ECHA
EUROPEAN CHEMICALS AGENCY

TRANSITIONAL GUIDANCE

Transitional Guidance on the Biocidal Products Regulation

Transitional Guidance on Efficacy Assessment for Product Type 22 Embalming Products

August 2014

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LEGAL NOTICE

This document aims to assist users in complying with their obligations under the Biocides Regulation (BPR). However, users are reminded that the text of the BPR is the only authentic legal reference and that the information in this document does not constitute legal advice. Usage of the information remains under the sole responsibility of the user. The European Chemicals Agency does not accept any liability with regard to the use that may be made of the information contained in this document.

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PREFACE

This Transitional Guidance is to be applied to applications for active substance approval and product authorisation submitted under the Biocidal Product Regulation (EU) No 528/2012 (the BPR). This document describes the BPR obligations and how to fulfil them.

A "Transitional Guidance" is a document that has been initiated under the "old" Biocidal Products Directive 98/8/EC and because it has been finalised before the relevant new BPR guidance document has been fully developed, it is being made available as a Transitional Guidance document until such time as the relevant new document is ready for publication.
This Transitional Guidance document has had a Public Consultation by the Commission and this document is now finalised and waiting for inclusion into Volume II Part B of the new BPR guidance structure: there will be no further consultation on this document and it will be added by a corrigendum when the relevant Volume is available.

This is a Transitional Guidance to support chapter 7 from TNsG on product evaluation for Product Type 22 Embalming and taxidermist fluids.

PRODUCT TYPE 22 – Embalming and taxidermist fluids

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NOTE to the reader:

This Transitional Guidance will be reformatted when it is incorporated into the New Guidance Structure. When this is completed, the finalised version will be uploaded onto the website of ECHA. No consultation will be made to do this

General introduction

Annex V of BPR defines Product Type 22 products as follows: "Embalming and taxidermist fluids. Products used for the disinfection and preservation of human or animal corpses, or parts thereof". Embalming for this purpose only aims at the temporary preservation of the deceased person, before burial. Taxidermy fluids and those intended for long-term preservation (e.g. repatriation as shipping cases) are not covered by this guidance document. These particular cases will be taken into account in a future update and inclusion into Volume II Part B of the new BPR guidance structure.

This guidance document is intended for applicants to assist them in compiling an authorisation request dossier regarding the efficacy aspect, and thus specifies the general conditions for carrying out efficacy assessments of biocidal products for marketing authorisations.

This guidance document may be reviewed in the event of regulatory changes or technical advances.

1. Use of the products

1.1 The issue of bodily decomposition

1.1.1 Physical, chemical and microbiological post-mortem activities

A body starts to decompose as soon as the blood ceases to circulate and oxygen is no longer supplied to the tissues. Under conditions favourable to decay, the body cools in the first few hours after death, dehydration sets in (lividity) together with rigor mortis resulting from anaerobic hydrolysis of muscle glycogen. The first stages of cell degradation can be seen with the onset of lividity.

The natural degradation of the body's organic matter results from the action of enzyme, tissue and microbial processes. The ecosystem whose characteristics determine the succession of physical, chemical and microbiological changes that occur post mortem can be defined as the set of interactions between ambient factors (temperature, hygrometry), individual factors, especially the body's water, muscle and fat composition, and the body's own microbial flora, both external (skin) and internal (digestive and respiratory). Together, these conditions affect the establishment, acclimatisation and development of the dominant indigenous flora, separately or in association, and thus steer the metabolism towards either speed or slow decomposition.

The activity of the microflora, initially latent, intensifies; the first stages of mineralisation of the organic matter, stages of the nitrogen, carbon, oxygen and hydrogen cycles, constitute both superficial and profound decomposition. This decay is defined partly by the decomposition of the organic tissues, mainly under the influence of the bacteria hosted by the individual, especially those in the intestinal flora, and then by fungi, and partly by the decomposition of the organic matter and the bacteria responsible for mineralisation that gradually invade the body, via the body fluids.

