

## DRUG DEVELOPMENT

**H** and  20    01  **B**ooks

Drug Development & Manufacture for Pharmaceutical Technology Professions

HANDBOOK OF GENERIC DRUG DEVELOPMENT

**READY-TO-GO™ SERIES**

**Copyright Records**

" TO PROMOTE THE PROGRESS OF SCIENCE AND USEFUL  
ARTS BY SECURING FOR A LIMITED TIME TO AUTHORS AND  
INVENTORS THE EXCLUSIVE RIGHTS TO THEIR WRITINGS  
AND DISCOVERIES "  
(US CONSTITUTION ARTICLE I SECTION 8)



DRUG DEVELOPMENT

Hand 20 Books

Drug Development &amp; Manufacture for Pharmaceutical Technology Professions

# TECHNICAL FILE



# CMC

Part II

# STABILITY

e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES

© 1994-1999 Locum International. All rights reserved.  
01/99 Part No. HBGDPI-II-V1

DRUG DEVELOPMENT

**Hand** 20  **Books**

Drug Development &amp; Manufacture for Pharmaceutical Technology Professions

# TECHNICAL FILE

GENERIC ACTIFED  
Pseudoephedrine 60mg  
Triprolidine 2.5 mg  
IMMEDIATE RELEASE SCORED TABLETS

Lot: 41B612 ; 10699/19 ; 10699/23 ; 167001/497 ; 167002/497  
Lot: BNC644 (200)

# STABILITY

May Contain: Stability Indicating Assay Method + Impurity Profile; SI Method Validation; Dissolution Stability Protocol and 25 & 40° C Profile (NLT 3 Pivotal Batches)

e-HANDBOOK of GENERIC DEVELOPMENT Ready-To-Go™ KNOW-HOW SERIES

Legal, copyright and privacy statement for public access at [www.iagim.org](http://www.iagim.org) and [www.locumusa.com](http://www.locumusa.com)

© 1994-2000 Locum International. All rights reserved.  
01/00 Part No. HBGDPI-II-V1

 **Copyright Records**

<http://www.iagim.org>

# Ready-To-Go™

## 120 plus

### KNOW-HOW

# Series

Ready-To-Go™

### **Expedited CMC for e-mail transmission only**

A complete set of TESTING Specifications is herewith provided for each strength of the solid oral dosage form.

**Pseudoephedrine**

60mg

**Triprolidine**

2.5 mg

IMMEDIATE RELEASE SCORED TABLETS

**Part 1 - Manufacturing CMC**

**- Part II - STABILITY CMC**

IAG172-00

e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES

Electronic version

Available on CD ROM DISKETTE and via E-MAIL ATTACHMENT

 Copyright Records

©2001 [www.iagim.org](http://www.iagim.org)

Legal, copyright and privacy statement for public access at [www.iagim.org](http://www.iagim.org) and [www.locumusa.com](http://www.locumusa.com)



©2001 www.iagim.org

© 1994-2000 Locum International Group. All rights reserved.  
01/00 Part No. HBGDPI-II-V1

" TO PROMOTE THE PROGRESS OF SCIENCE AND USEFUL ARTS BY  
SECURING FOR A LIMITED TIMES TO AUTHORS AND INVENTORS THE  
EXCLUSIVE RIGHTS TO THEIR WRITINGS AND DISCOVERIES "  
(US CONSTITUTION ARTICLE I SECTION 8)

This Print and **e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES** is supplied either in part or full in three formats, namely email version (expedited) or electronic disk or library Print Handbook. Any of the part components or formats complete the overall drug database as ordered and have been updated to **Jan 2001** Office of Generic Drugs regulatory requirements. Ready-To-Go™ end-users as a condition of purchase shall comply with the Copyright and EULA conditions.

The enclosed database is reviewed in **January/April** each year according to the product's update requirements (Stability, Assay, Manufacturing Process update data).

