

## 10286 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

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| STANDARD FORM 33, JULY 1963<br>GENERAL SERVICE ADMINISTRATION<br>GSA FPMR (41 CFR) 101-11.6 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | CONTINUATION SHEET |      | REP. NO. OF DOC. BEING CONTD. |        | PAGE |  | OF |  |
|                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                    |      | DSA 120-71-R-2364             |        |      |  |    |  |
| NAME OF OFFICE OR CONTRACTOR                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 March 1971       |      |                               |        |      |  |    |  |
| ITEM NO.                                                                                    | SUPPLIES/SERVICES                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | QUANTITY           | UNIT | UNIT PRICE                    | AMOUNT |      |  |    |  |
|                                                                                             | The following addition to the U.S.P. dissolution test is applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                    |      |                               |        |      |  |    |  |
|                                                                                             | <u>Determination of meprobamate in dissolution medium.</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                    |      |                               |        |      |  |    |  |
|                                                                                             | Internal standard solution. Transfer about 25 mg. of U.S.P. Phenacetin Reference Standard, accurately weighed to a 50-ml. volumetric flask. Add methylene chloride to volume and mix.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                    |      |                               |        |      |  |    |  |
|                                                                                             | Standard preparation - Transfer about 50 mg. of U.S.P. Meprobamate Reference Standard, accurately weighed, to a 50-ml. volumetric flask. Add methylene chloride to volume, and mix.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                    |      |                               |        |      |  |    |  |
|                                                                                             | Sample preparation - Withdraw a 10 ml. aliquot of the filtered dissolution medium after 30 minutes of rotation and transfer it to a 60 ml. separatory funnel containing 15 ml. of methylene chloride. Add two drops of sulfuric acid, shake vigorously, allow the layers to separate, and filter the organic layer through about 4 grams of anhydrous sodium sulfate suitably supported in a funnel. Repeat the extraction two additional times collecting the combined extracts in a suitable beaker. Evaporate to small volume with the aid of a stream of nitrogen and gentle warming and transfer to a small conical centrifuge tube or other suitable vessel, with the aid of additional small portions of methylene chloride and evaporate to dryness. Add, by pipette, 2.0 ml. of the internal standard solution. Dissolve the residue and mix.                                                                                                                                                                                                                                                                                                                                                               |                    |      |                               |        |      |  |    |  |
|                                                                                             | Standard Curve - Pipet into separate conical centrifuge tubes or suitable vessels, duplicate 1-, 3-, and 5- ml. portions, respectively of Standard preparation, and evaporate to dryness. Add, by pipette, 2.0 ml. of the Internal standard solution to each of the tubes and dissolve the residue. Inject 2.0 ml. from each solution, successively, into a suitable gas chromatograph (see page 793) equipped with a flame ionization detector. Under typical conditions, the instrument contains a 1.2 meter x 4- mm glass column packed with 3 percent (w/w) methylphenyl-silicone oil (OV-17) on 80 to 100-mesh silanized, acid-washed, flux-calcined siliceous earth suitably cured (see page 794). Maintain the column at 100° and maintain the injection port and detector at 170°. Use helium as the carrier gas, at a flow of 70 ml. per minute. Measure the heights, $H_p$ and $H_m$ , of the phenacetin and meprobamate peaks, respectively, in each chromatogram, and calculate the ratio $R_s$ , by the formula $H_m/H_p$ . Plot the standard curve of the values of $R_s$ against the amount, in mg. of U.S.P. Meprobamate Reference Standard contained in each portion of Standard preparation taken. |                    |      |                               |        |      |  |    |  |
|                                                                                             | Procedure - Inject 2.0 ml of Analysis preparation into the chromatograph, and obtain a chromatogram as directed under Standard curve. Measure the height of the meprobamate and phenacetin peaks, and calculate the ratio, $R_u$ , of the height of the meprobamate peak to that of phenacetin. Read from the Standard curve the quantity, in mg. of $C_{10}H_{18}N_2O_4$ , in the volume of the dissolution medium taken.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                    |      |                               |        |      |  |    |  |
|                                                                                             | 522                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                    |      |                               |        |      |  |    |  |