

# TECHNICAL PROPOXUR

Specification WHO/SIT/18.R3  
Approved 25 September 1989

## 1. Specification

### 1.1 Material

The material shall consist of propoxur together with related manufacturing compounds. It shall be in the form of a white to grey solid and free from extraneous impurities or added modifying agents.

### 1.2 Chemical and physical requirements

The material, sampled from any part of the consignment (see method WHO/M/1), shall comply with the requirements of section 1.1 and with the following requirements.

#### 1.2.1 *Propoxur content (g/kg)*

The propoxur content shall be declared (not less than 970 g/kg) and, when determined by the method described in section 2.1, the content obtained shall not differ from that declared by more than  $\pm 20$  g.

#### 1.2.2 *Acidity or alkalinity*

The acidity or alkalinity of the material, determined by the method described in WHO/M/3, shall not be higher than 0.5 g/kg, calculated as  $\text{H}_2\text{SO}_4$  or 0.1 g/kg calculated as NaOH.

#### 1.2.3 *Material insoluble in acetone*

The material insoluble in acetone, determined by the method described in WHO/M/21, shall not be higher than 1 g/kg.

#### 1.2.4 *Water content*

The water content, determined by the method described in section 2.2, shall not be higher than 2 g/kg.

#### 1.2.5 *Melting point range*

The melting point, determined by the method WHO/M/5.R1, shall be in the range 86°-91.5°C and shall not be depressed on admixture with an equal quantity of pure propoxur.

### 1.3 Packing and marking of packages

The technical propoxur shall be packed in suitable clean containers as specified in the order.

All packages shall bear, durably and legibly marked on the container, the following:

Manufacturer's name  
Technical propoxur to specification WHO/SIT/18.R3  
Batch or reference number, and date of test  
Net weight of contents  
Date of manufacture

and the following minimum cautionary notice:

Propoxur is a carbamate compound that inhibits cholinesterase. It is poisonous if swallowed or inhaled. Keep the material out of the reach of children and well away from foodstuffs and animal feed and their containers. If poisoning occurs, call a physician. Atropine is a specific antidote, and artificial respiration may be needed.

## 2. Methods of determining chemical and physical properties

### 2.1 Propoxur content

#### 2.1.1 *Outline of method*

The sample is dissolved in acetonitrile and n-butyrophenone is added as an internal standard. The propoxur content is determined by high-performance liquid chromatography (HPLC) using a reverse phase column and a 60:40 mixture of acetonitrile and water as the mobile phase.

#### 2.1.2 *Special apparatus*

1. *Liquid chromatograph.* The instrument should be one that is designed for use with stainless steel columns and that is equipped with a pumping system able to generate more than 10.5 MPa pressure and a UV spectrophotometer detector able to measure UV absorbance at 280 nm<sup>1</sup>.
2. *Liquid chromatographic column.* The column should be a stainless steel tube 25 cm long and 4.6 mm in internal diameter packed with £ 10-mm C-18 bonded silica gel (Partisil-10 ODS-3, or equivalent).

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<sup>1</sup> Check the linearity of the detector in the concentration zone used for the determination.

### 2.1.3 *Special reagents*

*Propoxur standard.* Analytical grade, of known purity, better than 995 g/kg.

*Internal standard.* *n*-Butyrophenone.

*Acetonitrile.* HPLC grade.

*Water.* HPLC grade.

*Mobile phase.* Degassed mixture of acetonitrile and water, 60 + 40 (v/v).

### 2.1.4 *Preparation of standard solutions*

*Internal standard solution.* Weigh a 6 g quantity of *n*-butyrophenone into a 200 ml volumetric flask, dissolve, and dilute to volume with acetonitrile.

*Propoxur calibration solution.* Weigh (to the nearest 0.1 mg) about 300 mg of propoxur standard into a 50 ml volumetric flask. Pipette 10.0 ml of internal standard solution into the flask, dilute to volume with acetonitrile, and mix well. Pipette 10.0 ml of this solution into a 100 ml volumetric flask, dilute to volume with acetonitrile, and mix well.

### 2.1.5 *Operating conditions for high-performance liquid chromatography*

The conditions given below are typical values and may have to be adjusted to obtain optimum results from a given apparatus.

Column temperature	ambient.
Flow rate	1.5 ml/min (at about 7 MPa).
Detector sensitivity	0.16 AUFS <sup>1</sup> .
Wavelength	280 nm.
Injection volume	20 ml.
Chart speed	0.5 cm/min.
Retention times:	
propoxur	about 3.75 min.
internal standard	about 6.50 min.

