1.3.1 SUMMARY PRODUCT CHARACTERISTICS (SmPC)

<table>
<tr><td>1</td><td>Name of the Finished Medicinal Product:</td></tr>
<tr><td>1.1</td><td>Product Name: Colecalciferol Injection BP 600000 IU/ml</td></tr>
<tr><td>1.2</td><td>Strength : 600000 IU/ml</td></tr>
<tr><td>1.3</td><td>Pharmaceutical Form: Injection</td></tr>
<tr><td>2</td><td>Qualitative and Quantitative Compositions:</td></tr>
<tr><td></td><td>Qualitative Declaration:
Active component
INN Name: Colecalciferol BP
Quantitative Declaration:
Each ml contains:
Colecalciferol BP …….600000IU

<table>
<tr><th>Sr. No.</th><th>Content Name</th><th>Quality Standard</th><th>Qty mg/ ml</th></tr>
<tr><td>1</td><td>Colecalciferol</td><td>BP</td><td>15.00</td></tr>
<tr><td>2</td><td>Butylated Hydroxy Toluene</td><td>BP</td><td>0.30</td></tr>
<tr><td>3</td><td>Butylated Hydroxy Anisole</td><td>BP</td><td>0.30</td></tr>
<tr><td>4</td><td>Vitamin E Acetate (Tocopheryl Acetate)</td><td>BP</td><td>1.00</td></tr>
<tr><td>5</td><td>Diethylene Glycol Monoethyl Ether (Transcutol H.P.)</td><td>BP</td><td>q.s. to 1.00ml</td></tr>
</table>

Note : 40000 IU Colecalciferol BP equivalent to 1mg Colecalciferol BP.
BP: British Pharmacopoeia.</td></tr>
<tr><td>3</td><td>Pharmaceutical Form: Injection
Almost clear colourless transparent liquid.</td></tr>
<tr><td>4</td><td>Clinical Particulars:</td></tr>
<tr><td>4.1</td><td>Therapeutic Indications:

Colecalciferol Injection BP 600000 IU/ml is indicated in prevention and treatment of Vitamin D deficiency states.</td></tr>
<tr><td>4.2</td><td>Posology and Method of Administration
The dosage is determined by the desired Vitamin D levels. Colecalciferol Injection BP 600000 IU/ml can be given once or as directed by the physician by intramuscular injection.
Method of administration: Intramuscular</td></tr>
<tr><td>4.3</td><td>Contra-indications: Known hypersensitivity to Vitamin D, hypercalcemia, abnormal sensitivity to the toxic effects of vitamin D, hypervitaminosis D.</td></tr>
<tr><td>4.4</td><td>Special warning and precautions for use:
Excessive intake may lead to development of hyperphosphataemia or hypercalcaemia. Infants, renal impairment or calculi, heart disease. Monitor plasma phosphate and calcium level.</td></tr>
</table>

4.5	**Interaction with other drugs, other forms of interactions:** Mineral Oil, Cholestyramine, Colestipol: Intestinal absorption of Vitamin D may be impaired when co-administered. Thiazides Diuretics: Concurrent administration of thiazide diuretics and Vitamin D to hypoparathyroid patients may cause hypercalcemia which may be transient or may require discontinuation of vitamin D. Antiepileptic (e.g. carbamazepine, phenobarbitone, phenytoin and primidone): may increase Vitamin D requirements. Rifampicin and Isoniazid : May reduce efficacy of Vitamin D. Corticosteroids : May counteract the effect of Vitamin D.
4.6	**Usage in pregnancy& Lactation** **Pregnancy** The use of Vitamin D in excess of the recommended dietary allowance during normal pregnancy should be avoided unless, in the judgment of the physician, potential benefits in a specific case outweigh the significant hazardous involved. **Lactation** Vitamin D is distributed into breast milk and concentration appears to correlate with the amount of Vitamin D in the serum of exclusively breast-fed infants hence its use should be weighted against the risks involved.
4.7	**Effects on ability to drive and operate machine:** It is unlikely to cause any effect on driving or on operate machinery. No impairment of mental ability has been reported.
4.8	**Undesirable effects:** Vitamin D analogs are well tolerated in normal daily doses. Chronic excessive dosing can lead to toxicity and hypervitaminosis D.
4.9	**Overdose :** Symptoms: Acute intoxication with vitamin D analogues may cause hypervitaminosis D (See Warning and precautions). Treatment: Treatment of acute chronic intoxication includes withdrawal of the vitamin D analogues and any calcium supplements, administration of oral or IV fluids and possibly corticosteroids or calciuric diuretics such as furosemide and ethacrynic acid. Peritoneal or hemodialysis with calcium free dialysate will help remove calcium. If acute ingestion is recent, gastric lavage or emesis may minimize further absorption. If the drug has already passed through the stomach, administration of mineral oil may promote faecal elimination. Hypocalcaemia is usually reversible; however if metastatic calcification has occurred, severe renal or cardiac failure or even death may result.
5	**Pharmacological Properties:**
5.1	**Pharmacodynamics Properties:** **Clinical Pharmacology** Colecalciferol, also called as Vitamin D3, is produced naturally by ultraviolet irradiation of the provitamin, 7-dehydrochlolesterol (a precursor of Vitamin D) in the skin. Absorbed Colecalciferol requires metabolic activation. The circulating vitamin undergoes hydroxylation in the liver with the help of the enzyme, Vitamin D 25-hydroxylase to form 25-hydroxy Colecalciferol (calcidiol), which is the predominant circulating metabolite.