As the proteins, lipids and certain carbohydrates that provide the substrate degrade; they produce malodorous soluble and gaseous substances, containing sulphur, nitrogen and carboxylates. Depending on the specific activities developed by the flora in place, the resulting foul odours can vary in nature and intensity. It is increased by higher temperatures and by interferences between chemical groups. As degradation progresses, the source of foul odours moves gradually from the body itself to the liquid products of decay, which rapidly become the principal source of foul odours. As the organic matter becomes hydrolysed into more soluble compounds it becomes easier for microorganisms to assimilate them, facilitating the production of foul odours.

1.1.2 The microorganisms involved

- in the early stages of decomposition of the liquids and soft tissues (with production of gases), only the following species are found: *Pseudomonas fluorescens* and *Micrococcus ureae*;
- at a later stage of lipid transformation, the following appear: *Pseudomonas* sp. and then *Pyogenes sp.*

The initial wave consists of aerobic bacteria while those following are anaerobic (*Diplococcus magnus, Streptococcus* sp., *Serratia liquefaciens, Bacteriodes* sp. *etc.*). This decomposition of the body due to bacteria and saprotrophic fundi gradually leads to autolysis of the remains, which is pursued later and over time by the bacteria active in the mineralisation of the organic matter, although this last stage is related to the level of humidity. Various factors concerning the environment of the body intervene (humidity, temperature, aeration) as well as its size, age, causes of death and place of storage.

The decay is predominantly influenced by the bacteria that had been hosted by the individual, especially those in the intestinal flora. The bacterial species frequently found in decomposing bodies are:

- of intestinal origin: enterobacteria, especially *Escherichia coli*; clostridia, especially *Clostridium tetani, C. welchii* and *C. difficile*; and faecal *Streptococcus*;
- of dermal origin: *Staphylococcus spp*.;
- of environmental origin: *Bacillus spp*.

The saprotrophic fungi and yeasts succeed one another in specific groups and the flora changes in line with the gradual alteration of the substrate, which thus provides a choice habitat for certain species of mycota at one moment and not at others.

The decomposition of the body due to bacteria and saprotrophic mycota accelerates the alteration started by autolysis, before the mineralising bacteria that invade the body later bring it into the cycle of waste material in the biosphere.

There may also be other pathogenic microorganisms, such as the tuberculosis bacillus (*Mycobacterium tuberculosis*) or other mycobacteria, or again viruses such as hepatitis or Human Immunodeficiency Virus (HIV), which can persist in the body.

1.2 Products for preserving human bodies and their uses

1.2.1 Types of application

The embalmer begins by physically working the limbs to reduce lividity and facilitate the flow of the preserving fluid. This is used for two separate purposes and at different concentrations:

- arterial fluid: an aquaeous solution injected under pressure into the vascular system (the embalmer adjusts the final concentration to the condition of the body). This liquid is injected in the arterial system via the carotid or the femoral artery (sometimes at several points if diffusion is poor). The injection is made under pressure (by pump) or by gravity. This result in venous drainage: replaced by the injected product, the blood leaves the body via the jugular vein. Six to ten litres are injected and four litres (of blood and other body fluids) are removed by suction;
- cavity fluids: these are usually used at high concentration to preserve the thoracic and abdominal cavities, which cannot be irrigated by arterial injection. Using a trocar connected to a pump, about two litres of the pure undiluted solution are injected into the peritoneal cavity through an incision close to the navel.

There are also preparations for dermal use. These are gels designed to limit the decomposition of the body by treating bedsores. For this type of product, applicants must complete the appropriate section of the assessment grid, demonstrating the efficacy of the product.

In addition to its biocidal active substance(s), such a formulation could include the following co-formulants, which must have no biocidal activity:

- anticoagulants: to fluidify the product and ensure correct diffusion (sodium chloride and sodium citrate);
- hydrating and moistening agents: to slow the drying out of the body by hydrating the tissues and making them more supple (glycerine, ethylene glycol, propylene glycol, hexylene glycol, urea);
- surface-active agents: to facilitate adsorption of the fluid and penetration of the membranes and to maintain the solubility of the other components of the formulation, which are generally cations, as these surfactants are often also antimicrobials;
- colouring agents: to ensure that the fluid is of a colour similar to blood; synthetic colouring agents are generally used (eosin, erythrosine or food colouring agents);
- perfumes.