**e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES**  
**Electronic version**  
**Available on CD ROM, Diskette, Online and via E-MAIL ATTACHMENT**

**Warning:**

Copyright © 1994-2001 by Locum Publishing House Inc. - All Rights Reserved. This publication is leased subject to the condition that it shall not, by way of trade or otherwise, be lent, resold, hired-out or otherwise circulated without the publisher's prior consent in any form or binding or cover other than that in which it is published and without a similar condition including this condition being imposed on the subsequent purchaser or lessor. Neither this CD, diskette, ELECTRONIC or PRINT FILE nor any part of the data contained therein may be reproduced, copied or transmitted in any form or by any means, electronic or mechanical, including printing photocopying, microfilming and recording, or by any information storage and retrieval system, without the prior written permission of the publishers. Any person who does any unauthorized act in relation to this publication may be liable to criminal prosecution and civil claims for damages. Legal, copyright and privacy statements for general access at [www.iagim.org](http://www.iagim.org) and [www.locumusa.com](http://www.locumusa.com) The right of IAGIM® [LIG®] to be identified as author of this work has been asserted to the author in accordance with the Copyright Designs and Patents Act 1988.

MAY 2000

™ Trademark - Microsoft Corporation, ™ Adobe Corporation ® Locum Corporation

©2001 www.iagim.org

COPYRIGHT &amp; INTELLECTUAL PROPERTY

## PROTECTED RECORDS

© 1994-2001 Locum International Group. All rights reserved.  
01/00 Part No. HBGDPI-II-V1



## IAG172-00

" TO PROMOTE THE PROGRESS OF SCIENCE AND USEFUL ARTS BY  
SECURING FOR A LIMITED TIMES TO AUTHORS AND INVENTORS THE  
EXCLUSIVE RIGHTS TO THEIR WRITINGS AND DISCOVERIES "  
(US CONSTITUTION ARTICLE I SECTION 8)



USA/CANADA

<http://www.locumUSA.com>  
[handbooks@locumUSA.com](mailto:handbooks@locumUSA.com)

EUROPE/EEU

<http://www.locumEURO.com>  
[handbooks@locumEURO.com](mailto:handbooks@locumEURO.com)

Middle East/Pacific Rim

<http://www.locum.co.il>  
[info@locum.co.il](mailto:info@locum.co.il)

**Copyright Records**

©2001 [www.iagim.org](http://www.iagim.org)

© 1994-2000 Locum International Group. All rights reserved.  
01/00 Part No. HBGDPI-II-V1

## DRUG DEVELOPMENT

**Hand** 20  01  **Books**

Drug Development &amp; Manufacture for Pharmaceutical Technology Professions

This Product presented on either the enclosed Printed version, or CD ROM; Diskette, Email attachment is suitable for viewing in PDF™ is Copyright © 2001 to Locum International Group Ltd. and leased to the purchaser under the conditions that the end-user/customer/client preserves the copyright conditions and EULA Agreement.

I hereby agree, prior to the use of the enclosed data and furthermore by placing my signature to this document to wholly preserve the stated copyright ©2001 and EULA agreement conditions pertaining to the above software electronic or print product and any future updates.

Company  
Responsible Officer

For and on behalf of the purchasing Company

**[FAX OR MAIL BACK THIS PAGE BEFORE USE]**

This Product is © Copyright 1992-2001 to Locum International Group Ltd. and is leased to the end-user on the conditions below (see WARNING) which is contingent on the end-user preserving full copyright conditions and further subject to the standard Locum International EULA agreement which is effective world wide. Failure to sign and return this copyright and EULA agreement form within 3 days of receipt shall invalidate and render null and void all and any future claims by the end-user. Utilising this product, data information or methodology therein in violation of copyright and EULA is prosecutable law under the global GATT and TRIPS agreements. In the United states it is further a felony offence prosecutable by law in all states. Signed for and on behalf of Locum International Group Ltd.

*Jennifer Anne Slemment*

Authorized signature of Locum International marketing director

Warning: Copyright © 1984 -2001 Locum Publishing House Inc. - All Rights Reserved.  
Neither this information nor any part of the data contained therein may be reproduced, copied or transmitted in any form, modification or merged portion or by any means, electronic or mechanical, including printing photocopying, microfilming and recording, or by any information storage and retrieval system, without the prior written permission of the publishers. Legal, copyright and privacy statement for public access at [www.iagim.org](http://www.iagim.org) and [www.locumusa.com](http://www.locumusa.com)

<http://www.locumUSA.com> - <http://www.locumEURO.com>  
<http://www.locum.co.il>  
[research@IAGIM.org](mailto:research@IAGIM.org)  
[info@locum.co.il](mailto:info@locum.co.il)