### 2.1.6 *Sample preparation and analysis*

Weigh (to the nearest 0.1 mg) a quantity of sample containing about 300 mg of propoxur into a 50 ml volumetric flask. Pipette 10 ml of internal standard solution into the flask, dilute to volume with acetonitrile and shake for 1 minute. Pipette 10 ml of this solution into a 100 ml volumetric flask, dilute to volume with acetonitrile, and mix well. Filter a portion of this solution and hold for HPLC analysis (use 0.45-mm porosity filters, Gelman Acrodisc-CR or equivalent). Pump the mobile phase through the column until the system is equilibrated (flat baseline). Allow 8 minutes between injections.

<sup>2</sup> Absorbance unit full scale.

Adjust operating parameters to cause propoxur to elute in 3.5-4.5 minutes. Adjust injection size and attenuation to give peaks with more than 60% full-scale deflection. Make repetitive injections of calibration solution and calculate response ratios by dividing peak area (or peak height) of propoxur by that of the internal standard peak. Response ratios must agree within  $\pm 1\%$ . Average the duplicate response ratios obtained with the calibration solution injections.

Inject duplicate aliquots of sample solution. Average the duplicate response ratios for the sample solution. Response ratios must agree within  $\pm 1\%$ . If not, repeat the analysis starting with the calibration solution injections. Reinject the calibration solution twice. Average the response ratios of the two calibration solution injections immediately preceding and following the sample injections. These must agree within  $\pm 1\%$ . If not, repeat the analysis.

### 2.1.7 Calculation

For each injection the response ratio  $r$  is given by the equation:

$$r = \frac{\text{area (or height) of propoxur peak}}{\text{area (or height) of internal standard peak}}$$

$$\text{Propoxur content (g / kg)} = \frac{r_2 \times m_1 \times P}{r_1 \times m_2}$$

Where

- $r_1$  = average response ratio for calibration solution
- $r_2$  = average response ratio for sample solution
- $m_1$  = mass of propoxur standard in the calibration solution (mg)
- $m_2$  = mass of sample taken (mg)
- $P$  = purity of propoxur standard (g/kg).

## 2.2 Water content

Determine the water content by the Karl Fischer electrometric titration method (see WHO/M/7.R1).

# PROPOXUR WATER-DISPERSIBLE POWDER

Specification WHO/SIF/30.R3  
Approved 25 September 1989

## 1. Specification

### 1.1 Description and ingredients

The material shall consist of a homogeneous mixture of technical propoxur together with filler(s) and other necessary formulants and shall be in the form of a fine, free-flowing, cream-coloured powder, which wets out readily on stirring into water. The technical propoxur used in the manufacture of the water-dispersible powder shall comply with the requirements of specification WHO/SIT/18.R3.

### 1.2 Chemical and physical requirements

The material, sampled from any part of the consignment (see method WHO/M/1), shall comply with the requirements of section 1.1 and with the following requirements.

#### 1.2.1 *Propoxur content (g/kg basis)*

The content of propoxur, determined by the method described in section 2.1, shall not differ from the nominal content by more than the following amounts:

<i>Nominal content</i>	<i>Tolerance permitted</i>
Up to 250 g/kg	± 6% of the nominal content
above 250 to 500 g/kg	± 5% of the nominal content
Above 500 g/kg	± 25 g/kg

The average content of all samples taken shall not be lower than the nominal content.

#### 1.2.2 *pH of the aqueous dispersion*

The pH of the aqueous dispersion, determined by the method WHO/M/25, shall be lower than 4 and higher than 7.

#### 1.2.3 *Sieving after heat stability treatment*

Not less than 98% of the powder after the heat stability treatment (section 2.3) shall pass through a 75 mm sieve when tested by the method described in WHO/M/4.R1.

#### 1.2.4 *Suspensibility*

*In standard hard water after heat stability treatment.* When tested by the method described in section 2.2, a minimum of 60% of the propoxur (15 g/l) shall be in suspension 30 minutes after agitating a suspension containing 25 g/l of propoxur prepared in standard hard water from powder subjected to the heat stability treatment described in section 2.3.

#### 1.2.5 *Heat stability*

The wettable powder, after treatment as described in section 2.3, shall comply with the requirements of sections 1.2.1 and 1.2.2 of this specification.

### 1.3 **Packing and marking of packages**

The propoxur water-dispersible powder shall be packed in suitable, clean drums, as specified in the order. The drums shall contain a lining or bag of polyethylene or equivalent, with a nominal thickness of 0.1 mm. The lining or bag shall be hermetically sealed after filling.

All packages shall bear, durably and legibly marked on the container, the following:

Manufacturer's name  
Propoxur water-dispersible powder to specification WHO/SIF/30.R3  
Propoxur, ...g/kg  
Batch or reference number, and date of test  
Net weight of contents  
Date of formulation

and the following minimum cautionary notice:

Propoxur is a carbamate compound that inhibits cholinesterase. It is poisonous if swallowed or inhaled.

Keep the material out of the reach of children and well away from foodstuffs and animal feed and their containers.

