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February 11, 2004

Dockets Management Branch  
Food and Drug Administration  
Department of Health and Human Services  
Room 1061, HFA-305  
5630 Fishers Lane  
Rockville, Maryland 20852

**RE: Fludarabine Phosphate  
Injection, 25 mg/mL**

**Docket No. 02P-0245/CP1**

On May 28, 2002, the undersigned submitted a Petition under the provisions of the Federal Food, Drug and Cosmetic Act, Section 505(j)(2)(c) and 21 CFR § 314.93, 10.20 and 10.30 to request the Commissioner of Food and Drugs to allow submission of an abbreviated new drug application (ANDA) for Fludarabine Phosphate Injection, 25 mg/mL, in a ready-to-use solution for injection.

At the time our petition was initially submitted, a request for a full waiver of pediatric studies for the proposed Fludarabine Phosphate Injection product as a treatment for B-cell chronic lymphocytic leukemia (CLL) was provided.

Pursuant to my conversation with Ms. Cecelia Parise, Regulatory Policy Advisor to the Director, Office of Generic Drugs, a request for a full waiver of pediatrics studies is being resubmitted.

A full waiver of pediatric studies for the proposed Fludarabine Phosphate Injection product is requested because it is impossible or highly impractical to conduct the necessary studies of this drug in a pediatric population due to the extremely small size of the affected population (i.e., nil occurrence of CLL in the population under 20 years of age).

**Request for Full Waiver of Pediatric Studies Requirement**

FDA regulations require that "each application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration" must contain "data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric populations..." Federal Food, Drug, and Cosmetic Act, Section 505B (Pediatric Research Equity Act).

Since the suitability petition requested permission to submit an ANDA for a new dosage form, this new dosage form may be subject to the pediatric studies requirement.

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Accordingly, the undersigned hereby requests a full waiver of that requirement for the proposed product under the Federal Food, Drug, and Cosmetic Act, Section 505B.

FDA may waive the pediatric study requirements for some or all pediatric age groups if it determines that:

- (i) The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used in a substantial number of pediatric patients,
- (ii) Necessary studies are impossible or highly impractical because, e.g., the number of such patients is so small or geographically dispersed, or
- (iii) There is evidence strongly suggesting that the drug product would be ineffective or unsafe in all pediatric age groups.

The undersigned requests this waiver in accordance with Federal Food, Drug, and Cosmetic Act, Section 505B because it is impossible or highly impractical to conduct the necessary studies for this drug in a pediatric population due to the extremely small size of the affected population (i.e., nil occurrence of CLL in the population under 20 years of age).

According to the National Cancer Institute SEER Cancer Statistics Review 1973-1999 (refer to the attached data), about 10,800 Americans will develop lymphocytic leukemia. Our research concluded that approximately 30 percent of CLL cases occur among men and women 65 – 74 and 74 – 84 years of age (representing a combined total of approximately 60 percent of CLL cases). Our research also showed nil occurrence of CLL among men and women under 20 years of age.

We trust you will find the information satisfactory for your review and approval. Should you have any questions or require further clarification, please contact me at (949) 455-4724.

Sincerely,



Elvia O. Gustavson  
Director, Regulatory Affairs

*SICOR Pharmaceuticals, Inc.*  
*FLUDARABINE PHOSPHATE INJECTION, 25 mg/mL*  
*Docket No. 02P-0245/CP1*

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**National Cancer Institute**  
**SEER Cancer Statistics Review 1973-1999**

