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SCREENING DATA SUMMARY  
 DEVELOPMENTAL THERAPEUTICS PROGRAM  
 DIVISION OF CANCER TREATMENT  
 NATIONAL CANCER INSTITUTE, BETHESDA, MD 20205  
 SYNTHETIC PRODUCTS

31  
 S99 DATE: 83/09/02 NSC 999999  
 PAGE 14  
 1ST SCR S.I. R.C./DATE PUB  
 \*\*

ACQ M.C./DATE QNS OTHER  
 7A 790617

29

CONTINUED

3LE31 TIS:1 LVL:5 RT:1 TRTMT SCHED: Q01DX05 DAY 1ST INJ= 1 TOTAL INJ= 15

24

25

26

27

28

ABOVE SCHED REPEATED ON DAYS : 010,020 } 20 1ST RX TIME = 13:15 HRS } 20

SMPLE SCR EXP # DATEON V FED TED TXSUR DOS/INJ/U BWD SOL C/NT/TS EVAL T/CX

9

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12

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ND00	90	12345	830726	02 030	005	WD1/2: 1/ 5	TSC:22P	SSC: L	SEX:M	CSC:1	
*	2017/04	018/01	019/01	KE=	4.43	06/06	200.00	-3.6	1	00 00 00	17.4 207
*	006/01	015/03	017/02	2 E=	2.57	06/06	100.00	-2.4	1	00 00 00	15.3 182
*	013/01	014/03	015/02	KE=	1.68	3 06/06	14 50.00	15 -2.2	6	1 30 00 00	21 14.3 170
*	012/01	013/01	014/04	KE=	1.33	06/06	25.00	-1.0	1	00 00 00	13.9 165
*	012/03	014/02		KE=	0.09	05/05	12.50	-0.8	1	00 00 00	12.5 148

1

2

3

14

15

6

30

21

22

23 { ##### COMMENT: ONE ANIMAL MISSING - WEIGHTS ADJUSTED  
 \* 008/18 009/10 010/01 30/30 CNTRL HOST:06 BWC= 2.0 8.4  
 011/01

16

23 { ##### COMMENT: RUN WITH 3LE31-12149

4

5

7

FOOTNOTE:

a MORTALITY IS GIVEN AS DAY/DEATH COUNT (NOT SURVIVORS)

SYN

999999

17

- 1 Blank = Not new this run.  
 \* = New this run.  
 C = Data modified this run by the DPC.  
 R = Packs revised by the Screener (these data affected).  
 S = Packs revised by the Screener (these data unaffected).
- 2 Death Pattern Data (DAY/DTHS) – Maximum of 3 entries per line; use multiple lines as necessary.
- 3 Log Cell Kill Reduction.
- 4 Designates data appearing on this and subsequent lines as applicable to Control (CNTRL) Group.
- 5 Host Code for all animals in the experiment (Test and Control).
- 6 BWD = Animal Body Weight Difference which is computed by subtracting the Control Group body weight change from the Test Group body weight change.
- 7 BWC = Body Weight Change calculated as final average body weight minus initial average body weight. This item is calculated for the Control Group only.
- 8 DATEON = Date the experiment was initiated. (YYMMDD)
- 9 SMPL = Compound Sample Number.
- 10 SCR = Screener Code.
- 11 V = Vehicle Code.
- 12 FED = Final Evaluation Day.
- 13 TED = Toxicity Evaluation Day.
- 14 TXSUR = Surviving animals/total animals on Toxicity Evaluation Day.
- 15 DOS/INJ/U Dose amount per injection, normally expressed as mg/kg of animal body weight/injection. Units other than mg/kg/inj are flagged with a "unit" code under the "U".
- 16 C/NT/TS = Cures(C)/No-Takes(NT)/Tumored Survivors (TS) as reported by the Screener.

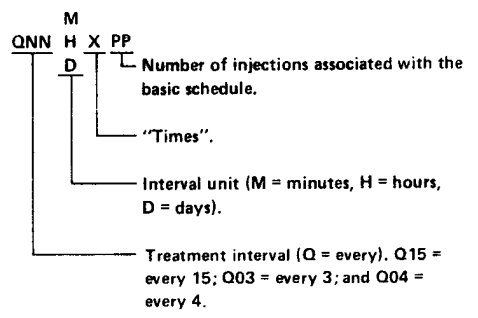
\*Varies by Test System.

- 17 "WD1:2:1; 5" = This item identifies initial (1) and final (2) animal weigh days. (In this example, the days are 1 and 5.)
- 18 "TSC:22P" = This item identifies the Test Status Code (TSC) and TSC suffix. P – Active Test, F – Inactive Test, or R – Erratic Test (unreliable data).
- 19 "SSC:L" = This item identifies any Special Study Code (SSC) associated with the test. (In this example, the SSC is "L".)
- 20 "CSC:1" = This item identifies the Control Status Code (CSC) associated with the experiment. (In this example, the CSC is "1".)
- 21 EVAL = The calculated value of the Test Group and/or Control Group evaluation based on the test system evaluation parameter.
- 22 T/C % = The test evaluation expressed as a percent of the control evaluation, providing a measure of effectiveness of the compound being tested. Survival systems indicate a degree of success when T/C percents exceed 125. \* Tumor inhibition systems indicate a degree of success when the T/C percents do not exceed 42. \* Minus values (only occurring for tumor inhibition systems) reflect the percent of tumor regression between initial and final tumor volume.
- 23 ##### Comment = Indicates a Screener comment applicable to the data immediately preceding the comment line.
- 24 3 L E 3 1 = Test System used
  - Site of inoculum implant.
  - Parameter of evaluation (i.e., 2 = mean survival time; 3 = median survival time; etc.).
  - Tumor Code (LE = L1210 Leukemia).
  - Animal Host Group (i.e., 3 = mice; 5 = rats; 7 = hamsters).

25 TIS:1 = Type of Tumor Inoculum.

- 26 LVL:5 = A one or two position field where the left-most position is a coded representation of the inoculum level, and the right-most position (if present) represents a multiplier value.
- 27 RT:1 = Route of Administration for compound (or vehicle) being tested. See pg. 11
- 28 TRTMT SCHED = The treatment schedule followed in administering the compound being tested, taking the form: See pg. 9

Basic Schedule:



DAY 1ST INJ = RR  
 First day basic schedule initiated.

