NIOSH Response to Peer Review Comments (April 6, 2009)			
Additions to Appendix A			
Proprietary Name	**Established Name**	**NIOSH Summary of all Comments and NIOSH Hazardous Drug Committee**	**Summary of Peer Review Comments**
Alimta®	pemetrexed	Antifolate antineoplastic drug, similar to methotrexate which is on the current list	Antifolate antineoplastic drug, similar to methotrexate which is on the current list, genotoxic
Amevive®	alafacept	Evidence of malignancies in treated patients, complex preparation process conducive to exposure	Evidence of malignanies in treated patients, immunosuppressive protein (decreases circulating T-Cells), complex preparation process condusive to exposure
Arranon®	nelarabine	Pregnancy Category D*, Antineoplastic agent	Analog of deoxyguanasine; acknowledged as cytotoxic; decreases incorporation of GTP into DNA, mutagenic in vitro
Avonex®	interferon beta 1a	Pregnancy Category C, but produces abortions at low doses in monkeys	Aborifacient in monkeys at 3X human dose eqivalent.; PI says "consider D/C if pregnant; reproductive adverse outcome registry established
Azilect®	rasagiline mesylate	Lung tumors seen in male and female mice, genotoxicity results mixed	Potent, carcinogenic, reproductive effects; increases in lung tumors (mice, males and females)
Baraclude®	entecavir	Lung, liver and other tumors seen in mice and rats	Tumors seen in mice and rats, Animal toxicity at dosing similar to human; Potent tumorigenicity
Betaseron®	interferon beta 1b	Pregnancy Category C, but produces abortions at low doses in monkeys	Aborifacient in monkeys at 2.8X human dose eqivalent.; PI says "consider D/C if pregnant;
Clolar™	clofarabine	Pregnancy category D, cytotoxic agent, antimetabolite	Purine nucleoside antimetabolite; cytotoxic; teratogenic; decreases DNA synth.; Genotoxic; bone marrow suppression

Dacogen™	decitibine	Pregnancy category D, cytotoxic agent, antimetabolite	Developmental and Reproductive Toxicity at low doses; Genotoxic mechanism, mutagenic; Cytosine analog nucleoside antimetabolite; cytotoxic; teratogenic
Depo-Provera®/ Provera®	medroxyprogesterone acetate	IARC, Group 2B Possible Human carcinogen**	Increased hypospadias, labial fusion, clitoral enlargement with exposure during 1st trimester; Mammary tumors in beagles; increase in breast & cervical cancer,; neonatal effects;
Kepivance™	palifermin	Developmental and reproductive toxicity at low doses	Developmental and Reproductive Toxicity at 0.15 mg/kg; human keratinocyte growth factor ; exhibited tumor cell growth in human models; low dose toxicity
Leustatin®	cladrabine	Pregnancy category D, antineoplastic drug	Developmental and Reproductive Toxicity at 1.5-3 mg/kg; Antineoplastic analog of adenosine; teratogenic and fetotoxic in mice and rabbits; genotoxic
Nexavar®	sorafenib	Pregnancy Category D, reproductive and developmental toxicty at low doses	Embryo-fetal toxicity in rats and rabbits (increased post-implantation loss, resorptions, skeletal retardations, lower fetal weight) at low doses; Clastogenic in in vitro CHO assay.; Deveopmental and Reproductive Toxicity at 1.2 mg/m2 ; significant toxicity seen in some animal models; "Multikinase" inhibitor that decreases cell proliferation by interacting with kinases involved in angiogenesis; teratogenic and embryotoxic

Paxil®	paroxetine HCl	Pregnancy Category D, Increased risk of cardiovascular malformations following exposure of fetus in 1st trimester and increased risk of overall major congenital malformations, numerous complications following exposure in 3rd trimester	Increased risk of cardiovasular malformations in women w/ 1st-trimester exposure. Various other neonatal/infant comorbidities when exposed 3rd trimester (including respiratory distress, persistent pulmonary hypertension of newborn). Increased rat pup deaths during first 4 days of lactation when exposed to 1/6th Maximum Recommended Human Dose during last trimester thru lactation; increased incidence of reticulum cell sarcomas and lymphoreticular tumors in male rats; Reduced pregnancy rate at 2.9x Maximum Recommended Human Dose; birth defects w/clinical use
Pentetate Calcium Trisodium	pentetate calcium trisodium	Severe teratogen in animal studies	Known severe teratogen in animals (depletes body stores of zinc). Zn-DTPA recommended during pregnancy
Rapamune®	sirolimus	Malignant lymphomas and other tumors in rats and mice at low doses, immunosuppressant	Embryo/feto-toxic at 0.2x Maximim Recommended Human Dose in rats. Manufacturer recommends contraception before, during, and 12 weeks after use. ; increased malignant lymphomas and hepatocellar adenomas/carcinomas in mice; Reduced sperm counts in male rats; tumors at low doses - 0.2 mg/kg/day ; Developmental and Reproductive Toxicity at 0.1 mpk; immunosuppressant; Potent; Low dose toxicity
Remicade®	infliximab	Increased risk of lymphomas and other cancers in treated patients	Very clear warning in PI about increased risk of lymphoma and other cancers in treated patients
Revlimid®	lenalidomide	Pregnancy category X, thalidomide analog	Manufacturer recommends

