ZEPHEX®

INDEPENDENT ACCEPTANCE TESTING SERVICE: VERSION 4

Independent Acceptance Testing Service

1. Introduction

It is a requirement of some regulatory authorities (e.g., US FDA) that pharmaceutical companies undertake independent testing as a means to maintain the validity of the supplier's Certificate of Analysis (CofA). This is often referred to as 'acceptance testing'.

Since January 2002 an independent testing service for Zephex® propellants has been offered by LGC Ltd, the UK's leading independent provider of analytical and diagnostic services.

The full range of analytical methods utilised by Koura, in its release testing of Zephex® propellants, is operated by LGC Ltd. This enables generation of independent results for comparison with those listed on Koura's CofA.

2. Validation

Full analytical method transfer has taken place, from Koura methods to LGC methods.

This process is covered in a validation report which can be requested from LGC, providing that a customer has a current confidentiality agreement with LGC.

3. Reporting

Upon completion of the testing, LGC Ltd prepares a CofA, as in Appendix 1, which includes a detailed summary of the results. The results are reported in the exact same way as the Koura CofA, being listed against the Zephex® 'C15' specification.

Strict confidentiality of data is maintained on a customer-by customer basis. Results are only discussed with Koura on the explicit agreement of the pharmaceutical customer.

European Pharmacopeia (Ph. Eur.) Methods & Specification

Koura can confirm compliance with the Ph. Eur methods and specification for Norflurane.

The methods and specification developed by Koura are equivalent, or superior, to that defined in the Ph. Eur. As indicated above, LGC report their results in the exact same way as Koura.

If a Ph. Eur CofA is required, this must be requested at the time of ordering. It should be noted that only Koura can provide a Ph. Eur. CofA format, this against the Ph. Eur. specification. LGC cannot provide a Ph. Eur. CofA format.

4. Requesting the Service

Customers wishing to use this independent acceptance testing service should make the request at the point of placing the order for a Zephex® propellant. Either 'full testing' or 'partial testing' can be performed, although in the latter case it is necessary for the customer to specify which aspects of the specification are to be tested. Koura will add the charge for this testing service to the cost of the product.

5. Testing Frequency

The customer is responsible for defining the frequency of independent acceptance testing, as it is not a regulatory requirement that all incoming material is completely re-tested. Koura can provide guidance for this frequency if required. Independent testing does not replace the need for a customer to do their own incoming checks required by the appropriate regulatory authority (e.g., identity test).

6. About LGC

LGC Ltd has a comprehensive system of quality accreditation, with the Acceptance Testing facilities being certified to various ISO standards including:

- ISO 9001 (business processes)
- ISO 17025 (laboratory testing and calibration standards)
- GLP
- GMP.

For more information see: https://www.lgcgroup.com/about-us/quality-and-compliance/

Appendix 1
Example CofA Version 1

Certificate of Analysis

(Customer Acceptance Analysis)

Name: 1,1,1,2-tetrafluoroethane

Synonyms: HFA 134a
Propellant
134a Zephex
134a

Grade: Pharmaceutical

Printed: 4th May 2019

Sample Ref. No:	19E0006	19E0007	**Batch No:**	RB19722-4
Container:	GLI		**Date Analysis Started:**	1st May 2019
I.D. No(S):	100789-0		**Order No:**	1110013333
Tag Seal (S):	A01814	148026	**Proposal Reference:**	LGC309540
Specification / Issue :	GCK134PGC15 / I13		**Sample Spec. Status:**	Pass