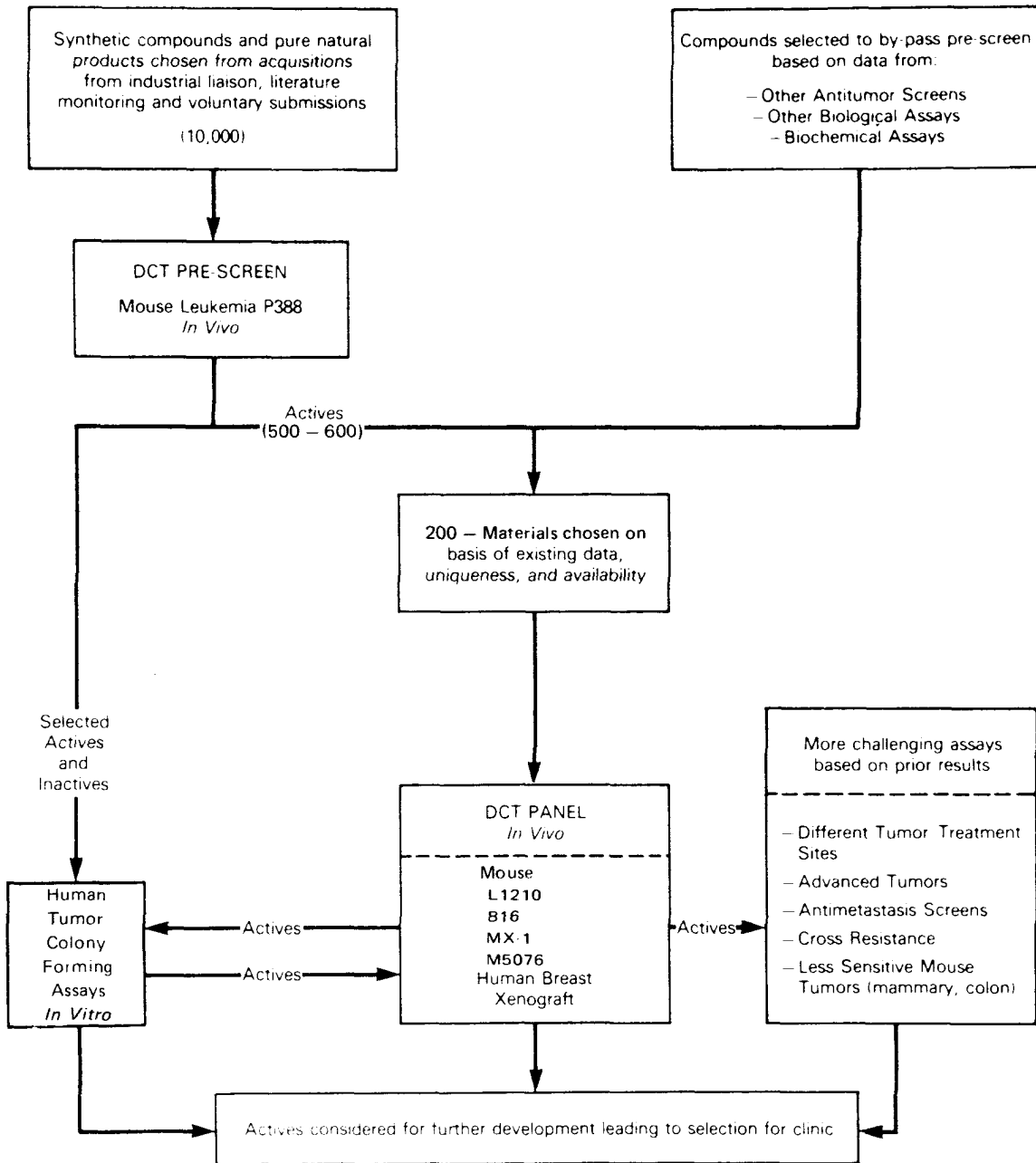
TOTAL INJ = SS  
 Total injections to be administered.

ABOVE SCHED REPEATED ON DAYS:  
TTT, TTT, TTT... TTT  
 Each day the basic schedule is to be re-initiated (if appropriate).

1ST RX TIME = 13:15 HRS  
 Time of 1st INJ (if provided) in military time (13:15 = 1:15 PM).

- 29 Same Test System, Tissue, Level, Route, and Treatment Schedule as from Previous Page.
- 30 SOL = Compound Solubility .
- 31 Screener or Supplier number.

# FLOW OF DRUGS THROUGH DCT SCREENS



# ACTIVITY THRESHOLDS OF COMMON SYSTEMS

<u>MODEL</u>	<u>CODE</u>	<u>DRUG RT/SCHED</u>	<u>PARAMETER</u>	<u>ACTIVE T/C%</u>	
				<u>MC1</u>	<u>DN2</u>
<b><u>PRESCREEN</u></b>					
IP P388 LEUKEMIA	3PS31	IP/Q1DX5	MED SURVIVAL TIME CONFIRMING TEST	≥ 127 ≥ 120	≥ 175 ≥ 175
<b><u>TRANSPLANTED MOUSE TUMORS</u></b>					
*IP B16 MELANOMA	3B131	IP/Q1DX9	MED SURVIVAL TIME	≥ 125	≥ 150
SC B16 MELANOMA	3B132	IP/Q1DX9	MED SURVIVAL TIME	≥ 140	≥ 150
SC CD8F1 MAMMARY	3CDJ2	IP/Q1DX1	MED TUMOR WT CHANGE	≤ 20	≤ 0
SC COLON 38	3C872	IP/Q7DX2	MED TUMOR WT	≤ 42	≤ 10
*IP L1210 LEUKEMIA	3LE31	IP/Q1DX9	MED SURVIVAL TIME	≥ 125	≥ 150
*IP M5 SARCOMA	3M531	IP/Q4DX4	MED SURVIVAL TIME	≥ 125	≥ 150
<b><u>HUMAN TUMOR XENOGRAFTS</u></b>					
SRC CX-1 COLON	3C2G5	IP/Q4DX4	MEAN TUMOR WT CHANGE	≤ 20	≤ 10
SC CX-1 COLON	3C2H2	IP/Q4DX3	MEAN TUMOR WT CHANGE	≤ 20	≤ 10
SRC LX-1 LUNG	3LKG5	IP/Q4DX3	MEAN TUMOR WT CHANGE	≤ 20	≤ 10
SC LX-1 LUNG	3LKH2	IP/Q4DX3	MEAN TUMOR WT CHANGE	≤ 20	≤ 10
*SRC MX-1 MAMMARY	3MBG5	IP/Q4DX3	MEAN TUMOR WT CHANGE	≤ 20	≤ 10
SC MX-1 MAMMARY	3MBH2	IP/Q4DX3	MEAN TUMOR WT CHANGE	≤ 20	≤ 10

\* DEB TUMOR PANEL

# SCREENING MODELS

AA Nontumored Animals (Toxicity Test)  
 \*AC Carcinoma, Adrenal Cortex (No.2)  
 AD ADJ-PC-22 Plasma Cell  
 AG L1210 Leukemia/8-Azaguanine; NSC 749  
 AK Lymphoma AKR (Transplanted)  
 AM Amelanotic Melanoma (No. 4)  
 AS Rat AC Glioma  
 A2 ADJ-PC-20 Plasma Cell  
 A3 Lieberman Plasma Cell No. 1 (LPC-1)  
 \*A5 ADJ-PC-5 Plasma Cell  
 A6 ADJ-PC-6  
 \*BA Clone Derived Amelanotic B16  
 BC L1210 Leukemia/BCNU; NSC 409962  
 \*BM Clone Derived Melanotic B16  
 BP P388 Leukemia/BCNU; NSC 409962  
 B1 B16 Melanoma  
 CA Adenocarcinoma 755  
 CD Mammary Adenocarcinoma CD8F1  
 CH Chang Liver (Cell Culture)  
 CL NCI-H460 Large Cell Carcinoma of the Lung  
 CM Dunning Leukemia/Mitomycin C; NSC 26980 (Solid)  
 CP P388 Leukemia/Cis DDPT; NSC 119875  
 \*CR L1210 Leukemia/Cytosin & Ara-C; NSC 26271, NSC 63878  
 CS Dunning Leukemia/Cycloleucine; NSC 1026 (Solid)  
 CX L1210 Leukemia/Cytosin; NSC 26271  
 \*CY Colon 36  
 CZ Colon 51  
 C2 HT29; CX-1 Human Adenocarcinoma (MER+)  
 \*C3 C3H Mammary Tumor  
 C4 CX-2 Colon Xenograft  
 C5 CX-3 Colon Xenograft  
 C6 Colon 26 Adenocarcinoma  
 C7 CX-4 Colon Xenograft  
 C8 Colon Carcinoma 38  
 C9 CX-5 Colon Xenograft  
 \*DA Dunning Leukemia (Ascites) (See DL)  
 DH Dunning Leukemia/Hexamethylmelamine; NSC 13875  
 (Solid)  
 DL Dunning Leukemia (Ascitic)  
 DM DMBA Induced Mammary Adenocarcinoma  
 DN Dunning Leukemia/A Nitrogen Mustard; NSC 51845  
 (Solid)  
 DP L1210 Leukemia/Cisplatin II; NSC 119875  
 \*DR Dunning Leukemia/A Thiopurine; NSC 29189 (Ascitic)  
 \*DX Dunning Leukemia/Cytosin; NSC 26271 (Ascitic)  
 \*D1 Adenocarcinoma, Duodenum (Hamster & Cell Culture)  
 EA Ehrlich Ascites Tumor  
 EC B-Galactoside Phage  
 EM Ependymoblastoma  
 \*EN Adenocarcinoma, Endometrium  
 EP Ependymoblastoma  
 FM Friend Virus Erythroleukemia Ascites  
 (P.Marks' Line DS-19)

