ii) plaque count;
iii) colony culture most probable number;
iv) non-growth-related methods:
v) microscopy;
vi) biochemical techniques;
vii) immunoassay;
viii) molecular biology techniques.

8.3.3 The choice of methods is not only influenced by the type of waste composition, concentration and kind of microorganism, but also by the methods of treatment.

8.3.4 To monitor the effectiveness of the treatment process, biological, chemical or other usable indicators should be used within a standard or "worst case" waste load.

Annex A

(informative)

Example of a continuous effluent sterilization by a thermal inactivation system

A.1 Continuous sterilization enables:

i) killing of microorganisms;
ii) reduction of cost of effluent treatment when compared to batch sterilization, because of the recovery of the heat in the sterilized effluent.

A.2 The following operations can be required:

i) storage of contaminated effluent in a small buffer tank, where pH adjustment can take place or other additives can be added;
ii) pumping of this fluid towards and through the sterilization unit and the energy recovery system;
iii) sterilization performed at temperatures above120 "C, depending on the holding time in the sterilization unit (for example, 140 "C for 2 min for most microorganisms).

A.3 The holding time at sterilization temperature depends on the flow rate through the system and the fixed volume of the holding tube. In the design, this volume has to be calculated to ensure the holding time necessary to kill the microorganism at the chosen sterilization temperature for the maximum flow rate.

A.4 The contaminated effluent is brought to the sterilization temperature by means of:

i. a heat exchanger where recovery of the heat of the sterilized effluent takes place through heat exchange with the incoming stream of contaminated effluent;
ii. a heater where steam is used to bring the temperature of the preheated fluid further up to the chosen sterilization temperature.

A.5 The final cooling is only necessary to ensure an acceptable temperature of the rejected sterile effluent, which very often goes into a wastewater station. At this position, an in-line pH control can be required,

A.6 To avoid corrosion problems (for example due to the presence of chlorine in the effluent), the installation is partially constructed in Uranus B6 stainless steel for the equipment which operates at high temperature, and in polyethylene for the equipment which operates at temperatures below 60 "C.

Annex B

(Informative)

Examples of application of disinfectants

Table B: Properties of some disinfectants

Disinfectant type	**Active against***							**Negative interference by**		
	Fungi	**Bacteria**		**Myco-bacteria**	**spores**	**Lipid viruses**	**Non-lipid viruses**	**Protein**	**Hard water**	**Detergent**
		Gram positive	Gram negative							
Phenolic compounds	xxx	xxx	xxx	Xx	-	x	v	+	+	C
Hypochlorites	X	xxx	xxx	Xx	xx	x	x	+++	+	C
Alcohols	-	xxx	xxx	Xxx	-	x	v	+	+	-
Formaldehyde	xxx	xxx	xxx	Xxx	xxx[a]	x	x	+	+	-
Glutaraldehyde	xxx	xxx	xxx	Xxx	xxx[b]	x	x	+	+	-
Iodophors	xxx	xxx	xxx	Xxx	x	x	x	+++	+	A

xxx: good
xx: fair
x: slight
-: nil
v: depend on virus
a: above 40^0C
b:above 20^0C
* If the manufacturer's data or the respective data of technical literature are observed

+++: very
++: partly
+: weakly
-: nil
C: cationic
A:anionic

NOTE: Attention is drawn to the toxicity and/or allergenicity of disinfectants and their environmental impact.