1.2.2 Products used for aesthetic purposes

Preservation may be supplemented with aesthetic treatment involving remodelling the face (modelling wax), sewing or bonding together the upper and lower jaws, placing eye caps under the eyelids to keep the eyes closed (or possibly gluing them shut). Finally, when all other treatment has been completed, cosmetic make-up may be applied, partly to give a more agreeable appearance but also partly to delay dehydration.

These products are not considered during assessment of the efficacy of the preservation product. However, if these products contain substantial amount of active substance and claim an effect on bodily composition, they should be considered as biocide.

2. Data required

2.1 Claims and labelling

When an application for the approval of a PT 22 substance is being assessed, the evaluation of the efficacy is focused on the efficacy of the biocidal product and not on the other products (as cosmetic) which can be also included in an embalming treatment, so this aspect must be demonstrated unambiguously in laboratory tests and tests on human bodies, the details of which must be available on request.

As a minimum, a PT 22 product must claim to be active against a broad spectrum of bacteria; yeasts, fungi and viruses are considered as an additional spectrum. As explained above, bacteria are the principal microorganisms targeted by PT 22 products. Yeast, fungi and viruses have less relevance in the early stages of bodily decomposition.

Nonetheless, an active substance with a broad spectrum on different types of microorganism would provide better protection for users (e.g. against tuberculosis bacilli, hepatitis viruses or HIV, etc.).

2.2 Efficacy tests

2.2.1 Laboratory tests

As there is currently no standardised method recognised at European level targeting the scope covered by PT 22 products, and as no technical reference documents were found either in France or throughout the world, it is important that methods used should achieve two different yet complementary goals:

- the rapid destruction of bacteria, representative of the bacterial sphere, in the presence of a strongly interfering organic load simulating the bodily fluids;
- to maintain this antibacterial activity for several days, thus demonstrating that there is no subsequent proliferation of these microorganisms.

2.2.2 Determining bactericidal activity

As already mentioned above, the minimum claim is a bactericidal activity. Other additional activities, such as fungicide or virucide activities must be supported by relevant tests.

From among the techniques available, the selection was made based on the following criteria:

- a method that has been standardised at least at European level – the bacterial "suspension" test used in the medical sector
- the presence of a standardised strong organic load accurately simulating organic bodily fluids.

In compliance with the classification of European standards (EN 14885), the two tests selected belong to the categories of tests in Phase 2, Step 1 which include quantitative suspension tests for establishing that a biocidal product has a bactericidal activity by simulating its use under real conditions:

a) tests according to the EN 13727 standard: this mandatory test determines the minimum bactericidal concentration of a product on the basis of a 5-log reduction in titre of a bacterial suspension, at a temperature of 20°C, for 60 minutes of contact, in the presence of a strong organic load (bovine albumin 3 g/L + ovine erythrocytes 3 ml/L), on three species of bacteria (*Staphylococcus aureus* ATCC 6538, *Pseudomonas aeruginosa* ATCC 15442, *Enterococcus hirae* ATCC 10541);

b) tests according to the EN 14348 standard: this additional test must be taken into account if the applicant advances any claim concerning activity against agents responsible for tuberculosis, or if complementary tests prove necessary to cover this particular need. This test has a methodology similar to that for the previous test, determining the minimum tuberculocidal concentration of a product on the basis of a 4-log reduction in titre of a bacterial suspension, at a temperature of 20°C, for 60 minutes of contact, in the presence of a strong organic load (bovine albumin 3 g/L + ovine erythrocytes 3 ml/L), on the bacterium *Mycobacterium terrae* ATCC 15755.

Any claim by applicants that a product targets a specific microorganism must be supported by supplementary studies. For example, a claim of activity against the agents responsible for tuberculosis must be verified in compliance with the EN 14348 standard. If there is no recognised standard for a specific microorganism, the EN 14348 standard may be used for the microorganism in question.

The most recent version of standards in force at the time of the tests must be used.

Furthermore, in accordance with the conclusions in Annex VI (77) *the level, consistency and duration of protection, control or other intended effects must, as a minimum, be*

similar to those resulting from suitable reference products, where such products exist, or to other means of control. Where no reference products exist, the biocidal product must give a defined level of protection or control in the areas of proposed use.

