BIOSPECTRA
100 Majestic Way, Bangor, PA 18013 / www.biospectra.us

BioSpectra External Validation Report

Validation Report for the Manufacture of:

6N HCl in IPA

To be Manufactured as the Following Codes:

6N HCl in IPA Bio Pharma and Below Compliance Grades IHCL-4100 Through IHCL-41XX

To be Manufactured at:

BioSpectra, Inc., 100 Majestic Way
Bangor, PA 18013

In Compliance with the Standards of:

IPEC / PQG
Joint Good Manufacturing Practice Guide

Manufactured to be Suitable for Use as:

GMP Manufactured Chemical

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1. INTRODUCTION:

The validation of a manufacturing process used to produce an IPEC Compliant GMP Manufactured Chemical is a requirement under IPEC Guidelines. This External Validation Report summarizes the execution of validation protocol for the Manufacturing of 6N HCl in IPA – Formosa Gas, 6N HCl in IPA Validation Protocol – Formosa Gas, DCN: BSI-PRL-0582, for three batches of 6N HCl in IPA Solution manufactured in Process Room N02 of Zone N at the BioSpectra, Bangor, PA facility. The objective of validation study was to demonstrate that the manufacturing process for 6N HCl in IPA utilizing Formosa Gas is a controlled and validated process capable of consistently producing material that meets pre-established specifications and critical quality attributes.

This 6N HCl in IPA validation was a Concurrent Validation to validate the process performed in Process Room N02 to ensure that the 6N HCl in IPA Bio Pharma Grade process continues to conform to the pre-developed validation parameters after the approval and implementation of one issued change controls since the last validation. A Concurrent Validation is a Validation Study in which the batches can be released for commercial distribution based on the monitoring and analysis of the lot.

2. OBJECTIVE:

The objective of this Validation Report is to verify and assure that the manufacturing process for 6N HCl in IPA Bio Pharma Grade in Bangor's process room N02 consistently produces material that meets a set of pre-determined specifications as listed in Table 1 and quality attributes. This validation was performed due to change controls BCC22-58, Additional Anhydrous Hydrogen Chloride Gas Manufacturer, to add an additional manufacturer of Anhydrous Hydrogen Chloride (AHCl), Formosa Plastics, who Airgas USA LLC will utilize to fill cylinders.

The Validation batches of 6N HCl in IPA were manufactured according to the current revision of the Batch Record. Once the manufacture of the batches was completed, representative samples were submitted to the QC Laboratory and were tested against Finished Good specifications. This was conducted to verify that the process is capable of consistently producing material that meets Finished Good Specifications.

3. SCOPE:

This Report applies to the manufacturing process for 6N HCl in IPA Bio Pharma Grade which includes the following process steps: charging the raw materials, recirculating, filtering, packaging, and the testing of the finished goods. Specifications and approval requirements for all Raw Materials (RM) and components have been created; therefore, these RM and components are not covered by this Report except that only approved RM and components were used.

4. REFERENCES:

4.1. BSI-MPR-0020, 6N HCl in IPA Batch Record

4.2. BSI-PRL-0160, Degradation and Impurity Profile Protocol: 6N HCl in IPA

4.3. BSI-PRL-0582, 6N HCl in IPA Validation Protocol – Formosa Gas

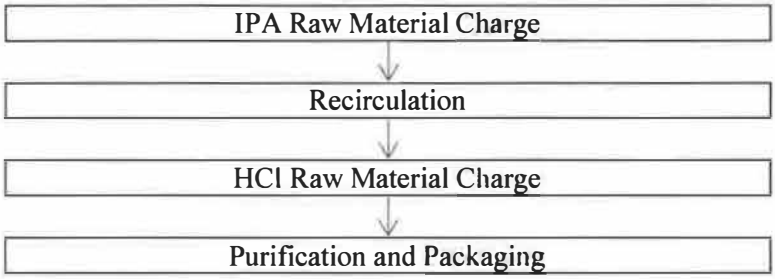
4.4. BSI-RPT-1354. Degradation and Impurity Profile Report: 6N HCl in IPA (Formosa Gas)