# PRODUCT MASTER FORMULA

Generic Name: <b>Pseudoephedrine 60mg / Triprolidine 2.5mg Tablets</b>	<h2 style="margin: 0;">IAGIM</h2> Edition No: 02	Signatures ↻ Development	
DEPARTMENT: Granulation & Tableting	Edition Status: Spsds. 01	Validation ↻	
PRECAUTION: Wear mask and gloves <b>CAUTION: 1. Wear Masks with air filters 2. Potent Active Materials</b>	Effective Date: <b>Jan/15/2001</b> Cat. No: <b>IAG-167-2000</b>	Production ↻  Q.A. ↻  R.A. ↻	

CHANGE : No change

Page 1 of 1

BATCH NO.

Weighing Date : \_\_\_\_\_

Per Unit Dose	Ex- cess	Raw Materials 300 000 units	Per 91.220 Kg					Signatures Weighing Depart.	
			kg	g	mg	L	mL	A	B
<b>PART I</b>									
62.0		Lactose Monohydrate NF (200 mesh)	18	600					
2.5		Triprolidine HCl	0	750					
60.0	6.0	Pseudoephedrine HCl	19	800					
<b>PART II</b>									
60.0		Starch NF	18	000					
<b>PART III</b>									
90.0		Lactose Monohydrate NF (200 mesh)	27	000					
<b>PART IV</b>									
-		Purified Water USP (85-95°C)	23	000					
2.3		PVP K-30 (Povidone USP)	0	690					
14.0	1.4	Starch NF	4	620					
<b>PART V</b>									
-		Purified Water USP q.s. (up to 6.0 kg)	qs	000					
<b>PART VI</b>									
5.6		Ac-Di-Sol™ (Croscarmellose Sodium NF)	1	680					
3.6		Magnesium Stearate NF	1	080					
300.0	7.4	Theoretical End Volume	<u>91</u>	<u>220</u>					

10% Excess Starch NF added to compensate the loss of water during the granulation/drying process

ED. NO: 02 Replaces 01	Effective Date:  Jan / 15 / 2001	<b>APPROVED:</b>			
Ed. Status : 02 - EU		Department	R&D	RA	QC / QA



**STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg****PSEUDOEPHEDRINE ASSAY**

**Batch number:** AIG/167-02-597  
**Batch size:** 180,000 tablets  
**Manufacturing date:** 28.04.1997.  
**Storage conditions:** 25°C (±2°) / 60%RH (±5%)  
**Packaging:** Blister: PVC / PVdC film laminate into Aluminium foil.  
**HPLC I Assay:** Pseudoephedrine 60mg/Tab - Percentage of labelled Amount

Page 1 of 4

<b>Parameter</b> 🔄	<b>Test</b>	<b>Specification</b>	<b>T<sub>0</sub></b>		<b>6 month</b>		<b>12 months</b>		<b>24 months</b>		<b>36 months</b>	
<b>Analysis date</b> 🔄	<b>Method</b>	<b>Criteria Accept -Reject</b>	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
<b>Appearance Description Score</b>	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface	
<b>(%) Dissolution labeled amount</b>	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	102.9		102.4		99.7		98.1		101.1	
<b>Assay I (%)</b>	PSD-01404	95.0 - 105.0% of the labelled amount	100.0		100.2		101.0		99.9		99.1	
<b>Impurities/ Degradation Products Determination (%)</b>	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%  Total UNKNOWN	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.09 <0.03 0.04  0.13	<u>RRT</u> 0.93 Imp.E 1.10 Imp.F	<u>%</u> 0.03 0.09 <0.03 0.04  0.16	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.09 <0.03 0.04  0.13	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.06 <0.03 0.02  0.08	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.08 <0.04 0.04  0.15
<b>Total Viable Count</b>	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
<b>Test for specified micro-organism</b>	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

HPLC Assay I Pseudoephedrine HCl 60mg - Percentage of Labelled Amount

HPLC Assay II Triprolidine HCl 2.5 mg - Percentage of Labelled Amount

**STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg**

**TRIPROLIDINE ASSAY**

**Batch number:** AIG/167-02-597  
**Batch size:** 180,000 tablets  
**Manufacturing date:** 28.04.1997.  
**Storage conditions:** 25°C (±2°) / 60%RH (±5%)  
**Packaging:** Blister: PVC / PVdC film laminate into Aluminium foil.  
**HPLC II Assay:** Triprolidine 2.5mg/Tab - Percentage of labelled Amount