	Further hydroxylation in the kidneys (in response to the need for phosphorus and calcium) forms 1, 25-dihydroxy Colecalciferol (calcitriol) with the help of 1 alpha –hydroxylase. Calcidiol possesses some intrinsic activity, but calcitriol is the most active Vitamin D metabolite with respect to initiating intestinal transport of calcium and phosphate and mobilizing calcium from bone. Calcitriol may prevent phosphaturia by inhibiting parathyroid hormone secretion. Conversion to calcitriol, as well as decreases in serum inorganic phosphate levels is stimulated by the parathyroid hormone. Reduced renal conversion of calcidiol to calcitriol contributes to altered calcium haemostasis and osteodystrophy in uraemia.
5.2	**Pharmacokinetic Properties:** **Absorption :** Vitamin D is well absorbed from the GI tract. Presence of bile is essential for adequate intestinal absorption. After intramuscular administration it gets rapidly absorbed into the systemic circulation. **Distribution :** Vitamin D and its metabolites circulate in the blood, bound to a specific alphaglobulin. Vitamin D can be stored in adipose and muscle tissue for long periods of time. It is slowly released from such storage sites and from the skin where it is formed in the presence of sunlight or ultraviolet light. Colecalciferol has a slow onset and a long duration of action. **Metabolism :** Colecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxy Colecalciferol. It is then further converted in the kidneys to 1, 25-dihydroxy Colecalciferol. 25-dihydroxyl Colecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D that is not metabolized is stored in adipose and muscle tissues. **Elimination :** Vitamin D compounds and their metabolites are excreted mainly in the bile and faeces with only small amounts appearing in urine.
5.3	**Pre-clinical Safety Data:** Pre-clinical studies conducted in various animal species have demonstrated that toxic effects occur in animals at doses much higher than those required for therapeutic use in humans. In toxicity studies at repeated doses, the effects most commonly reported were increased calciuria and decreased phosphaturia and proteinuria. Hypercalcaemia has been reported in high doses. At doses equivalent to those used therapeutically, Colecalciferol has no teratogenic activity. Colecalciferol has no potential mutagenic or carcinogenic activity.
6	**Pharmaceuticals Particulars:**
6.1	**List of Excipients:** Butylated Hydroxyl Toluene BP Butylated Hydroxyl Anisole BP Vitamin E Acetate (Tocopheryl Acetate) BP Diethylene Glycol Monoethyl Ether BP (Transcutol H.P)
6.2	**Incompatibilities:** Not Applicable
6.3	**Shelf Life:** 24 Months

6.4	**Special Precaution for Storage:**
6.5	**Nature and Contents of Container:** Colecalciferol Injection BP 600000IU/ml is packed in 1ml USP Type I amber ampoule with yellow ring. 5 such ampoules are available in a PVC tray packed in a carton along with pack insert.
6.6	**Special Precautions for Disposal:** Not applicable
7	**Registrant:** **Marketing Authorization Holder:** **M/s PHILLIPS PHARMACEUTICALS (NIGERIA) LTD.** Address : Afprint Industrial Estate, Plot 122-132, Apapa Oshodi Expressway Lagos Country : Nigeria. Telephone : +234 806761764 Fax : --- E-mail : --- **Manufacturing Site Address:** **M/s THEMIS MEDICARE LIMITED** Sector 6A, Plot No. 16, 17 & 18, IIE, SIDCUL, Haridwar – 249 403, Uttarakhand, INDIA. Telephone: 91-1334-239321/22 Fax: 91-334-239217 E-mail: hwdgmtech@themismedicare.com
8	**Date of Revision of the Text:** Not Applicable
9	**Dosimetry (if applicable):** Not Applicable
10	**Instruction for preparations of Radiopharmaceutical (if applicable):** Not Applicable