If poisoning occurs call a physician. Atropine is a specific antidote, and artificial respiration may be needed.

## 2. Methods of determination chemical and physical properties

### 2.1 Propoxur content

#### 2.1.1 *Outline of method*

The propoxur is extracted from the sample with acetonitrile and n-butyrophenone is added as internal standard. The propoxur content is determined by high-performance liquid chromatography (HPLC) using a reverse-phase column and a 60:40 mixture of acetonitrile and water as the mobile phase.

#### 2.1.2 *Special apparatus*

1. *Liquid chromatograph.* The instrument should be one that is designed for use with stainless steel columns and that is equipped with a pumping system able to generate more than 10.5 MPa pressure and a UV spectrophotometer detector able to measure UV absorbance at 280 nm<sup>1</sup>.
2. *Liquid chromatographic column.* The column should be a stainless steel tube 25 cm long and 4.6 mm in internal diameter, packed with  $\phi$  10 mm C-18 bonded silica gel (Partisil-10 ODS-3, or equivalent).

#### 2.1.3 *Special reagents*

*Propoxur standard.* Analytical grade, of known purity, better than 995 g/kg.

*Internal standard.* n-Butyrophenone.

*Acetonitrile.* HPLC grade.

*Water.* HPLC grade.

*Mobile phase.* Degassed mixture of acetonitrile and water, 60 + 40 (v/v).

#### 2.1.4 *Preparation of standard solutions*

*Internal standard solution.* Weigh a 6 g quantity of n-butyrophenone into a 200 ml volumetric flask, dissolve, and dilute to volume with acetonitrile.

*Propoxur calibration solution.* Weigh (to the nearest 0.1 mg) about 300 mg of propoxur standard into a 50 ml volumetric flask. Pipette 10.0 ml of internal standard solution into the flask, dilute to volume with acetonitrile, and mix well. Pipette 10.0 ml of this solution into a 100 ml volumetric flask, dilute to volume with acetonitrile, and mix well.

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<sup>1</sup> Check the linearity of the detector in the concentration zone used for the determination.

2.1.5 *Operating conditions for high-performance liquid chromatography*

The conditions given below are typical values and may have to be adjusted to obtain optimum results from a given apparatus.

Column temperature	ambient
Flow rate	1.5 ml/min (at about 7 MPa)
Detector sensitivity	0.16 AUFS <sup>2</sup>
Wavelength	280 nm
Injection volume	20 ml
Chart speed	0.5 cm/min
Retention times:	
propoxur	about 3.75 min
internal standard	about 6.50 min

2.1.6 *Sample preparation and analysis*

Weigh (to the nearest 0.1 mg) a quantity of sample containing about 300 mg of propoxur into a 50 ml volumetric flask. Pipette 10.0 ml of internal standard solution into the flask, dilute to volume with acetonitrile, and shake for 1 minute. Pipette 10.0 ml of this solution into a 100 ml volumetric flask, dilute to volume with acetonitrile and mix well. Filter a portion of this solution and hold for HPLC analysis (use 0.45 mm porosity filters, Gelman Acrodisc-CR or equivalent). Pump the mobile phase through the column until the system is equilibrated (flat baseline). Allow 8 minutes between injections.

Adjust operating parameters to cause propoxur to elute in 3.5-4.5 minutes. Adjust injection size and attenuation to give peaks with more than 60% full-scale deflection. Make repetitive injections of calibration solution and calculate response ratios by dividing peak area (or peak height) of propoxur by that of the internal standard peak. Response ratios must agree within  $\pm 1\%$ . Average the duplicate response ratios obtained with the calibration solution injections.

Inject duplicate aliquots of sample solution. Average the duplicate response ratios for the sample solution. Response ratios must agree within  $\pm 1\%$ . If not, repeat the analysis starting with the calibration solution injections.

Reinject the calibration solution twice. Average the response ratios of the two calibration solution injections immediately preceding and following the sample injections. These must agree within  $\pm 1\%$ . If not, repeat the analysis.

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<sup>2</sup> Absorbance unit full scale.

### 2.1.7 Calculation

For each injection the response ratio  $r$  is given by the equation:

$$r = \frac{\text{area (or height) of propoxur peak}}{\text{area (or height) of internal standard peak}}$$

$$\text{Propoxur content (g / kg)} = \frac{r_2 \times m_1 \times P}{r_1 \times m_2}$$

Where  $r_1$  = average response ratio for calibration solution  
 $r_2$  = average response ratio for sample solution  
 $m_1$  = mass of propoxur standard in the calibration solution (mg)  
 $m_2$  = mass of sample taken (mg)  
 $P$  = purity of propoxur standard (g/kg).