\*FR P815/5-Fluorouridine; NSC 27640 (Ascitic)  
 \*FS Fibrosarcoma (No. 2)  
 FU P815/5-Fluorouracil; NSC 19893 (Ascitic)  
 FV Friend Virus Leukemia (Solid)  
 GA Lymphosarcoma Gardner 6C3HED  
 GE Adl Gardner 6C3HED Lymphosarcoma/1-Asparaginase;  
 NSC 109229  
 \*GL Lymphosarcoma LePage Gardner 6C3HED Sensitive to  
 Ara-A; NSC 404241  
 \*GS 239PU-Induced Osteogenic Sarcoma  
 G1 Glioma 261  
 G2 Glioma 26  
 HD Hepatoma 134  
 HE Hepatoma 129 (Mouse)  
 \*HE Cystadenocarcinoma, Liver (No. 1) (Hamster)  
 HE HeLa Human Carcinoma (Cell Culture)  
 HF Hep 2/2-Fluoroadenine; NSC 27364  
 HG Hep 2/2-Fluoroadenine & 2-Fluoroadenosine;  
 NSC 27364, NSC 30605  
 HH HEP 2/6-MP & 6-Methylthiopurine Ribonucleoside &  
 2-Fluoroadenine; NSC 755, NSC 4911, NSC 27364  
 HL HL-60 Human Promyelocytic Leukemia Xenograft  
 HM Hep 2/6-Methylthiopurine Ribonucleoside;  
 NSC 4911  
 HN HEP 2/6-MP & 6-Methylthiopurine Ribonucleoside;  
 NSC 755, NSC 4911  
 HR Hep 2/6-Mercaptopurine; NSC 755  
 HU L1210 Leukemia/Hydroxyurea; NSC 32065  
 HX Hep 2/Methotrexate; NSC 740  
 H1 HSI Human Sarcoma (Egg)  
 H2 Hep 2 Human Epidermoid Carcinoma  
 H3 Hep 3 Human Epidermoid Carcinoma  
 \*IC L1210 Intracerebral Inoculation (See LE)  
 \*IC Dunning Leukemia Intracerebral Inoculation (See DL)  
 JA NCI-H23 Human Lung Adenocarcinoma  
 JB NCI-H324 Human Lung Adenocarcinoma  
 JC NCI-H522 Human Lung Adenocarcinoma  
 JD NCI-H125 Human Lung Adenosquamous Carcinoma  
 JE NCI-H358 Human Lung Bronchiolo-Alveolar Carcinoma  
 JF NCI-H292 Human Lung Mucoepidermoid Carcinoma  
 KB Human Epidermoid Carcinoma of the  
 Nasopharynx (Cell Culture)  
 K4 AK4 Lymphoid Leukemia  
 \*LA L1210 Leukemia/Azacytidine; NSC 102816  
 \*LB L1210 Leukemia/BIC; NSC 82196  
 LC L1210 Leukemia/Cytosine Arabinoside; NSC 63978  
 LD L1210 Leukemia/DTIC; NSC 45388  
 LE L1210 Leukemia  
 \*LF L1210 Leukemia/Methotrexate & Dichloromethotrexate;  
 NSC 740, NSC 29630  
 \*LG L1210 Leukemia/Guanazole; NSC 1895  
 LH L1210 Leukemia/Cycloctidine; NSC 145668  
 LJ L1210 Leukemia/L-Alanosine; NSC 153353

# SCREENING MODELS

LK Human Lung LX-1 Xenograft  
 LL Lewis Lung Carcinoma  
 LM L1210 Leukemia/Dichloromethotrexate; NSC 29630  
 LN A549 Human Adenocarcinoma of Lung with characteristics of Type II Alveolar Epithelial cells  
 LO Human Amelanotic Melanoma (LOX)  
 \*LP Liposarcoma (No. 1)  
 \*LQ L1210 Leukemia/Methane Sulfonate; NSC 102627  
 \*LR L1210 Leukemia/6-MMPR; NSC 40774  
 LS L1210 Leukemia/L-PAM; NSC 8806  
 LT L1210 Leukemia/Ftorafur; NSC 148958  
 LU L1210 Leukemia/5-Fluorouracil; NSC 19893  
 LV NCI-H322 Human Lung Bronchiolo-Alveolar Carcinoma  
 LW L1210 Leukemia/A Terephthalanilide; NSC 38280  
 LX L1210 Leukemia/Methotrexate; NSC 740  
 LY Lewis Lung Carcinoma/PALA; NSC 224131  
 L2 Lymphoma 2  
 L2 Leiomyosarcoma (No. 2)  
 L4 Lymphoma 4  
 L8 L5178Y Lymphatic Leukemia  
 L8 Lymphoma 8  
 L9 L5178Y Lymphatic Leukemia/L-Asparaginase; NSC 109229  
 MA 13762 Mammary Adenocarcinoma  
 MB Human Mammary Carcinoma MX-1 Xenograft  
 \*MC Adenocarcinoma, Breast  
 MD Madison 109 Lung Carcinoma  
 ME Lymphosarcoma Mecca  
 MF Human Breast MX-2 Xenograft  
 MG Human Breast MX-3 Xenograft  
 \*MH EMT6 Fibrosarcoma  
 ML L1210 Leukemia/Methyl-GAG; NSC 32946  
 MM Melanotic Melanoma  
 MP L1210 Leukemia/6-MP & 6-Thioguanine; NSC 755, NSC 752  
 MS Lymphosarcoma Murphy-Sturm  
 MT Human Mesothelioma  
 MX MXT Hormone Dependent Transplantable Mammary Adenocarcinoma  
 \*MY Myeloid Leukemia in RFM/UN Mouse  
 M2 MPC-2 Plasma Cell  
 M5 Sarcoma M5076  
 M6 M5076/Cisplatin II; NSC 119875  
 M7 Agrobacterium Tumefaciens Microbial Assay  
 M8 Candida Albicans Microbial Assay  
 M9 Zanthomona Compestris Microbial Assay  
 NH Novikoff Hepatoma  
 \*NL Nova Leukemia NRL-1871  
 \*NP Plasmacytoma No. 1/BCNU; NSC 409962  
 \*NR Neurilemmoma No. 1  
 OC Human Ovarian Carcinoma  
 OG Osteogenic Sarcoma  
 OS Osteogenic Sarcoma HE 10734  
 OT Human Ovarian Sarcoma