Page 2 of 4



<b>Parameter</b> ↻	<b>Test</b>	<b>Specification</b>	<b>T<sub>0</sub></b>		<b>6 month</b>		<b>12 months</b>		<b>24 months</b>		<b>36 months</b>	
<b>Analysis date</b> ↻	<b>Method</b>	<b>Criteria Accept -Reject</b>	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
<b>Appearance Description Score</b>	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface	
<b>(%) Dissolution labeled amount</b>	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	100.3		102.5		100.2		108.9		100.2	
<b>Assay II (%)</b>	PSD-01404	95.0 - 105.0% of the labelled amount	100.9		101.3		100.3		101.1		100.8	
<b>Impurities/ Degradation Products Determination (%)</b>	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D
<b>Total Viable Count</b>	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
<b>Test for specified micro-organism</b>	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

**STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg**

**PSEUDOEPHEDRINE ASSAY**

**Batch number:** AIG/167-02-597  
**Batch size:** 180,000 tablets  
**Manufacturing date:** 28.04.1997.  
**Storage conditions:** 25°C (±2°) / 60%RH (±5%)  
**Packaging:** HDPE Securitainer 30cc round white bottle -Quantum Resin LR-7340-43 - 29mm Techniplex cap  
**HPLC I Assay:** Pseudoephedrine 60mg/Tab - Percentage of labelled Amount

Page 3 of 4

Parameter 	Test	Specification	T <sub>0</sub>	6 month	12 months	24 months	36 months			
Analysis date 	Method	Criteria Accept -Reject	21. May 1997	23. Nov 1997	24. May 1998	20. May 1999	27. May 2000			
<b>Appearance Description Score</b>	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface			
<b>(%) Dissolution labeled amount</b>	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	101.2	102.5	100.3	99.6	100.2			
<b>Assay I (%)</b>	PSD-01404	95.0 - 105.0% of the labelled amount	97.3	98.7	99.3	100.7	100.9			
<b>Impurities/ Degradation Products Determination (%)</b>	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%  Total UNKNOWN	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F  0.13	<u>%</u> <0.03 0.09 <0.03 0.04  0.14	<u>RRT</u> 0.93 Imp.E 1.10 Imp.F  0.14	<u>%</u> 0.03 0.10 <0.03 0.04  0.13	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F  0.10	<u>%</u> <0.03 0.07 <0.02 0.03  0.10	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F  0.13	<u>%</u> <0.03 0.09 <0.03 0.04  0.13
<b>Total Viable Count</b>	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10	- -	< 1000 < 10		< 1000 < 10			
<b>Test for specified micro-organism</b>	Ph.Eur.	Absence of E. coli in 1 g of product	conforms	-	conforms		conforms			

**STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg****TRIPROLIDINE ASSAY**

**Batch number:** AIG/167-02-597  
**Batch size:** 180,000 tablets  
**Manufacturing date:** 28.04.1997.  
**Storage conditions:** 25°C (±2°) / 60%RH (±5%)  
**Packaging:** HDPE Securitainer 30cc round white bottle -Quantum Resin LR-7340-43 - 29mm Techniplex cap  
**HPLC II Assay** Triprolidine 2.5mg/Tab - Percentage of labelled Amount

Page 4 of 4

<b>Parameter</b> 🚫	<b>Test</b>	<b>Specification</b>	<b>T<sub>0</sub></b>		<b>6 month</b>		<b>12 months</b>		<b>24 months</b>		<b>36 months</b>	
<b>Analysis date</b> 📅	<b>Method</b>	<b>Criteria Accept -Reject</b>	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
<b>Appearance Description Score</b>	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface	
<b>(%) Dissolution labeled amount</b>	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	99.4		101.1		100.1		101.2		100.2	
<b>Assay II (%)</b>	PSD-01404	95.0 - 105.0% of the labelled amount	98.4		98.8		99.5		100.9		98.5	
<b>Impurities/ Degradation Products Determination (%)</b>	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D
<b>Total Viable Count (Euro Lot)</b>	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
<b>Test for specified micro-organism</b>	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

HPLC Assay I Pseudoephedrine HCl 60mg - Percentage of Labelled Amount

HPLC Assay II Triprolidine HCl 2.5 mg - Percentage of Labelled Amount .