Considering the history of the use of formaldehyde, it may therefore be worthwhile to include with the application information about the bactericidal efficacy of formaldehyde, if available.

In France, formaldehyde is most commonly used at concentrations of about 28% for cavity fluid and 1.5% for arterial fluid. As formaldehyde is currently under assessment in the review programme, efficacy data may become available when the assessment report is published by the evaluating Competent Authority (eCA). The standards proposed above for validating claims may be reviewed at a later stage in the context of the review of this guidance document as a result of the conclusions published by the eCA on the efficacy of formaldehyde, or in the event of other data for this same substance becoming available in the future.

2.2.3 Verifying that antibacterial activity is maintained

When embalming, the biocidal product must remain effective over several days, until burial. The persistence indicated on the label must be proven, e.g. by challenge tests. The following protocol may be used, adapted from the French NF X30-503 standard (Healthcare waste - Reduction by disinfection pre-treatment appliances in microbiological and mechanical risks involving infections and other comparable healthcare waste).

- In order to ensure that bacteria are destroyed and not merely subjected to stress or inhibition by the biocidal product, and to confirm the absence of bacterial revival, the bacterial suspension, treated according to the EN 13727 standard, is held at ambient temperature for four to six days and then the bacteria are counted. In the laboratory, it is held at 20°C until analysis.
- The bacteria in the bacterial suspension are counted on the day of treatment and again after four to six days.
- Lasting disinfection is shown by the absence of bacterial revival, i.e. the bacterial count on day 4-6 must not be increased by more than one log compared to the bacterial load measured in the sample taken on the day of treatment (Day 0).
- The "effective" dose of the product must be in a range bounded by upper and lower limits, which are:
  - a lower concentration for which bacterial recrudescence is observed after 4-6 days;
  - a higher concentration.

2.2.4 Tests on human bodies

To complement *in vitro* efficacy tests for the biocidal product used for the preservation of human bodies, tests on bodies are necessary to assess product performance.

Because of the number of factors that can influence the efficacy of a biocidal product, such as the cause of death or the time lapsed or the condition of the body before embalming begins, a sufficient number of bodies (at least 20) satisfying the requirements of the grid in Appendix 1 and the claims for the product, must be available for optimum assessment of the results in terms of preservation of the body for viewing by families.

⚠ Note: the applicant has to inquire about the legislation in force in the Member State (MS) where the tests on human bodies are performed (e.g. current French regulations only allow bodies donated to science to be used to test a product that

has not yet been approved.

Every centre for the donation of bodies participating in these tests on human bodies must declare the number of bodies undergoing tests in its establishment. This declaration is supplied to the applicant and must be submitted with the application).

In all cases, whatever the legislation in force in each MS, tests on human bodies with good quality and in line with this guidance will be accepted by MS when the dossier will be submitted for authorisation.

The assessment grid for specific biocidal products is shown in Appendix 2. Its purpose is not to assess the overall embalming treatment but only the biocidal product for which authorisation is being requested.

The grid consists of:

- general information: date and place of the treatment, identification of the deceased (gender, age), weight, corpulence, adiposity, date and causes of death, etc.;
- the preoperative body examination: bodily integrity, autopsy, external prostheses, surgery, visible anomalies (decomposition, rigidity, dehydration, lividity, colouring of tissues, dermal lesions, distension of the abdomen, bruising, etc.). The bodies used must be representative of the range of criteria listed in this section;
- the techniques used to inject the biocidal product: timetable, sites and types of injection, biocidal product used, drainage and puncture;
- observations concerning the injection of the biocidal product: observations during treatment, 48 hours after treatment and after different periods in accordance with the applicant's claims;
- where necessary, the use of other products during the preservation process: products for cosmetic purposes, humidifiers and other products.

The embalmer thus assesses the efficacy of the embalming product on a series of human bodies, using the grid provided. The efficacy is judged for the duration claimed by the manufacturer according to observations concerning odour, colouring and the suppleness of the skin after injection of the biocidal product. In the event that the tests on these human bodies have to be interrupted for any reason, the results already obtained remain valid for three years following the official decision to halt the tests.