PA P388 Leukemia/Adriamycin; NSC 123127, Developed at Scr 08  
 PB P388 Leukemia/Daunomycin; NSC 82151  
 PC P388 Leukemia/ARA-C; NSC 63878  
 PD P388 Leukemia/Actinomycin-D; NSC 3053  
 PE P388 Leukemia/AMSA; NSC 249992  
 \*PF P388 Leukemia/Dihydroxy Anthracenedione; NSC 299195  
 PG P388 Leukemia/DON; NSC 7365  
 PH P388 Leukemia/Acivicin; NSC 163501  
 PJ P388/Bleomycin; NSC 125066  
 PK P388 Leukemia/Ellipticine; NSC 71795  
 PL P815/Vinblastine; NSC 49842  
 \*PM Plasmacytoma No. 1/Triethylenemelamine; NSC 9706  
 PN Adenocarcinoma, Pancreas No. 1  
 PO P388 Leukemia/Cytoxan; NSC 26271  
 PP P388 Leukemia/L-PAM; NSC 8806  
 PQ P388 Leukemia Bristol Strain  
 \*PR Adenocarcinoma, Prostate  
 PS P388 Leukemia  
 \*PT Carcinoma, Pitutary  
 PU P388 Leukemia/5-Fluorouracil; NSC 19893  
 PV P388 Leukemia/Vincristine; NSC 67574  
 PW P388 Leukemia/A Terephthalanilide; NSC 38280  
 \*PX Plasmacytoma No. 1/Cytoxan; NSC 26271  
 \*PY PY89 Sarcoma  
 PZ P388 Leukemia/5-Azacytidine; NSC 102816  
 \*PI Plasmacytoma No. 1  
 P2 P388 Leukemia/ARA-A & 2'-Deoxycoformycin; NSC 404241, NSC 218321 (ADL)  
 \*P3 P1534/Methotrexate; NSC 740  
 P4 P1534 Leukemia  
 P6 P388 Leukemia/L-Alanosine; NSC 153353  
 P7 P388 Leukemia/Methotrexate; NSC 740  
 P8 P815 Mast Cell Leukemia (Ascitic)  
 P9 P329 Reticulum Cell Sarcoma  
 RC Adenocarcinoma, Kidney  
 \*RE Renal Cell Carcinoma  
 RO Osteogenic Sarcoma Ridgway  
 RS Reticulum Cell Sarcoma (Kelley Mouse)  
 \*RS Reticulum Cell Lymphosarcoma No. 5 (Hamster)  
 \*RX Ros/Cytoxan; NSC 26271  
 SA Sarcoma 180  
 SB Adenocarcinoma, Small Bowel (Ileum)  
 SC Human Tumor Colony Forming Assay  
 ST Special Testing, Biochemical Assay (Host98)  
 \*TC L1210 Leukemia/Picolinaldehyde, Thiosemicarbazone; NSC 729  
 TE TE-671 Human Meduloblastoma  
 TG Dunning Leukemia/Thioguanine Riboside; NSC 29422  
 TR P388 Leukemia/Tiazofurin; NSC 286193, Developed at Scr 08  
 UG U-251 Human Glioma  
 VA Colon Xenograft CS-1

# SCREENING MODELS

VG BREAST XENOGRRAFT BS-3  
 VH BREAST XENOGRRAFT BS-4  
 VI LUNG XENOGRRAFT LS-1  
 VJ PANCREAS XENOGRRAFT PS-1  
 VK SARCOMA XENOGRRAFT SS-1  
 VL SARCOMA XENOGRRAFT SS-2  
 VM MELANOMA XENOGRRAFT MS-1  
 VN MELANOMA XENOGRRAFT MS-2  
 VO MELANOMA XENOGRRAFT MS-3  
 VP MELANOMA XENOGRRAFT MS-4  
 VQ MELANOMA XENOGRRAFT MS-5  
 VR MELANOMA XENOGRRAFT MS-6  
 VS MELANOMA XENOGRRAFT MS-7  
 VT MELANOMA XENOGRRAFT MS-8  
 WA WALKER CARCINOSARCOMA 256 (SUBCUTANEOUS)  
 \*WJ WALKER CARCINOMA/CYTOXAN; NSC 26271  
 \*WI WALKER CARCINOSARCOMA 256 (INTRAPERITONEAL) (SEE WA)  
 \*WM WALKER CARCINOSARCOMA 256 (INTRAMUSCULAR) (SEE WA)  
 \*WP WALKER CARCINOSARCOMA 256 (PULMONARY) (SEE WA)  
 XE ERLICH ASCITES TUMOR ENZYMES (BIOCHEMICAL ASSAY)  
 XL L1210 LEUKEMIA (BIOCHEMICAL ASSAY)  
 XM HUMAN LEUKEMIA CELL ENZYME (BIOCHEMICAL ASSAY)  
 XN HUMAN ERYTHROCYTE ENZYME (BIOCHEMICAL ASSAY)  
 XR HUMAN RBC [HOLE] (BIOCHEMICAL ASSAY)  
 XS HUMAN RBC [UNSPECIFIED] (BIOCHEMICAL ASSAY)  
 XX HUMAN RBC [BROKEN] (BIOCHEMICAL ASSAY)  
 XY HUMAN LIVER  
 \*YC MYELOID LEUKEMIA/ARA-C; NSC 63878 IN RFM/UN MOUSE  
 \*10 COLON CYSTADENOCARCINOMA 10/A  
 \*11 COLON ADENOCARCINOMA 11/A  
 \*12 COLON CYSTADENOCARCINOMA 12/A  
 13 C3H MAMMARY ADENOCARCINOMA 13/C

14 C3H MAMMARY ADENOCARCINOMA 14/C  
 16 C3H MAMMARY ADENOCARCINOMA 16/C  
 17 C3H MAMMARY ADENOCARCINOMA 17/C  
 18 C3H MAMMARY CYSTADENOCARCINOMA 18/C  
 2P PANCREATIC CARCINOMA 02  
 \*2R P338 LEUKEMIA/TIAZOFURIN; NSC 286193, DEVELOPED AT  
 LMGB, DTP, DCT, NCI  
 2S P338 LEUKEMIA/AMETANTRONE, NSC 287513  
 2T P333 LEUKEMIA/ADRIAMYCIN; NSC 123127, DEVELOPED AT  
 SCR 06 & 41  
 2U P328 LEUKEMIA/ADRIAMYCIN; NSC 123127, DEVELOPED AT  
 SCR 01  
 2X P288 LYMPHOCYTTIC LEUKEMIA/METHOTREXATE; NSC 740  
 23 C3H MAMMARY ADENOCARCINOMA 23/C  
 25 CARCINOMA 1025  
 28 P288 LYMPHOCYTTIC LEUKEMIA  
 \*4A L4946 LYMPHATIC LEUKEMIA/AZASERINE; NSC 742  
 49 L4946 LYMPHATIC LEUKEMIA (SOLID)  
 5P P335 LEUKEMIA  
 \*6A COLON 06/A  
 \*6M L1210 LEUKEMIA/6-MP & 6-MMPR & 6-THIOGUANINE;  
 NSC 755, NSC 40774, NSC 752  
 6T L1210 LEUKEMIA/6-THIOGUANINE; NSC 752  
 7A COLON 07/A  
 \*7P CA 755/6-MERCAPTOPYRINE; NSC 755  
 \*8A COLON 08/A  
 8C P1798/CORTISONE; NSC 9703  
 8P P1798 LYMPHOSARCOMA  
 81 P1081 CHLOROBLASTOMYXOMA  
 91 S-91 CLOUDMAN MELANOTIC MELANOMA  
 98 C1498 MYELOID LEUKEMIA