Component	Result Value	Specification	Status
Identity Tests			
Identity by I.R.	Agrees With Std Spectra	Agrees With Std Spectra	Pass
Identity by GC	Agrees With Std Chromatogram	Agrees With Std Chromatogram	Pass
Specified Related Impurities			
125	N/D	<=3 ppm w/w	Pass
22	N/D	<=3 ppm w/w	Pass
12	N/D	<=3 ppm w/w	Pass
124	N/D	<=3 ppm w/w	Pass
133a	N/D	<=3 ppm w/w	Pass
12B1	N/D	<=3 ppm w/w	Pass
115	N/D	<=3 ppm w/w	Pass
143a	N/D	<=10 ppm w/w	Pass
114	N/D	<=3 ppm w/w	Pass
114a	N/D	<=3 ppm w/w	Pass
134	58.6 ppm w/w	<=90 ppm w/w	Pass
Unsaturated Impurities			
1243zf	0.3 ppm w/w	<=5 ppm w/w	Pass
1122	1.6 ppm w/w	<=5 ppm w/w	Pass
C-1122a	0.2 ppm w/w	<=5 ppm w/w	Pass
T-1122a	N/D	<=5 ppm w/w	Pass
T-1131	0.2 ppm w/w	<=5 ppm w/w	Pass
1131a	N/D	<=5 ppm w/w	Pass
1112a	N/D	<=5 ppm w/w	Pass
1123	N/D	<=5 ppm w/w	Pass
1234yf	N/D	<=5 ppm w/w	Pass
1225ye	N/D	<=5 ppm w/w	Pass
1122a	0.2 ppm w/w	<=5 ppm w/w	Pass
Total Unsaturates	2.3 ppm w/w	<=5 ppm w/w	Pass

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Sample Ref. No: 19E0006 19E0007

Component	Result Value	Specification	Status
Any Other Saturated Impurities			
218	N/D	<=3 ppm w/w	Pass
32	N/D	<=3 ppm w/w	Pass
C-318	N/D	<=3 ppm w/w	Pass
152a	0.6 ppm w/w	<=3 ppm w/w	Pass
263fb	N/D	<=3 ppm w/w	Pass
40	N/D	<=3 ppm w/w	Pass
Iso-butane	N/D	<=3 ppm w/w	Pass
31	N/D	<=3 ppm w/w	Pass
123	N/D	<=3 ppm w/w	Pass
123a	N/D	<=3 ppm w/w	Pass
11	N/D	<=3 ppm w/w	Pass
132b	N/D	<=3 ppm w/w	Pass
245cb	0.1 ppm w/w	<=3 ppm w/w	Pass
227ea	N/D	<=3 ppm w/w	Pass
Total Other Saturated Impurities	0.7 ppm w/w	<=10 ppm w/w	Pass
Total Unknowns	N/D	<=3 ppm w/w	Pass
Total Organics	61.6 ppm w/w	<=100 ppm w/w	Pass
134a Purity	99.994 % w/w	>=99.99 % wt	Pass
Other Tests			
Water	3 ppm w/w	<=10 ppm w/w	Pass
Appearance	Clear & Colourless	Clear & Colourless	Pass
High Boiling Impurities	<0.01 % v/v	<=0.01 % v/v	Pass
Malodour	No Malodour Present	No Malodour Present	Pass
Halides	Test Pass	Not detected	Pass
Acidity as HCl	<0.1 ppm w/w	<=0.1 ppm w/w	Pass
Involatile Residue	<1 ppm w/w	<=5 ppm w/w	Pass
Non-Absorbable Gases	0.38 % v/v	<=1.5 % v/v	Pass

Deviations
None.

Compliance Statement
This study has been conducted in compliance with the principles of Good Manufacturing Practice (GMP) as laid down in Directive 2003/94/EC.
Methods used for the analysis were controlled, appropriate and references can be supplied on request.

Additional Information
We certify that this material has been analysed and conforms to the Zephex 134a Specification.
The product was analysed at LGC, Fordham, Cambridgeshire.
The product was manufactured at the Zephex 134a Plant , Rocksavage Site, Runcorn, Cheshire.

Issued By
Laboratory Analyst **Name** ..... **Signature** ..... **Date** .....

Technical Approval **Name** ..... **Signature** ..... **Date** .....

Approved By: **Name** ..... **Signature** ..... **Date** .....

Position: (Deputy) Head of Quality Control

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Author:	Tim Noakes & Richard Greenhough

Amendments from previous issue:
Introduction updated Section 5 added

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