2.2.5 Choice of dose

The usage dose[1] claimed is a matter for the applicant. Indeed, related to the body conditions, it can be necessary to test several doses above the dose determined in laboratory and then define a range of doses, adapted to difficult cases. They must choose the usage dose claimed according to the efficacy sought and the precautions for use that will be imposed on embalming technicians by their employers, depending on the health risks created by the full preparation (active substance at the chosen concentration plus excipients and solvents). In cases where little is known about the pathogenic microorganisms that might present a risk to the embalmer, it is essential that protective measures be taken during the preservation process. These measures should not be primary criteria for choosing the biocidal product used for the treatment.

If the applicant chooses a range of doses instead of a single value, the lower must be justified with appropriate tests, as defined in the preceding section (and also the higher

[1] Concentration and volume injected

dose in the case where different doses have been tested in the human body tests to cover difficult cases). The applicant may also request approval for two different doses, one of them more concentrated for special or difficult cases (bodies found some time after death or in contact with water, for example).

3. Assessing the application for authorisation

The assessment of the embalming product shall be favourable if it satisfies the following efficacy criteria:

- laboratory test: bactericidal properties (EN 13727 and/or EN 14348 standards): obligatory test conditions;
- laboratory test: e.g. challenge test: no bacterial recrudescence for at least 4-6 days by more one log compared to the bacterial load measured in the sample taken on the day of treatment (Day 0), with the bacterial suspension being held at ambient temperature;
- field test: 80% of the bodies must meet the satisfaction criteria at T+48 hours. Satisfaction criteria are according to the grid: normal or fair odour, colouring and suppleness of the skin, related to the initial conditions of the body.

SUMMARY OF THE PARAMETERS ASSESSED

EFFICACY CLAIMS ON THE LABEL SUBMITTED

1. Does the applicant make any specific claims? Y/N

2. Have the efficacy claims on the label been judged and dealt with according to the parameters described in this guidance document for this type of product? Y/N

ASSESSING THE DATA

3. Has each study (or supplementary item) been assessed individually for robustness? Y/N

4. Has each study (or supplementary item) been assessed individually for quality assurance? Y/N

5. Has each study (or supplementary item) been assessed individually for suitability (i.e. for reliability and relevance concerning the claims)? Y/N

DECISION-MAKING

Considering all the available data:

6. Are the claims on the label sufficiently supported? Y/N

7. Do the claims on the label require modifications? Y/N

8. On the basis of the efficacy data submitted, can authorisation for the use of the product be recommended? Y/N

Appendix 1. PT 22 active substances in the review programme

Active Substance	RMS	CAS No
Formaldehyde	DE	50-00-0
Bronopol	ES	52-51-7
Iodine	SE	7553-56-2
Quaternary ammonium compounds, benzyl-C12-18-alkyldimethyl, chlorides	IT	68391-01-5
Quaternary ammonium compounds, benzyl-C 12- 16-alkyldimethyl, chlorides (ADBAC)	IT	68424-85-1
Quaternary ammonium compounds, benzyl-C12-14-alkyldimethyl, chlorides	IT	85409-22-9
Quaternary ammonium compounds, C12-14-alkyl[(ethylphenyl)methyl]dimethyl, chlorides	IT	85409-23-0
Polyvinylpyrrolidone iodine	SE	25655-41-8

Appendix 2. Assessment grid for tests on human bodies

This grid is for use in the assessment of the biocidal product itself, but not for assessing the overall embalming process with its hygiene and cosmetic aspects.

Number of the report:

Name and signature of the embalming professional:

Company:

Address of company:

1. General information

Date of the operation:

Place:

Type of place:

☐ Funeral parlour

☐ Morgue

☐ Establishment without a morgue (fewer than 200 deaths per year)

☐ Home or other (please specify):

Identification:

Gender: ☐ Male ☐ Female

Age:

Estimated weight (kg):

Estimated corpulence: ☐ cachectic ☐ thin ☐ medium ☐ stout

Adiposity: ☐ low ☐ medium ☐ high

Date of death (if known):

Date and time of treatment:

Body refrigerated: ☐ yes ☐ no. If "yes", for how long:
Temperature:

Causes of death (if known):

Therapeutic treatment (if known):