# TEST SYSTEMS

5 position Test System<sup>1</sup> = Host Group, Tumor, Parameter, Site (See indicated pages for definition)

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5.6.7

17

21

3AAH	3CP31	3EA31	3LC29	3LNJ2	3MH22	3PG31	3TR31	32P32	5H112	8H118
3AA2	3CR31	3EA32	3LC31	3LN31	3MH36	3PH31	3UG37	32R31	5H312	9ASK
3AA21	3CX21	3EM12	3LD21	3LOG5	3ML21	3PJ31	3VAH2	32T31	5L822	9CH5
3AA3	3CX29	3EM32	3LD31	3L03F	3ML22	3PJ32	3VBH2	32U31	5MS16	9C25
3AA4	3CX31	3EM37	3LE1E	3L03S	3MP21	3PK31	3VCG5	32X31	5NH12	9D15
3AD12	3CX39	3EP12	3LE12	3L031	3MP22	3PL31	3VDG5	32332	5NH16	9ECL
3AG21	3CY32	3EP32	3LE21	3L032	3MP29	3PM21	3VEG5	32512	5NH31	9HE5
3AKF3	3CY37	3EP37	3LE22	3L039	3MP31	3P031	3VEH2	32831	5NL32	9HF5
3AK31	3CY72	3FM31	3LE27	3LQ31	3MP37	3P039	3VFG5	32841	5NL37	9HG5
3AK33	3CZ31	3FR41	3LE29	3LR21	3MT3F	3PP31	3VGG5	34A22	5TG42	9HL5
3A212	3CZ32	3FS32	3LE3E	3LS21	3MT3S	3PQ31	3VHG5	34922	5WA12	9HM5
3A331	3CZ37	3FU21	3LE31	3LS31	3MT31	3PS21	3VIG5	35P21	5WA16	9HR5
3A332	3CZ72	3FV12	3LE32	3LT31	3MT32	3PS31	3VIH2	36A32	5WA21	9HX5
3A336	3C2G5	3GA31	3LE36	3LU21	3MT39	3PS32	3VJG5	36M21	5WA27	9H25
3A512	3C2H2	3GA41	3LE37	3LU31	3MX32	3PS36	3VKH2	36T21	5WA31	9JA5
3A631	3C3D2	3GE31	3LE39	3LVG5	3MX72	3PS37	3VLG5	36T31	5WA32	9JB5
3A632	3C3E2	3GL31	3LF21	3LW21	3MY39	3PS39	3VMG5	37A31	5WA36	9JC5
3BA31	3C33B	3GS32	3LF31	3LW31	3M212	3PU31	3VNG5	37A32	5WA46	9JD5
3BA32	3C332	3GS37	3LF32	3LX21	3M5J2	3PV31	3VNH2	37P12	5WA86	9JE5
3BC21	3C339	3G137	3LG21	3LX22	3M51E	3PW31	3VOG5	38A32	5WC12	9JF5
3BC27	3C4G5	3G232	3LH31	3LX32	3M512	3PY12	3VPG5	38C12	7AA4	9KB5
3BC32	3C4H2	3G233	3LJ21	3LY32	3M53E	3PZ31	3VQG5	38C82	7AC12	9LE5
3BM31	3C5G5	3G237	3LKG5	3L221	3M531	3P231	3VRG5	38P12	7AM12	9LN5
3BP31	3C5H2	3HD31	3LKH2	3L431	3M532	3P331	3VRH2	38P22	7D112	9L05
3BU31	3C631	3HE12	3LL1E	3L829	3M539	3P421	3VSG5	38P31	7EN12	9LV5
3B1D2	3C632	3HE31	3LL12	3L831	3M572	3P431	3VTG5	38P32	7FS12	9PS5
3B1E2	3C637	3HL31	3LL16	3L841	3M631	3P631	3WA16	38P82	7HE12	9SCM
3B11E	3C639	3HL32	3LL22	3L931	3M632	3P731	3YC39	38121	7LP12	9XEB
3B13E	3C672	3HL72	3LL29	3MBG5	3M672	3P831	31032	39112	7L212	9XLC
3B131	3C682	3HU21	3LL3B	3MBH2	3OC3F	3P841	31132	39131	7MC12	9XMC
3B132	3C8J2	3HU31	3LL3E	3MBH5	3OC3S	3P931	31232	39831	7MM12	9XNC
3B136	3C816	3JAG5	3LL31	3MD32	3OC31	3RE35	31332	5AA	7NP12	9XRB
3B137	3C83B	3JBG5	3LL32	3MD36	3OC32	3R032	31339	5AA3	7NR12	9XSB
3B139	3C831	3JCG5	3LL36	3MD72	3OC39	3R039	31432	5AA4	7OG12	9XXB
3B172	3C832	3JDG5	3LL37	3ME31	3OS12	3R072	31437	5CM42	7PM12	9XYC
3CA12	3C872	3JEG5	3LL39	3ME41	3OT31	3RS31	31472	5CS42	7PN12	
3CCJ2	3C876	3JFG5	3LL72	3MFG5	3PA31	3RX32	31631	5DH42	7PR12	
3CD12	3C882	3K431	3LL76	3MFH2	3PB31	3SA12	31632	5DL31	7PT12	
3CD32	3C9G5	3LA31	3LL82	3MGG5	3PC31	3SA31	31637	5DL32	7PX12	
3CD72	3C9H2	3LB21	3LL86	3MGH2	3PC37	3SA32	31639	5DL37	7P112	
3CD82	3DP21	3LB31	3LM21	3MGH5	3PD31	3SA82	31672	5DN42	7RC12	
3CLG5	3DP31	3LC21	3LM32	3MHEF	3PE31	3TC21	31732	5DR31	7RS12	
3CL31	3EA11	3LC27	3LNG5	3MH3F	3PF31	3TE37	31832	5DX31	7SB12	

<sup>1</sup> Frequently test system is specified as a 6 position field. In this instance, the two position host strain code is used in lieu of the single position host group codes now in this table. A four position test system always infers the absence of an inoculum site.

# TREATMENT SCHEDULE

The treatment schedule for administration of a compound in a test is comprised of six parts as follows:

Interval  
 Interval unit  
 Basic number of injections per cycle  
 Time of day of administration of initial dose (optional)  
 Day of 1st injection  
 Restart days (optional)  
 Total injections

Interval – The time between treatments expressed in terms of minutes (M) or hours (H) or days (D).

Interval Unit – Designation of the interval as either minutes (M) or hours (H) or days (D).

Basic Number of Injections – The number of injections associated with one cycle of the treatment schedule (e.g., daily 1-9 would involve nine injections in one complete cycle).

