

**AMENDMENT  
to  
Time and Extent Application**

**Triclosan USP**

**Prepared to support the Inclusion of Triclosan into FDA's Monograph for Topical Acne Drug Products for Over-the-Counter Human Use; Docket No. 81N-0114, (21 CFR 333.301; 56 FR 41008, August 16, 1991; and subsequent amendments)**

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## 1. INTRODUCTION

This TEA is being submitted by Ciba Specialty Chemicals Corporation ("Ciba"), Home and Personal Care Business Line. It contains the most current and factual information on the ingredient IRGASAN® DP300 (triclosan) being proposed for inclusion into FDA's Monograph for Topical Acne Drug Products for Over-the-Counter Human Use; 21 CFR 333.301.

Ciba is the pioneer manufacturer of triclosan for topical and oral care applications worldwide. Triclosan has been used safely in human dermal and oral care applications for the past thirty-five years. Triclosan became the United States Adopted Name (USAN) for the drug substance in 1992. The trade name IRGASAN DP300 has historically been used by Ciba to present the dermal applications (i.e., OTC, cosmetic, preservative uses) of triclosan.

Ciba requests that the Agency include triclosan in the Topical Acne Drug Monograph on the basis of the information contained herein. This information was developed by Ciba and contains confidential and commercial trade secret information. Further information is available as necessary.

### 1.1 BASIC INFORMATION ABOUT THE ACTIVE INGREDIENT (IRGASAN DP300)

#### 1.1.1 Description and Identity

The generic name of the active ingredient is triclosan. Triclosan became the United States Adopted Name (USAN) for the drug substance in 1992. Triclosan is recognized as an official drug substance by the United States Pharmacopeia (USP 28).

The tradename: IRGASAN® DP300 was adopted by Ciba in 1989 to denote the pharmaceutical grade of triclosan, which is manufactured and distributed specifically for use in topical products

#### 1.1.2 Intended OTC Use

The intended use is as an active ingredient for human OTC acne drug products.

#### 1.1.3 OTC Strength

Proposed concentrations in topical OTC acne drug formulations:

- 0.2 to 0.5% dosage strength in leave-on applications, alone or in combination with other monograph active ingredients, and;
- 0.3 to 1.0 % dosage strength in rinse-off applications, alone or in combination with other monograph active ingredients.

### 1.1.4 Route of Administration

Route of administration would be via topical ointments, creams, gels and wash formulations. Directions for use would fall under FDA's New Acne Monograph.

### 1.1.5 Applicable OTC Monograph

Topical Acne Drug Products for Over-the-Counter Human Use; Final Monograph; Docket No. 81N-0114, (21 CFR 333.301; 56 FR 41008).

## 1.2 PHYSICAL-CHEMICAL CHARACTERISTICS OF ACTIVE INGREDIENT

### 1.2.1 Chemical Names

2,4,4'-trichloro-2'-hydroxydiphenyl ether  
5-chloro-2-(2,4-dichlorophenoxy)phenol