			contraception 4 weeks before, during, and 4 wks after use. Analog of thalidomide
Risperdal®/ Risperdal Consta®	risperidone	Multiple tumors in rats and mice at low doses, developmental and reproductive toxicity at low doses	Tumors at 0.2 mg/kg (prolactin elevation); Developmental and Reproductive Toxicityat less than 0.2 mg/kg; Tumorigenicity at low doses; increased pituitary, mammary, and endocrine pancreas neoplasms in rodents at doses 1.5x Maximum Recommended Human Dose or less; Impaired mating in rats, decreased sperm count and motility in beagles
Sprycel®	dasatinib	Pregnancy Category D, fetal toxicity in rats and rabbits, clastogenic in vitro	Retrospective reports of neural tube defects in women exposed during 1st trimester. Crosses the placenta in rats and rabbits.; increased hepatic and pulmonary neoplasms in female mice; Malformations in monkeys (anencephaly, microophalthmia, cleft palate); teratogenic in monkeys
Sutent®	sunitinib malate	Pregnancy Category D, duodenal carcinomas in mice	Increased embryolethality and structural abnormalities in rats and rabbits at concentrations as low as 0.3 AUC. Decreased follicular development and endometrial atrophy in monkeys.; Duodenal carcinoma in mice at 200mg/kg/day; multi kinase inhibitor angiogenesis inhibitor; Animal toxicity seen at low exposures.; effects on reproductive organs noted in repeat-dose studies in monkeys; Developmental toxicity at low doses
Tracleer®	bosentan	Pregnancy Catogory X, teratogenic in rats, carcinogenic in mice and rats	Expected to cause fetal harm if administered to pregnant women; increased hepatic neoplasms in mice; colon adenomas and brain astrocytomas, resp; Likely irreversible testicular atrophy and

			decreased fertility in male rats when treated for more than 10 weeks; fetal harm; liver injury, Endothelian receptor antagonist for pulmonary arterial hypertension; carcinogenic findings in rats and mice; clearly teratogenic in rats; testicular atrophy
Velcade®	bortizomib	Pregnancy Category D, post-implantation loss in rabbits	Increased post-implantation loss and decreased fetal weight in rabbits at 0.5x Maximum Recommended Human Dose during organogenesis; Clastogenic in CHO cells; Animal toxicity seen at low exposure doses; antineoplastic; cytotoxic; Developmental and organ tox at low doses
Zolinza™	vorinostat	Pregnancy Category D, Genotoxic in vitro and in vivo	Crosses placenta, causes decreased fetal weight, incomplete ossification in rats and rabbits at 0.5x Maximum Recommended Human Dose; increased gallbladder malformations in rabbits; increased peri-implantation losses in female rats, Mutagenic in vitro and in vivo; Animal toxicity seen at low exposures
Zonegran®	zonisamide	Teratogenic in several species, mixed genotoxicity	increased fetal abnormalities (external, visceral, and skeletal) and death at doses equivalent to Maximum Recommended Human Dose in multiple animal models; Teratogenic in mice, rats, and dogs and embryolethal in monkeys when given during organogenesis at levels equivalent or less than Maximum Recommended Human Dose; Mutagenic in CHO cells; Animal toxicity seen at exposure lower than therapeutic dosing

Deletions to Appendix A			
Theracys®	Bacillus Calmette-Guerin	BCG requires special handling and should not be prepared along with other hazardous drugs because of cross-contamination issues	

NIOSH did not include these drugs as the majority of reviewers did not recommend that they be included on the Hazardous Drug List.	
Abilify	aripiprazole
Apokyn	apomorphine HCl
Avastin	bevacizumab
Azilect	rasagiline mesylate
Baraclude	entecavir
Chantix	varenicline
Cordarone	amidarone HCl
Depacone	valproate Na
Depakene	valproic acid
Depakote	divalproex Na
Elidel	pimecrolimus
Erbitux	cetuximab
Geodon	ziprasidone
Gleevec	imatinib mesylate
Increlex	mecasermin (rDNA origin)
Lunesta	eszopicline
Lyrica	pregagalin
Mycamine	micafungin sodium
Myozyme	alglucosidase alfa
Orencia	abatacept
Photofrin	porfimer sodium
Rituxan	rituximab
Rozerem	ramelteon
Seroquel	quetiapine fumerate
Spiriva Handihaler	titropium bromide
Sustiva	efavirenz
Tarceva	erlotinib HCl
Tindamax	tinidazole
Trileptal	oxcarbazepine
Tygacil	tigcycline
Tysabri	natalizumab
Viramune	nevirapine
Viread	tenofovir
Vision Blue	trypan blue

NIOSH did not include these drugs on the Hazardous Drug List although the majority of reviewers recommended that they be included on the Hazardous Drug List.		
Proprietary Name	**Established Name**	**NIOSH Summary**
Amitiza	lubiprostone	Effects seen at high does; formulation limits occupational exposure
Hivid	zalcitibine	Effects seen at high doses; formulation limits occupational exposure

NIOSH did not include these drugs on the Hazardous Drug List as they are radiopharmaceuticals.	
Proprietary Name	**Established Name**
Metastron	strontium-89 chloride
Quadramet	samarium 153 lexidronam

*The FDA-assigned pregnancy categories as used in the Drug Formulary are as follows:

Category A
Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).

Category B
Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Category C
Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Category D
There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Category X
Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

** International Agency for Research on Cancer. www.iarc.fr