Time of Day of Administration of Initial Dose – An optional field permitting the screener to specify the time of day for the initial injection. Times are expressed in military time (e.g., 00:01 thru 24:00 representing 12:01 AM thru 12:00 midnight).

Day of 1st Injection\* – The day, relative to day zero (inoculation day), when the 1st treatment is to be initiated.

Restart Day(s) – An optional field specifying day(s) when the complete treatment cycle is to be reinitiated.  
 Example: A treatment schedule of Q01D×9 Time: 13:30 Day = 1,17 would be interpreted – daily treatment at 1:30 PM on days 1-9 and 17-25. Day 17 is defined as a restart day.

Total Injections – The total number of injections intended to be administered for this test. In the case of infusion or perfusion indicates the total number of hours involved.

Special Codes – The following special treatments may be used and are coded in the interval field Q\_\_\_ with the interval unit left blank:

Code	Meaning
#A	Daily, twice a day (hourly interval not specified)
#B	Daily, three times a day (hourly interval not specified)
#C	Ad lib in water
#D	Ad lib diet
#(1-9; A-M)	Hourly interval specified but daily interval irregular (consult input data)
##	Other (see input data)
#X	Infusion – The continuous administration of a compound to an entire animal over a period of time with the compound entering the general body circulation. (See total injections field)
#Y	Perfusion – The continuous administration of a compound to an isolated site (tumor, organ, or a limb) over a period of time without the compound entering the general body circulation. (See total injections field)

## INPUT INTERVAL CODES FOR COMBINATION CHEMOTHERAPY

### MINUTES

00 thru 60 – actual minutes

### HOURS

+ – blank  
 1-9 – hours 1-9  
 0 – 10 hours  
 A – 11 hours

B – 12 hours etc. thru  
 M – 23 hours  
 X – infusion  
 # – See Special Codes

### DAYS

1 – daily (also single)  
 2 – every other day  
 3 – every 3rd day

4 – every 4th day etc. thru  
 9 – every 9th day  
 0 – every 10th day

A – every 11th day etc. thru  
 Z – every 36 days  
 # – See Special Codes

Time interval between each treatment. If # symbol is used in either hours or day columns, the individual codes for hours and day do not apply; see Special Codes above for definition.

\* an asterisk in lieu of an actual day means day 27 or greater for pre-October 1978 testing only. Consult the microfilm for actual day.

# EVALUATIONS

## CONTROL (CONTL)

Measure of tumor progression in untreated animals using indicated parameter. (See page 17, survival time, tumor weight, etc.) Units are specified in individual protocol.

**NOTE:** For parameters G, H & J this field deviates from the norm. Because an optimum evaluation day is selected from two or more possible evaluation days for each dose, control evaluation may vary from dose to dose within a dose response. What is displayed is the actual control evaluation for the evaluation day determined to be optimum for a particular test. Additionally, where the test evaluation and the T/C% column are negative, the control evaluation column for parameters G, H and J does not contain a control evaluation at all but the initial weight of the test group. In these instances the test tumor weight change (test evaluation) is divided by the test tumor initial weight so that the T/C% column is actually a T/T% and reflects the amount of actual test regression, i.e., "- 50%" in the T/C% column means the test tumor diminished to one half of its initial size.

## TEST

Measure of response in treated animals using indicated parameter. (See page 17, survival time, tumor weight, etc.) Units are specified in individual protocol.

# T/C (PERCENT)

Ratio of test (T) evaluation to control (C) evaluation expressed as a percentage.

## SPECIAL STUDY CODES (SSC)

Special Study Code (SSC) is a two position field. Where the code is only one position in length, it should be right justified in the two position field.

CODE	DATA TYPE
A	Comparison Study (analogs)
B	Schedule Dependency
C	Combination Chemotherapy
D	Not Processable
E	Special Request
F	Special Colon Tumor Protocol Testing
G	Special Statistical Studies
H	Radiation Sensitizers
J	Comparison-Schedule Dependency
K	Spontaneous AKR Testing
L	L1210 1-5 VS 1-9 Study
M	Special Synthetic Protocol
N	Special Natural Products Protocol
P	Delayed Treatment Schedule
R	Sensitive Matching Control for Resistant Tumor Experiment
S	Not Submitted
T	Screener 28 only
U	Special P388 Testing
W	Panel Statistical Studies

# CONTROL STATUS CODE (CSC)

### In Vivo

- 1 -- Satisfactory control
- 2 -- Excessive control deaths by control early death day
- 3 -- Excessive control no-takes on control no-take day \*
- 4 -- Mean or median tumor weight or survival time outside limits
- 5 -- Other reasons (contamination, etc.)
- 6 -- Excessive deaths and excessive no-takes (2 + 3)
- 7 -- Excessive deaths and mean tumor weight or survival time outside limits (2 + 4)
- 8 -- Excessive no-takes and mean tumor weight or survival time outside limits (3 + 4)

- 9 -- T/C of positive control outside limits at standard dose
- A -- Test of positive control compound at standard dose is toxic in otherwise satisfactory control
- E -- Quality control limits not established. Screener assigned only if other CSC codes are not applicable.

\* for TSC 85 and a parameter of G indicates more than 10% control regressors.

### In Vitro

- (Blank) -- Satisfactory Control (CSC-1)
- 4 -- Fold growth outside limits
- 9 -- Positive control outside limits

## DATE ON

Date experiment started.

Left to right,

First two positions: Last two digits  
of calendar year  
Second two positions: 1-12 number of month  
Third two positions: 1-31 day of month

## CONTROL NUMBER

Experiment identification number. Numbers are assigned by screening laboratory sequentially within each test system. Control numbers are comprised of a prefix, core and suffix defined as follows:

**Prefix** The prefix is optional and can be used in any manner developed by the screener provided its use is approved in advance by DEB. Once approved, the prefix must be consistently used by the screener(s) for which it was approved.

**Core** The control number core is the equivalent of the old four position

control number. It is comprised of 5 digits and permits control numbers up to 99,999. Those screeners previously representing the number 10,001 with P001 will now enter 10,001.

**Suffix** The suffix is a one position field that permits the screener to relate series of control packs (e.g. 10,001A; 10,001B; 10,001C; etc.). When this convention is used, all control packs in the series must contain a suffix including the first.

## ROUTE OF ADMINISTRATION (RT)

0 - None (Controls Only)  
1 - iP (Intraperitoneal)  
2 - SC (Subcutaneous)  
3 - Oral (nonfasting)  
4 - Other

5 - iV (Intravenous)  
6 - IM (intramuscular)  
7 - Oral with prior fast  
8 - Inhalation  
9 - Ad lib in water

## 1ST SCREENER

First Laboratory to test a compound.  
\*\*= Not designated

## SCREENER (SCR)

\*01 - Microbiological Assoc.  
\*02 - Hazleton Labs. - in vivo  
03 - Battelle Columbus Labs. - in vivo  
\*04 - Stanford Research Inst.  
\*05 - Raltech Scientific Services, Inc. - in vivo  
\*06 - A.D. Little, Inc. - in vivo  
\*07 - Abbott Labs.  
A8 - Southern Research Inst. in vivo  
08 - Southern Research Inst. - in vivo

09 - IIT Research Inst. - in vivo  
\*10 - Chas. Pfizer and Co.  
\*11 - Pitman-Moore Co.  
\*12 - Schering Corp.  
\*13 - Wm. S. Merrill Co.  
\*14 - Univ. of Miami - in vivo  
\*15 - Wyeth Labs.  
\*16 - Univ. of Miami - in vitro  
\*17 - A.D. Little, Inc. - in vitro  
\*18 - Southern Research Inst. - in vitro