### 1.2.2 Chemical Abstracts Service Number

3380-34-5

### 1.2.3 Molecular Weight

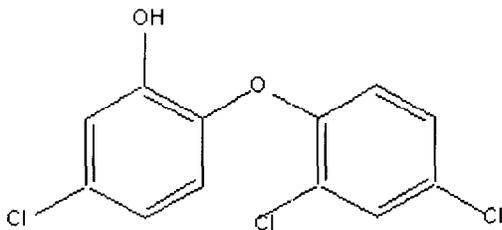
289.6

### 1.2.4 Molecular Formula

$C_{12}H_7Cl_3O_2$

### 1.2.5 Molecular Structure

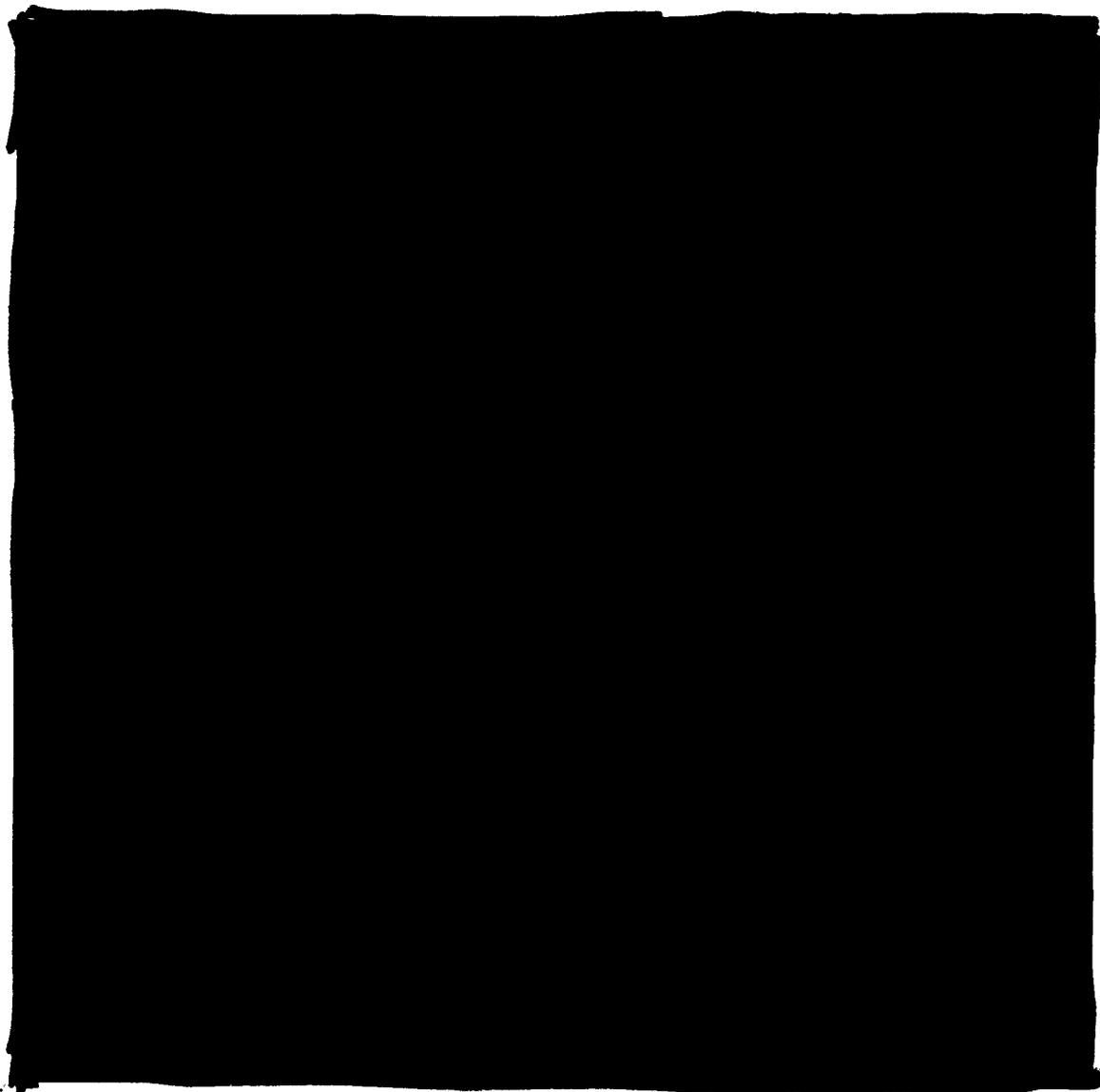
Figure 1. Structure of Triclosan



### 1.2.6 Melting Point

$57 \pm 1^\circ \text{C}$

### 1.2.7 Method of Synthesis and Purification



### 1.2.8 Specifications and Analytical Methods

Specifications for purity are dictated under USP 28 (triclosan). Analytical methods are contained in Ciba's FDA Type II DMF for triclosan (No. 12097) and also available upon request.

## 2.0 MATERIAL TIME AND EXTENT DATA

Triclosan (IRGASAN DP300) is currently incorporated into a variety of consumer acne products worldwide. Table 1 presents a summary of 19 diverse countries where Triclosan has been marketed for acne use for a minimum of five (5) continuous years or more.

