Note AGFAR#s: 161549

浙江华海药业股份有限公司
HUAHAI ZHEJIANG HUAHAI PHARMACEUTICAL CO.,LTD.

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CERTIFICATE OF ANALYSIS

Product name	Captopril		
Batch no.	5102-16-030	Batch Size	300.34Kg
Batch Type	Commercial	Report Date	2016-06-22
Retest Date	2019-05	Storage Condition	Preserved in a well-closed container
Manufacture Date	2016-06-08	Manufacture Site	Xunqiao,Linhai,Zhejiang,317024 China.
Reference	EP8 Specification		
Test Items	Specifications		Results
Appearance	White or almost white crystalline powder		White crystalline powder
Solubility	Soluble in water, freely soluble in methanol and in methylene chloride, it dissolves in dilute solutions of alkali hydroxides.		Conforms
Identification	Specific optical rotation: -127~-132°		-131°
	Infrared absorption spectrum concordant with spectrum obtained with captopril CRS.		Conforms
Appearance of Solution S	Clear and colorless		Clear and colorless
pH	2.0~2.6		2.4
Related substances (HPLC)	Impurity A ≤ 1.0%		0.14%
	Impurity B ≤ 0.15%		N.D
	Impurity C ≤ 0.15%		N.D(LOD=0.01%)
	Impurity D ≤ 0.15%		N.D
	Impurity E ≤ 0.15%		N.D(LOD=0.02%)
	Impurity J ≤ 0.20%		<LOD(LOD=0.006%)
	Any unspecified impurity ≤ 0.10%		<LOQ(LOQ=0.05%)
	Total Impurities ≤ 1.2%		0.14%
Related Substances (GC)	Impurity F ≤ 0.2%		0.08%
Heavy Metals	≤20ppm		<20ppm
Loss on Drying	≤1.0%		0.1%
Sulphated Ash	≤0.2%		0.1%
Assay (Titration)	98.0~101.5% (calculated on dried basis)		100.0%
Conclusion	Complies with EP8 Specification		

Signature : Lin zhenghui (QC manager) Issued Date: 2016.06.22

Signature : Zhao Xiaohong (QA manager) Issued Date: 2016.06.23

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CONFIRMATION ON RESIDUAL SOLVENTS IN ACTIVE AND INACTIVE SUBSTANCES ACCORDING TO GUIDELINE CPMP / ICH / 283 / 95

We, (*name of manufacturer*) Zhejiang Huahai Pharmaceutical Co., Ltd.
hereby confirm that the (*active substance / inactive substance*) Captopril
(*material name*) (2S)-1-[(2S)-2-methyl-3-sulphanylpropanoyl]pyrrolidine-2-carboxylic acid
is evaluated according to "Note for Guidance on Impurities: Residual Solvents"(CPMP / ICH / 283 / 95) as follows:

1. Are Class 1 solvents (see Table 1 of the guideline) likely to be present according to the above mentioned Guideline?
"Likely to be present" refers to the solvent used in the final manufacturing step and to solvents that are used in earlier manufacturing steps and not removed consistently by a validated process.

Yes ☐ No ■

If yes, please list the solvents concerned and their maximum concentration in the material:

Name of Class 1 solvent	Maximum concentration (ppm)

2. Are Class 2 solvents (see Table 2 of the guideline) likely to be present? "Likely to be present " refers to the solvent used in the final manufacturing step and to solvents that are used in earlier manufacturing steps and not removed consistently by a validated process.

Yes ☐ No ■

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If yes, please fill in the following information:

Name of Class 2 solvent	Concentration Limit as listed in Table 2 of the guideline (ppm)	Material complies with this Conc. Limit (yes/no)	If no, please state the maximum concentration (ppm)

3. Are Class 3 solvents (see Table 3 of the guideline) likely to be present?
"Likely to be present" refers to the solvent used in the final manufacturing step and to solvents that are used in earlier manufacturing steps and not removed consistently by a validated process.

Yes ☐ No ■

If yes, loss on drying is less than 0.5 %

Yes ☐ No ☐

If no, please fill in the following information:

Name of Class 3 solvent	Maximum concentration (ppm)

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4. Are any other solvents likely to be present (e.g. solvents that are listed in Table 4 of the referred guideline)?
"Likely to be present" refers to the solvent used in the final manufacturing step and to solvents that are used in earlier manufacturing steps and not removed consistently by a validated process.

Yes ☐ No ■

If yes, please list the name of the solvents:

Responsible Person: Lucy Liu

Function: Manager of Regulatory Affairs, API Group

Linhai, March 26, 2012
Place, Date

Signature of Responsible Person