\*19 - Carver Fdn.  
\*20 - Sloan-Kettering Inst. - in vivo  
\*21 - Cancer Research Inst.-Bombay - in vivo  
\*22 - Central Drug Research Inst. - Lucknow - in vivo  
23 - Mason Research Inst. - in vivo  
\*24 - Research Triangle inst. - in vitro  
\*25 - The Weizmann Institute of  
Science, Rehovot - in vivo  
\*26 - The Catholic Medical Center of  
- Brooklyn & Queens, Inc. - in vivo

\* Discontinued Screener

# SCREENER (CONTINUED) (SCR)

- \*27 - Institute for Pharmacological Research "Mario Negri," Milan - in vivo
- 28 - Institut Jules Bordet, Brussels - in vivo
- \*29 - Japanese Foundation for Cancer - in vivo
- 30 - Bristol Laboratories - in vivo
- \*31 - Univ. of Wisc. - in vitro
- \*32 - Upjohn Co. - in vivo
- \*33 - Univ. of Alberta - Biochemical Assay
- \*34 - Yale Univ. - Biochemical Assay
- \*35 - University of Arizona - in vitro
- \*36 - Southern Research Institute - in vitro/BC
- 37 - Parke Davis/Warner Lambert - in vivo
- \*38 - Yale Univ. School of Medicine - in vivo
- \*39 - Southwest Foundation for Research and Education - in vitro

- \*40 - Screening Section, DEB
- \*41 - Assoc. Chief Lab. Res., DTP - in vivo
- \*42 - Biochem. Section, DEB
- \*43 - Molecular Biol. & Methods Dev. Lab.
- \*44 - Litton Bionetics - in vitro - antiviral
- \*45 - IITRI Life Science Division - in vitro
- \*46 - Biotech Research Laboratories - in vitro - antiviral
- \*47 - Purdue University - in vitro
- \*48 - Department of Public Health, Mich. - in vitro
- 49 - Parke Davis/Warner Lambert - in vitro
- \*50 - Upjohn Co. - in vitro
- \*51 - W.R. Grace & Co. - in vitro
- \*52 - Stehlin Foundation for Cancer Research - in vivo
- \*53 - Arizona State University - in vitro

- 54 - Institut Jules Bordet - in vivo
- 55 - V.A. Sepulveda Hospital - in vitro
- 56 - Mayo Medical School - in vitro
- 57 - Cancer Therapy & Research Foundation of South Texas - in vitro
- 58 - University of Arizona - in vitro
- \*80 - University of Georgia Inst. for NP Research - in vitro
- \*92 - Leo Goodwin Institute for Cancer Research - in vivo
- 93-99 - NCI information only
- 9C - Tumor Bank
- 9F - Southern Research Inst.
- 9G - Southern Research Inst.

\*Discontinued Screener

## DOSE UNITS (UNT)

In mg/kg/injection or dilution unless otherwise noted.

- A - Nanoliters/mouse/injection
- B - ml/mouse/injection
- C - Dilution factor  $10^2$
- E - mg/mouse/injection
- G - Grams/kg/injection
- J - Micrograms per hour
- K - Dilution factor  $10^3$
- L - Microliters/mouse/injection
- M - Micrograms/kg/injection
- N - 1/1000 micrograms/kg/injection
- P - Micrograms/mouse/injection
- R - Units of radiation
- T - Micromoles per kilogram
- U - International Units/animal/injection
- V - 10,000 International Units/ animal/injection
- % - % drug inhaled or offered in feed or water
- Z - % concentration in a 0.5 ml injection volume

Dilution expressed a/bcdef where a = volume of original material, bcdef = final volume

## CELL CULTURE

- W - Micrograms/ml/duration
- D - Dilution

## TOXICITY DAY SURVIVORS (TOXD SURV)

First column shows the number of survivors on Toxicity Day (or the special indicator \*\* which indicates that drug-induced deaths cannot be determined because of the time of drug treatment.)

Second column shows the total number of animals started on test.

In a tumor-weight model, Toxicity Day is normally the same as day of evaluation. (Exceptions: 3CD12, 3CD13, 3CD72, 3CDJ2)

Toxicity Day is normally four days after day of first injection. Survivors are recorded on this day as a measure of drug toxicity. In experiments where treatment is initiated prior to implant, Toxicity Day is never designated earlier than day 0.

## DOSE PER INJECTION

- Seven position field
- 0005000 = 50.00 mg/kg
- 1/00010 = Dilution 1 in 10

## TOXICITY DAY (TOX)

TOXICITY day is a day specified by the screener that will serve as a toxicity evaluation point for the compound under test. Toxicity day often coincides with the second weigh day. When it does, excessive deaths (>34%) or excessive weight loss on this day in an otherwise inactive test are indications of toxicity in a survival model or false activity in tumor inhibition model.

Usually toxicity determination is only performed where treatment is initiated prior to experiment day 4. (Exception - all tumor inhibition systems)

Test toxicity day may never exceed the control early death day for the specified test system. Where the screener specifies a toxicity day that exceeds the early death day for the operative test system, the computer will automatically revert to the early death day.

# LOG CELL KILL REDUCTION FIELDS

## 1.0 INTRODUCTION

The Screening Data Summary (SDS) Report contains, for some data lines, an information field that can be valuable in the evaluation of compounds. This information field provides log cell kill information for selected tests on the screening data summary, and is identified on the report as " $K_E$ ". This field is an estimate of the number of logs (or fractions of a log) of cells killed by the chemotherapeutic agent at the indicated dose level and on the indicated treatment schedule. In the future an additional field, the  $K_I$  field, will appear just to the right of the  $K_E$  field. The  $K_I$  field will be an estimate of the log cell kill of a single injection of the chemotherapeutic agent. Log cell kill ( $K_E$ ) and log cell kill per injection ( $K_I$ ) provide a measure of the relative tumor population changes during treatment. These values are related to the fraction of cells killed rather than to the absolute number of cells killed. According to Skipper, Schabel, and Wilcox, Cancer Chemotherapy Reports 35: 1-111, 1964, and Wilcox, Cancer Chemotherapy Reports 50: 541-542, 1966, in tumor populations for which all cells have adequate exposure to drug and for which the growth fraction does not change appreciably with population size, a given dose of drug will kill about the same fraction of cells regardless of population size. Relative reduction in tumor burden is therefore considered a more meaningful measure of drug effectiveness than the absolute number of cells killed.

