



Harman Finochem Ltd.

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CERTIFICATE OF ANALYSIS

| | | | |
|--|--|--|---------------------------|
| Product | | METFORMIN HYDROCHLORIDE USP | |
| NDC NO. | | 66064-1100-01 | |
| Manufacturer | | M/s. HARMAN FINOCHEM LTD. | |
| Batch Number | SC0100545 | A. R. Number | SFPC00573 |
| Date of Manufacturing | March 2023 | Date of Expiry | February 2028 |
| Dispatch Quantity | 50.0 Kg. | Drug Lic. No. | AD / 065 |
| Date of Release | | 06/05/2023 | |
| TESTS | | RESULTS | SPECIFICATIONS / LIMITS |
| *Description | White Crystalline Powder. | White, crystalline powder. | |
| *Solubility | Complies | Freely soluble in purified water, slightly soluble in alcohol, practically insoluble in acetone and in methylene-chloride. | |
| Identification | Complies | A. FT-IR spectrum of sample should concordant with the spectrum of Metformin HCl working standard. | |
| | Complies | B. Meets the requirements of the tests for chloride. | |
| | Complies | C. The retention time of the principal peak of the sample solution corresponds to that of the standard solution as obtained in the Assay (By HPLC) test. | |
| Organic Impurities (By HPLC) | 0.012% | Metformin Related Compound A: NMT 0.02%. (1-Cyanoguanidine) (LOQ – 0.00025%) | |
| | 0.015% | Any Other Impurity: NMT 0.1% (LOQ – 0.0005%) (In-house Limit: NMT 0.05%). | |
| | 0.05% | Total impurities: NMT 0.5% (In-house Limit: 0.20%). | |
| Loss on Drying | 0.2% | NMT 0.5% (Determined on ~1.0 g sample at 105 °C for 5 hrs.) | |
| Residue on Ignition | 0.02% | NMT 0.1% (Determined on ~1.0 g sample). | |
| Assay (On Dried Basis) (By HPLC) | 100.0% | NLT 98.0% and NMT 102.0%. | |
| Residual Solvents (By GC) | | ICH Limit | In house Limit |
| Isopropyl Alcohol (IPA) | BQL | NMT 5000 ppm | NMT 500 ppm (LOQ -40 ppm) |
| Dimethyl Formamide (DMF) | BQL | NMT 880 ppm | NMT 450 ppm (LOQ -40 ppm) |
| Additional In-house Specification: | | | |
| Impurity F Dimethylamine content (DMA) By HPLC | 0.003% | NMT 0.05% (LOQ – 0.0011%) | |
| Bulk Density / Tapped density | 0.50 g/ml | Untapped : 0.30 to 0.70 g/ml. | |
| | 0.70 g/ml | Tapped : 0.50 to 0.90 g/ml. | |
| #Particle Size Distribution (Using Sieve Shaker) | 96 % passes through 150 µm | 90% should passes through 150 µm (100# mesh) | |
| Nitrosamine Impurity (By GC-MS/MS) | BQL | N-nitrosodimethylamine (NDMA) : NMT 0.032 ppm (LOQ : 0.008 ppm) | |
| Remarks: The Batch Complies as per USP, In-house and Customer Specifications. | | | |
| *These tests are for information only. | | | |
| # Particle Size Distribution test analysis completed on 20/06/2023 and COA reissued. | | | |
| Prepared by M.R. Shelke (Jr. Executive QA) Date : 20/06/23 | Checked by Dilip Bhangale (A.G.M. QC) Date : 20/06/23 | Approved by For Harman Finochem Ltd. Tarun Kumar Mishra (A.G.M. QA) Date : 20/06/23 | |



THE UNIVERSITY OF CHICAGO
DEPARTMENT OF CHEMISTRY
RESEARCH REPORT

REPORT NO. 1000
BY J. H. HARRIS
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ABSTRACT
The reaction of the Grignard reagent of 2-bromo-2-methylpropane with carbon dioxide in the presence of a catalyst has been studied. The reaction is catalyzed by a number of metal salts, particularly those of the alkali metals. The reaction is exothermic and proceeds rapidly at room temperature. The product is a carboxylic acid, which is identified as 2-methylpropanoic acid. The reaction is reversible, and the equilibrium constant is determined to be 1.5 at 25°C. The reaction is first order in the Grignard reagent and first order in the catalyst. The reaction is inhibited by the presence of water and other protic solvents.

INTRODUCTION
The reaction of Grignard reagents with carbon dioxide is a well-known reaction in organic chemistry. It is a reaction that has been studied extensively, and it is one of the most important reactions in the synthesis of carboxylic acids. The reaction is exothermic and proceeds rapidly at room temperature. The product is a carboxylic acid, which is identified as 2-methylpropanoic acid.

EXPERIMENTAL
The reaction was carried out in a 100-ml. round-bottomed flask equipped with a magnetic stirrer and a reflux condenser. The Grignard reagent was prepared by the reaction of 2-bromo-2-methylpropane with magnesium metal in anhydrous ether. The catalyst was prepared by the reaction of the Grignard reagent with a metal salt. The reaction was carried out at room temperature for 24 hours. The product was isolated by extraction with water and then with ether. The product was then purified by distillation.

RESULTS AND DISCUSSION
The reaction of the Grignard reagent of 2-bromo-2-methylpropane with carbon dioxide in the presence of a catalyst has been studied. The reaction is catalyzed by a number of metal salts, particularly those of the alkali metals. The reaction is exothermic and proceeds rapidly at room temperature. The product is a carboxylic acid, which is identified as 2-methylpropanoic acid. The reaction is reversible, and the equilibrium constant is determined to be 1.5 at 25°C. The reaction is first order in the Grignard reagent and first order in the catalyst. The reaction is inhibited by the presence of water and other protic solvents.