**Table 1. Countries where Triclosan Sold or Marketed in OTC Acne Products**

<b>COUNTRY</b>	<b>On Market for a Minimum of 5 Continuous Years</b>
CHINA	YES
FRANCE	YES
GERMANY	YES
INDIA	YES
INDONESIA	YES
JAPAN	YES
KOREA	YES
MALAYSIA	YES
PHILIPPINES	YES
SINGAPORE	YES
SWITZERLAND	YES
TAIWAN	YES
THAILAND	YES
UK	YES
VIETNAM	YES

**Table 1a. Additional countries where Triclosan Sold/Marketed in OTC Acne Products**

<b>COUNTRY</b>	<b>On Market for a Minimum of 5 Continuous Years</b>
AUSTRALIA	YES
BRAZIL	YES
MEXICO	YES
SOUTH AFRICA	YES

## 2.1 Marketing Information

### 2.1.1 Amount of Active Ingredient Sold

Table 2 presents a summary of the amount (Kg) of IRGASAN DP300 (triclosan) sold by country/geographical region in acne products during the past six (6) continuous years.



## 2.2 Estimates of Number of Units Sold and Exposed Populations

Table 4 provides an estimate of the total number of acne product units containing triclosan sold in 19 countries and geographical regions during the past 6 continuous years. From the data in Table 4, it is estimated that over 21 million units of acne products containing triclosan have been sold in these select countries during the past six years. These data are based on actual Ciba sales of IRGASAN DP300 for acne product use and are considered proprietary.

The total number of units sold was derived using the following information: A typical unit size contains approximately 100 grams of acne product. Assuming triclosan is incorporated into such products at an average concentration of 0.3%. It is estimated that one kilogram of triclosan yields approximately 350 units (unit weight: 100 grams) at a formulation concentration of 0.3 %.

Assuming that the estimates derived from Table 4 can be used a surrogate for potential human exposure, it is estimated that approximately 21 million consumers have been exposed to triclosan in acne products during the past six years in the 19 countries selected.

**Table 4. Estimation of Units Sold For Six Continuous Years (1999-2004) in Six Geographic Regions (Millions of Units)**

CONFIDENTIAL BUSINESS INFORMATION: Ciba Specialty Chemicals						
Country	1999	2000	2001	2002	2003	2004
Asia	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Australia	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Brazil	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Europe	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Mexico	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
South Africa	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
TOTALS	4.10	4.06	3.99	3.28	3.22	2.83

Cumulative total across all countries : 21.48 Million Units

## 2.3 Description of population Demographics

It is expected that the population demographics of the countries where triclosan is sold for acne applications are similar to that of the United States.

## 2.4 Use Pattern

The use patterns associated with the majority of global acne products utilizing triclosan as an active ingredient are consistent with those that appear in FDA's acne monograph. In most cases, directions for use and claims for these products appear on the product packaging and containers. Examples of specific product brand claims by country (including active ingredient concentrations) for various acne products are presented in Table 5. Actual examples of product labeling are presented in Appendix 1. Ciba certifies that the label translations presented in Appendix 1 are accurate to the best of its knowledge.

**Table 5a. Summary of Some Typical Leave-on Acne Products, Claims and Triclosan Content Concentrations**

Thailand	Dr. Montri Acne Cream	Anti-acne	Leave-on	1.0
Vietnam	Hazeline Anti-acne cream	Reduces and prevents pimple/acne/blemishes	Leave-on	0.20
South Africa	Oxy Medicated Pads	Dries and clears pimples. Helps kill acne-causing bacteria.	Leave-on	0.20
Germany	Jade Hautklar anti-acne gel	With activity against acne specific claims	Leave-on	0.15
UK	ACT Overnight Prevention Gel	Helps prevent spots	Leave-on	0.10
South Africa	Clearasil Pimple & Acne Cream	For treatment of pimples, acne, and blackheads	Leave-on	0.10