5. EXECUTIVE SUMMARY:

The 6N HCl in IPA manufacturing process is a manufacturing/purification process with Critical Process Parameters as detailed in the Validation Protocol. The CPP's were developed based on prior validation studies and the FMEA analysis conducted for the process and were found to be in accordance with BioSpectra's Manufacturing Process Validation Master Plan. The utilities and process used in the manufacture of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The manufacturing of the validation batches for this validation study were deemed successful when following the current 6N HCl in IPA Batch Record and CPP parameter values detailed in the Validation Protocol. The finished goods batches will be released in accordance with the Validation protocol based on the approval of the manufacturing records and associated quality control testing.

6. PROCESS FLOW DIAGRAM:

6N HCl in IPA Process Flow Diagram



7. ANALYSIS:

The three 6N HCl in IPA validation batches manufactured in accordance with the current 6N HCl in IPA Bio Pharma Grade Batch Record, DCN: BSI-MPR-0020 has met the BioSpectra analytical requirements associated with Finished Good Release Code IHCL-4101. The results can be found in Table 2.

Table 1: Critical Quality Attributes Results from the Current Validation

CQA	Test Method	Specification
Purity	Appearance and Color	Clear, Colorless to slightly yellowish fuming liquid
	Assay (Acid Titration)	> 5.9 N
Impurity	Identification (Chloride)	Passes Test

Table 2: Composite CQA Testing Results for IHCL-4101 Product Code

Validation Batch Composite Sample CQA Results				
Analysis	**Specification**	**IHCL-0122-00013-PV**	**IHCL-0122-00014-PV**	**IHCL-0122-00015-PV**
Appearance and Color	Clear, Colorless to slightly yellowish fuming liquid	Clear, Colorless to slightly yellowish fuming liquid	Clear, Colorless to slightly yellowish fuming liquid	Clear, Colorless to slightly yellowish fuming liquid
Assay (Acid Titration)	≥ 5.9 N	6.0 N	6.2 N	6.1 N
Identification (Chloride)	Passes Test	Passes Test	Passes Test	Passes Test

8. ADDITIONAL INFORMATION:

8.1. Degradation and Impurity Profile

8.1.1. A Degradation and Impurity profile was performed for this validation in accordance with Degradation and Impurity Profile Protocol, DCN: BSI-PRL-0160. The degradation and impurity profile will be reported on in the Degradation and Impurity Profile Report, BSI-RPT-1354.

8.2. Stability Study

8.2.1. The Stability Analysis for 6N HCl in IPA consists of an evaluation of the following analyses and associated specifications detailed in Table 3. These analyses were selected based on the finished goods requirements. The Stability analyses and specification criteria is listed below. Each validation batch is placed on the Stability program.

Table 3: Stability Analysis

Analysis	Stability Specification
Appearance and Color	Clear, Colorless to slightly yellowish fuming liquid
Assay (Acid Titration)	≥5.9 N
Identification (Chloride)	Passes Test

9. CONCLUSION:

BioSpectra has successfully manufactured and validated the 6N HCl in IPA manufacturing process in Process Room N02 to be compliant with key compliance grades up to and including the Bio Pharma grade. This Bio Pharma grade classification requires that the material be manufactured in accordance with IPEC/PQG Joint Good Manufacturing guidelines to be suitable for use as a GMP manufactured chemical. The results obtained during this validation study and subsequent analysis provide evidence that the 6N HCl in IPA manufactured using the approved process will consistently meet the approved specifications. The utilities and process used in the manufacture of this product have been qualified in accordance with BioSpectra's Equipment Qualification Master Plan. The results reported from the validation batches of 6N HCl in IPA for this validation study provided the evidence necessary to confirm that the process for 6N HCl in IPA is a validated process capable of consistently producing Bio Pharma Grade material that meets Finished Good Specifications (IHCL-4101).

All Raw Materials used for the processing of 6N HCl in IPA were approved before use in accordance with RM specifications. The Validation samples of 6N HCl in IPA will be placed into Long Time Stability and will be reported on annually. The data obtained from the Stability Study will be utilized to continue to support the current retest date.