## 2.2 Suspending ability after heat stability treatment

### 2.2.1 Outline of method

A suspension of known concentration of propoxur in standard hard water is prepared, poured into a 250-ml graduated cylinder maintained at a constant temperature, and allowed to remain undisturbed for 30 minutes. The top 9/10ths are drawn off and the content of propoxur in the bottom 1/10th is determined, so allowing to evaluate the active ingredient mass still in suspension after 30 minutes.

### 2.2.2 Special apparatus

1. A 250 ml graduated cylinder with a ground-glass stopper and a distance of 20-21.5 cm between the bottom and the 250 ml calibration mark.
2. A glass tube, about 40 cm long and about 5 mm in internal diameter, pointed at one end to an opening of 2-3 mm, the other end being connected to a suitable source of suction.

### 2.2.3 Special reagents

*Standard hard water.* Dissolve 0.304 g of anhydrous calcium chloride and 0.139 g of magnesium chloride hexahydrate in distilled water and make up to 1 litre. This provides water with a hardness of 342 mg/l, calculated as calcium carbonate. Check the hardness by method WHO/M/26 and correct if appropriate.

#### 2.2.4 Procedure

Weigh (to the nearest 10 mg) into a 100 ml beaker an amount of the sample to form 250 ml of a suspension containing 25 g/l of propoxur. Add a volume of water<sup>3</sup> at 30°C ± 1°C equal to at least twice the mass of the sample taken. Allow to stand for 30 seconds and then stir by hand for 30 seconds with a glass rod, 4-6 mm in diameter, at not more than 4 revolutions per second, making no deliberate attempt to break up any lumps. Then immediately transfer the mixture quantitatively to the 250 ml graduated cylinder, using water at 30°C ± 1°C for rinsing and again avoiding mechanical disintegration of lumps. Immediately add sufficient water at 30°C ± 1°C to bring the volume to the 250 ml mark.

Stopper the cylinder and mix by inverting and righting it 30 times at a rate of one complete cycle every 2 seconds. During agitation the cylinder must be thermally insulated from the hands to maintain the prescribed temperature of the suspension. Allow the graduated cylinder to stand for 30 minutes in a water-bath at 30°C ± 1°C, taking care that the bath is free from vibrations.

Should excessive flocculation occur during the test, the material is unsatisfactory.

At the end of the 30 minutes settling period, insert the glass tube into the cylinder and, with a minimum of disturbance, withdraw during 10-15 seconds by means of the suction tube 9/10ths of the suspension, i.e. 225 ml. This is achieved by maintaining the tip of the glass tube just below the sinking top level of the suspension. Discard the suspension withdrawn.

Quantitatively transfer the retained one-tenth of the suspension into a 100 ml volumetric flask, rinsing several times with acetonitrile. Dilute to about 90 ml with acetonitrile. Shake for 1 minute, dilute to volume with acetonitrile and homogenize. Filter rapidly to avoid any solvent loss, or centrifuge. Pipette 10.0 ml of this solution into a 50 ml volumetric flask, add 10.0 ml of internal standard solution (section 2.1.4), dilute to volume with acetonitrile, and mix well. Pipette 10.0 ml of this last solution into a 100 ml volumetric flask, dilute to volume with acetonitrile, and homogenize. Hold this sample solution for HPLC analysis and proceed as described in section 2.1.

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<sup>3</sup> Whenever water is mentioned in this section use standard hard water.

### 2.2.5 Calculation

Mass (g) of propoxur<sup>4</sup> in the retained one-tenth of the suspension

$$m_1 = \frac{r_1 \times m_0 \times 10}{r_0}$$

Where  $r_0$  = average response ratio for calibration solution  
 $r_1$  = average response ratio for sample solution  
 $m_0$  = mass (g) of propoxur standard in the calibration solution.

From the value obtained in section 2.1 for the propoxur content, calculate the mass of propoxur in the initial sample taken for the suspensibility test.

$$\text{Suspensibility (\%)} = \frac{(m_2 - m_1) \times 111.1}{m_2}$$

Where  $m_1$  = mass (g) of propoxur found in the retained one-tenth of the suspension (section 2.2.3)  
 $m_2$  = mass (g) of propoxur in the initial sample.

## 2.3 Heat stability treatment

Fill a 50 ml<sup>5</sup> wide-mouthed glass bottle to within 1 cm of the top with the sample. Seal the bottle with a phenolic plastic cap having a soft liner. Turn the cap firmly to ensure a tight seal and place the bottle in a forced-draught oven maintained at  $54 \pm 2^\circ\text{C}$  for 3 days.

At the end of the heating period, remove the bottle from the oven and allow it to come to room temperature before removing the cap.

After completion of the heat stability treatment, the sample should not be exposed to heat, bright sunshine, or high atmospheric humidity.

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<sup>4</sup> If the volume of sample solution, to which the internal standard is added is not 10 ml, correct the equation accordingly.

<sup>5</sup> If a larger quantity of the sample is required for the tests, use a 100 ml bottle.