**Table 5b. Summary of Some Typical Rinse-off Acne Products, Claims and Triclosan Content Concentrations**

Australia	pHisohex	For clearer skin and fewer pimples	Rinse-off	1.0
Thailand	Dr. Montri Liquid Soap	Anti-acne	Rinse-off	0.40
Brazil	Clean & Clear Sabonete Liquido Facial	Combats acne causing bacteria	Rinse-off	0.25
Thailand	Bionic Acne Facial Foam	Anti-acne	Rinse-off	0.20
Japan	Clearex Face Wash	Pimple prevention	Rinse-off	0.20
South Africa	Gill Gentle Moisturising Face Wash	To protect skin from bacteria which may cause pimples	Rinse-off	0.20
Mexico	Clean & Clear Jabon Facial	Combats acne causing bacteria	Rinse-off	0.20
Brazil	Salisoap	Adjuvant for acne	Rinse-off	0.20
Thailand	Biore Acne Control	Controls acne	Rinse-off	0.05

## 2.5 Description of Method for Collecting Adverse Drug Experience Data

Most companies selling acne products with triclosan employ a “customer attendance service” system for collecting adverse drug experience data. In general, the systems work as follows.

- Information regarding customer adverse drug experience or information address/telephone number is provided on the product label;
- Acne product company receives a complaint via phone call or mail.
- Company investigates incident and requests that a sample be sent by consumer.
- Sample is analyzed and compared to standard.
- If the sample is okay and without any external interference, company writes a letter to the customer indicating test results with technical information regarding product safety, etc.
- If medical emergency, company provides relevant toxicity information to doctor and pays for doctor to treat the problem. Quality Assurance Department and Customer

Attendance Service Department have all the data related to these complaints in their files to be checked and audited as per GMP.

- Active ingredient manufacturer is advised of serious incidents and follows up accordingly.

To our knowledge, as of the date of this transmittal, there have been no serious or adverse drug experiences filed for any acne products containing IRGASAN DP300 (triclosan).

## **2.6 Prescription Drug information**

All acne products containing IRGASAN DP300 (triclosan) are sold OTC (directly to the consumer) and not via prescription.

## **2.7 Marketing Withdrawals**

There have been no marketing or product withdrawals in any countries where IRGASAN DP300 is used as an active ingredient in acne formulations.

## **2.8 Certification**

The undersigned certifies that, to the best knowledge and belief, this petition includes all information and views on which the petition relies and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

Respectfully Submitted,



Lisa Navarro, Ph.D., D.A.B.T.  
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Home & Personal Care Business Line

### 3.0 APPENDIX: Examples of Acne Product Labels

1. AUSTRALIA	14
a. Clean & Clear Facial Cleansing Bar	
b. Neutrogena Acne Sin Cleanser (Bar)	
c. pHisoHex Anti-Bacterial Face Wash	
d. Young Solution Cleansing Bar	
e. Young Solution Face Wash	
f. Young Solution Oil Controlling Toner	
g. Young Solution Wash Up	
2. BRAZIL	21
a. Clean & Clear Facial Soap (Bar)	
b. Clean & Clear Liquid Facial Soap	
c. Salisoap (Bar)	
3. CHINA	24
a. Clean & Clear Facial Wash	
4. FRANCE	25
a. Garnier Synergie Pure	
5. GERMANY	26
a. Jade Hautklar	
6. INDONESIA	27
a. Biore Antiacne Facial Foam	
7. JAPAN	28
a. Clearex Face Wash	
b. Clearasil Medicated Face Wash	
8. MEXICO	32
a. Clean & Clear Facial Soap (Bar)	
b. Axel Facial Bar	
9. SOUTH AFRICA	34
a. Clean & Clear Facial Cleansing Bar	
b. Clearasil Cream	
c. Cuticura Face Washes	
d. Gill Gentle Moisturising Face Wash	
e. Oxy Face Wash/Medicated Pads	
f. Pond's Lasting Oil Control Face Wash	
g. Pure SOS Anti-Blemish Pen	
10. SWITZERLAND	41
a. Antebor N	
b. Louis Widmer Acne Gel	

11. THAILAND	44
a. Biore Massaging Facial Wash – Acne Control	
b. Bionic Acne Facial Foam	
c. Dr. Montri Acne Cream	
d. Dr. Montri Liquid Soap	
12. UK	48
a. ACT Overnight Protection Gel	
b. Sainsbury’s Skin Deep Medicated Pads	
c. Skin Clear Face Mask	
13. VIETNAM	51
a. Hazeline Anti-Acne Cream	
b. Hazeline Anti-Acne Facial Foam	