2. Preoperative examination of the body

Body intact: ☐ yes ☐ no, description:

Autopsy before treatment: ☐ yes ☐ no

Presence of external prostheses: ☐ yes ☐ no

Surgical intervention before death (if apparent or known): ☐ yes ☐ no

If yes, type of intervention:

Other visible anomaly(ies):

Decomposition: ☐ none ☐ commencing ☐ problematic

Rigidity: ☐ none ☐ minimal ☐ moderate ☐ problematic

Dehydration: ☐ none ☐ normal ☐ high

Lividity: ☐ none ☐ minimal ☐ moderate ☐ problematic, location:

Coloration of tissues (yellowing): ☐ no ☐ slight ☐ moderate ☐ intense, description:

Dermal lesions (sores, blisters, wounds, etc.): ☐ yes ☐ no, description:

Distension of the abdomen: ☐ no, ☐ slight ☐ moderate ☐ intense, ☐ liquid ☐ gas

Bruising: ☐ yes ☐ no, ☐ abdomen ☐ thorax ☐ leg, ☐ arm, ☐ face, specify degree and place:

Comments:

3. Techniques used for injection of the biocidal product

Time of start of treatment:

Time of end of treatment:

Site(s) of injection:

Carotid(s): ☐ right ☐ left.

Femoral(s): ☐ right ☐ left

Axillary(ies): ☐ right ☐ left
Other(s), description:

Ease of finding: ☐ easy ☐ normal ☐ deep

Condition: ☐ good ☐ atheromatous / ☐ hardened

Injection: ☐ manual ☐ by electric pump ☐ by gravity

Diffusion: ☐ good ☐ fair ☐ bad

Puncture before treatment: ☐ yes ☐ no. If "yes", type:
Biocidal product used:

Pre-injection: ☐ yes ☐ no

Injection:

Hypodermic: *product:*

Site:

Topical: *product:*

Site:

Name of the biocidal product:

Active substance(s):

Duration of efficacy claimed:

Number of litres:

Arterial fluid:

Name of fluid:

% of dilution:

Number of litres injected:

Start time for the injection:

End time for the injection:

Cavity treatment:

Name of fluid:

% of dilution:

Number of litres injected:

Start time for the injection:

End time for the injection:

Corrective injection:

☐ yes ☐ no

Drainage method:

☐ Cardiac, ☐ Venous

Vein(s) chosen: ☐ jugular, ☐ femoral, ☐ axillary

Volume drained by circulatory system (*litres*):

Total volume drained (*litres*):

Type of drainage: ☐ drain tube(s) ☐ forceps ☐ intermittent / ☐ continual

Quality of drainage: ☐ considerable clotting ☐ medium ☐ slight ☐ no clotting

General puncture:

Quantity*:*

4. Observations concerning the injection of the biocidal product

Observations during the treatment:

Odour: ☐ normal ☐ fair ☐ bad

Colouring: ☐ good ☐ fair ☐ bad

Suppleness of the skin: ☐ good ☐ fair ☐ bad

Observations following the treatment:

Odour: ☐ good ☐ fair ☐ bad

Colouring: ☐ good ☐ fair ☐ bad

Suppleness of the skin: ☐ good ☐ fair ☐ bad

Mandatory observation 48 hours after the treatment:

Odour: ☐ good ☐ fair ☐ bad

Colouring: ☐ good ☐ fair ☐ bad

Suppleness of the skin: ☐ good ☐ fair ☐ bad

Optional observation (at times relevant to the manufacturer's claims):

Time after treatment:

Odour: ☐ good ☐ fair ☐ bad

Colouring: ☐ good ☐ fair ☐ bad

Suppleness of the skin: ☐ good ☐ fair ☐ bad

Other products used during the preservation process:

Reasons for their use:

Description:

Products for cosmetic purposes:

☐ yes, ☐ no. If yes: ☐ normal, ☐ make-up, ☐ significant, ☐ restorative

Other restoration: _____

Moisteners and other products used (cauterising agents, disinfectants, skin tone correctors, etc.):

Name of the fluid: _____, % dilution: _____, litres injected: ___

Name of the fluid: _____, % dilution: _____, litres injected: ___

Explanations:

5. Comments

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