Table I-1  
ESTIMATED NEW CANCER CASES AND DEATHS FOR 2002

All Races, By Sex

Primary Site	Estimated New Cases			Estimated Deaths		
	Total	Males	Females	Total	Males	Females
All Sites	1,284,900	637,500	647,400	555,500	288,200	267,300
Oral Cavity and Pharynx	28,900	18,900	10,000	7,400	4,900	2,500
Tongue	7,100	4,700	2,400	1,700	1,100	600
Mouth	9,800	5,200	4,600	2,000	1,100	900
Pharynx	8,600	6,500	2,100	2,100	1,500	600
Other Oral Cavity	3,400	2,500	900	1,600	1,200	400
Digestive System	250,600	130,300	120,300	132,300	70,800	61,500
Esophagus	13,100	9,800	3,300	12,600	9,600	3,000
Stomach	21,600	13,300	8,300	12,400	7,200	5,200
Small Intestine	5,300	2,500	2,800	1,100	600	500
Colon	107,300	50,000	57,300	48,100	23,100	25,000
Rectum	41,000	22,600	18,400	8,500	4,700	3,800
Anus, Anal Canal, and Anorectum	3,900	1,700	2,200	500	200	300
Liver and Intrahepatic Bile Duct	16,600	11,000	5,600	14,100	8,900	5,200
Gallbladder and Other Biliary	7,100	3,400	3,700	3,500	1,300	2,200
Pancreas	30,300	14,700	15,600	29,700	14,500	15,200
Other Digestive	4,400	1,300	3,100	1,800	700	1,100
Respiratory System	183,200	100,700	82,500	161,400	94,100	67,300
Larynx	8,900	6,900	2,000	3,700	2,900	800
Lung and Bronchus	169,400	90,200	79,200	154,900	89,200	65,700
Other Respiratory	4,900	3,600	1,300	2,800	2,000	800
Bones and Joints	2,400	1,300	1,100	1,300	700	600
Soft Tissues	8,300	4,400	3,900	3,900	2,000	1,900
Skin (excl. basal & squamous)	58,300	32,500	25,800	9,600	6,200	3,400
Melanomas of Skin	53,600	30,100	23,500	7,400	4,700	2,700
Other non-epithelial skin	4,700	2,400	2,300	2,200	1,500	700
Breast	205,000	1,500	203,500	40,000	400	39,600
Genital Organs	279,100	187,700	81,400	57,100	30,900	26,200
Cervix (uterus)	13,000	-	13,000	4,100	-	4,100
Endometrium (uterus)	39,300	-	39,300	6,600	-	6,600
Ovary	23,300	-	23,300	13,900	-	13,900
Vulva	3,800	-	3,800	800	-	800
Vagina and other genital organs, female	2,000	-	2,000	800	-	800
Prostate	189,000	189,000	-	30,200	30,200	-
Testis	7,500	7,500	-	400	400	-
Penis and other genital organs, male	1,200	1,200	-	200	200	-
Urinary System	90,700	62,200	28,500	24,900	16,200	8,700
Urinary Bladder	56,500	41,500	15,000	12,600	8,600	4,000
Kidney and Renal Pelvis	31,800	19,100	12,700	11,600	7,200	4,400
Ureter and other urinary organs	2,400	1,600	800	700	400	300
Eye and Orbit	2,200	1,100	1,100	200	100	100
Brain and Other Nervous System	17,000	9,600	7,400	13,100	7,200	5,900
Endocrine System	22,700	6,000	16,700	2,300	1,000	1,300
Thyroid	20,700	4,900	15,800	1,300	500	800
Other Endocrine	2,000	1,100	900	1,000	500	500
Lymphoma	60,900	31,900	29,000	25,800	13,500	12,300
Hodgkin's Disease	7,000	3,700	3,300	1,400	800	600
Non-Hodgkin's Lymphoma	53,900	28,200	25,700	24,400	12,700	11,700
Multiple Myeloma	14,600	7,800	6,800	10,800	5,500	5,300
Leukemia	30,800	17,600	13,200	21,700	12,100	9,600
Lymphocytic Leukemias	10,800	6,300	4,500	5,900	3,400	2,500
Myeloid Leukemias	15,000	8,400	6,600	9,400	5,100	4,300
Other leukemia	5,000	2,900	2,100	6,400	3,600	2,800
All Other Sites	30,200	14,000	16,200	43,700	22,600	21,100

Source: Cancer Facts & Figures - 2002, American Cancer Society (ACS), Atlanta, Georgia, 2002. Excludes basal and squamous cell skin and in situ carcinomas except urinary bladder. Incidence projections are based on rates from the NCI SEER Program 1979-1998.

Table I-11

AGE DISTRIBUTION (%) OF INCIDENCE CASES BY SITE, 1995-99

All Races, Both Sexes

Site	<20	20-34	35-44	45-54	55-64	65-74	75-84	85+	All Ages	Cases
All Sites	1.1	3.2	6.4	12.7	19.0	28.2	22.3	7.2	100.0%	791,807
Oral cavity & Pharynx	0.6	3.1	8.1	18.2	22.0	25.7	17.0	5.3	100.0%	18,703
Esophagus	0.0	0.5	2.7	11.7	21.9	32.5	23.3	7.2	100.0%	7,504
Stomach	0.1	1.6	5.0	9.4	15.8	27.5	28.1	12.6	100.0%	15,253
Colon & Rectum	0.0	1.0	3.3	9.0	16.5	28.5	29.4	12.3	100.0%	89,391
Males	0.1	1.0	3.5	9.8	18.8	30.7	27.7	8.5	100.0%	44,899
Females	0.0	0.9	3.1	8.2	14.3	26.3	31.1	16.2	100.0%	44,492
Colon	0.0	0.9	2.8	7.8	15.2	28.4	31.2	13.7	100.0%	64,538
Rectum	0.1	1.3	4.4	12.1	20.0	28.8	24.6	8.6	100.0%	24,853
Liver & Intrahep	1.4	1.3	4.9	14.7	20.1	28.0	22.5	7.1	100.0%	9,525
Pancreas	0.1	0.5	2.6	9.0	16.7	29.4	29.4	12.4	100.0%	18,188
Larynx	0.0	0.5	4.2	14.2	26.4	33.3	17.7	3.6	100.0%	6,726
Lung & Bronchus	0.0	0.3	2.2	8.9	20.5	35.6	26.4	6.0	100.0%	104,990
Males	0.0	0.3	2.2	8.9	21.1	36.2	25.9	5.4	100.0%	58,716
Females	0.0	0.3	2.3	8.9	19.8	34.7	27.2	6.8	100.0%	46,274
Melanomas of skin	0.8	9.9	16.2	19.4	16.8	18.7	13.7	4.6	100.0%	28,297
Breast (females)	0.0	2.1	11.0	21.6	20.4	22.4	17.0	5.5	100.0%	123,380
Cervix uteri	0.3	16.3	27.0	22.0	13.7	11.2	7.1	2.6	100.0%	9,223
Corpus & Uterus, NOS	0.0	1.4	6.1	17.3	24.6	26.4	18.9	5.2	100.0%	22,654
Ovary	1.3	6.6	10.9	19.0	18.3	21.4	16.7	5.9	100.0%	15,634
Prostate	0.0	0.0	0.4	6.6	23.8	40.6	23.6	5.0	100.0%	119,342
Testis	5.6	48.1	31.1	10.9	2.4	1.2	0.7	0.0	100.0%	4,974
Urinary bladder	0.1	0.7	2.6	8.0	16.6	31.6	30.0	10.5	100.0%	33,304
Kidney & Renal pelvis	2.1	1.4	6.1	15.0	21.7	27.7	20.3	5.7	100.0%	18,199
Brain & Other nervous	13.3	10.1	11.3	13.9	15.6	18.7	13.9	3.3	100.0%	11,227
Thyroid	2.4	22.0	23.5	21.0	13.3	10.2	6.1	1.5	100.0%	11,909
Hodgkin's disease	12.7	34.7	17.7	11.3	8.6	7.5	5.9	1.5	100.0%	5,021
Non-Hodgkin's lymphomas	1.6	6.0	9.9	13.6	16.2	23.8	21.7	7.1	100.0%	32,633
Multiple myeloma	0.0	0.6	3.4	11.0	18.0	29.5	28.6	9.0	100.0%	9,112
Leukemias	11.6	5.4	6.1	9.7	13.1	22.1	22.3	9.7	100.0%	20,673
Acute lymphocytic	65.1	9.6	5.8	5.1	4.4	4.8	3.9	1.2	100.0%	2,837
Chronic lymphocytic	0.0	0.2	2.4	9.7	17.1	30.0	28.2	12.4	100.0%	5,800
Acute myeloid	6.0	7.6	7.7	10.2	13.4	23.6	23.1	8.4	100.0%	6,150
Chronic myeloid	1.5	9.1	10.2	12.2	13.4	21.9	21.9	9.7	100.0%	2,876
All other leukemias	4.5	3.3	6.6	10.6	12.7	20.4	26.8	15.0	100.0%	3,010

Source: SEER 12 areas.