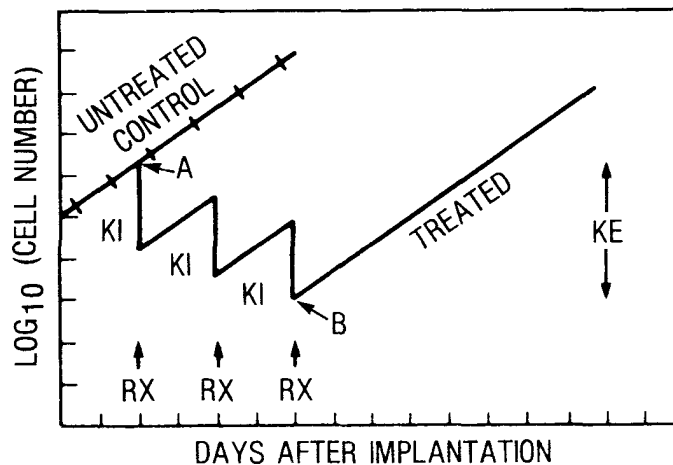
## 2.0 BACKGROUND

If the intent of chemotherapy is to reduce a tumor cell population extensively, then some quantitative measure of this reduction would be useful in evaluating the effectiveness of a drug against a tumor when applied at a given dose and schedule. The log cell kill and log cell kill per injection provide a measure of tumor population changes during treatment, and indicate the extent to which the population was reduced during treatment and the amount of tumor remaining after treatment. Figure 1 idealizes the treatment of a leukemia population and will be useful in explaining and defining log cell kill. The figure depicts cell number for an exponentially growing cell population *in vivo*. Both an untreated control population and a population treated three times with chemotherapy are illustrated. The effect of each dose of chemotherapy is idealized as being an instantaneous reduction of the tumor population. The cells that survive treatment immediately begin to regrow at the rate of the untreated population. Although not illustrated, it is further assumed that both the untreated control animals and the treated animals will die when the tumor burden reaches some particular size, which for P388 and L1210 in the mouse is assumed to be  $10^9$  cells. The following definitions are now made:

$K_I$ : The log kill per injection is the tumor size reduction for each dose of drug assuming equal doses produce the same affect (the treated group vertical lines in the figure).

$K_E$ : The log kill at end of treatment is the number of log<sub>10</sub> units by which a tumor population is reduced relative to its size at the beginning of treatment (point A to point B in the figure).

It is necessary to know the doubling time of the tumor cell population to estimate either the treatment log cell kill or the log cell kill per injection. This doubling time is routinely determined from daily titrations included with each experiment submission. In the event of an unacceptable titration accompanying the experiment, the log cell kill is calculated using an average doubling time based on the prior quarter's titration input. (Where no prior quarter data exist, a value is derived empirically from small numbers of titrations performed by selected laboratories.)



# LOG CELL KILL REDUCTION FIELDS (CONT.)

## 3.0 INTERPRETATION

The numerical values of  $K_E$  and  $K_I$  are no more precise than the data used to make the estimates, and any interpretation attributed to these values must be further qualified according to the validity of the assumptions previously described. Recognizing these limitations, the following general considerations are useful in interpreting  $K_E$  and  $K_I$ :

- $K_E > 0$ : The cell population was reduced by the drug, drug dose, and schedule being tested. The cell population at end of treatment was less by this number of log 10 units than its size at the beginning of treatment. Example: Suppose the cell population at the beginning of treatment was  $8 \times 10^5$  cells and the  $K_E = 3.0$ , then the number of cells at the end of treatment was  $8 \times 10^2$  cells. This means that 99.9% of the  $8 \times 10^5$  cells were killed (800,000 initial cells minus 800 final cells equal 799,200). The larger the value of  $K_E$ , the greater the cell kill achieved. There are some practical cases where the computer value of  $K_E$  can be very large, i.e., in test groups where some animals are cured and the median or mean life span is large. When this occurs, the value of  $K_E$  displayed is the value to reduce the population to one cell, but preceded by a ">" sign.
- $K_E = 0$ : The cell population at end of treatment was the same as at the beginning of treatment. Note that this means that each dose reduced the cell population by some amount ( $K_I > 0$ ), but that regrowth between injections compensated for the cell reduction.
- $K_E < 0$ : The cell population at end of treatment was greater than the cell population at the beginning of treatment. The negative value is an estimate of the number of log10 units of cell growth that occurs during the course of treatment. For a completely ineffective drug, drug dose, or schedule, the cell kill per dose is zero and the treated cell population will follow the growth curve of the untreated control population.

In addition to numeric values providing the actual log cell kill calculated, the  $K_E$  value may at times contain error codes identifying why a log cell kill calculation is not possible. The possible non-numeric  $K_E$  codes and their meaning are described in section 6.0.

## 4.0 FORMAT

The format of the new field is as follows:

$K_E = > \pm \underline{xxx}$



This field is the actual log10 value to a single decimal place.

The sign of the log kill. A negative sign always infers a net cell increase during treatment.

The greater than (>) symbol appears whenever the calculation routine overestimates the log kill. The routine then sets  $K_E$  (and eventually  $K_I$ ) to a value that would reduce the cell population to a single cell. The greater than symbol is used to indicate that the actual value is probably a little larger than the displayed value. This condition can occur whenever test survival time is unusually large. It suggests a bad test, too many cures for an accurate estimate of survival time, or a test in which cure is closely approached.

# LOG CELL KILL REDUCTION FIELDS (CONT.)

## 5.0 SDS DATA AFFECTED

Currently log cell kill calculations are determined for the following test systems:

3B131  
3CDJ2 (single injection only)  
3LE21  
3LE31  
3M531  
3PS21  
3PS31

It is anticipated that information in the  $K_E$  field will be added for other test systems in the future, and the user of the SDS should be aware that  $K_E$  data for additional test systems will be added to the SDS without additional notification.

## 6.0 SPECIAL LOG CELL KILL MESSAGES

When a log cell kill calculation is not possible, special codes are provided to indicate why. The following table provides a listing of each such special code and its interpretation. The absence of any information on the SDS, with respect to log cell kill, means that the test system is not one for which log cell kill is being calculated, or it is an appropriate test system but the testing date is prior to the period for which necessary data are available to permit the calculation (July, 1977).

TABLE OF SPECIAL MESSAGES

<u>Special Code</u>	<u>Interpretation</u>
$K_E$ = Toxic	The test is clearly toxic (too many deaths prior to toxicity evaluation day) and no log cell kill calculations have been attempted.
$K_E$ = Toxic?	The log cell kill calculation has determined that the test is a probable toxic test.
$K_E$ = TSC 33 or $K_E$ = TSC 34	Test to be repeated. No log cell kill calculation attempted.
$K_E$ = ERR001	Insufficient data available to permit the log cell kill calculation.
$K_E$ = ERR002	Final treatment day listed as occurring before initial treatment day (mistake). No log cell kill calculation attempted.
$K_E$ = ERR003	First treatment day negative. No log cell kill calculation attempted.
$K_E$ = ERR005	Unable to use the specified inoculum level. No log cell kill calculation attempted.



# CALCULATIONS FOR MEAN AND MEDIAN SURVIVAL TIME

## MEAN SURVIVAL TIME

$$\frac{\Sigma S + AS(A-1) - (B+1)NT}{S(A-1) - NT}$$

Day A = Day on which deaths are no longer considered due to drug toxicity.

Day B = Day beyond which control group survivors are considered "no-takes."

$\Sigma S$  = If there are "no-takes" in the treated group (as defined in Protocol 11.103),  $\Sigma S$  is the sum from Day A through Day B. If there are no "no-takes" in the treated group,  $\Sigma S$  is the sum of daily survivors from Day A onward.

$S(A-1)$  = Number of survivors at the end of Day (A-1).

NT = Number of "no-takes" according to the criteria given in Protocols 7.300 and 11.103.

## MEDIAN SURVIVAL TIME

$$L + c \cdot j/f_M$$

L = lower boundary of class containing median animal, =  $D_M - 0.5$   
 where:  $D_M$  = that day when total deaths  $\geq A$

$$A = \left( \frac{\text{initial animal count} + 1}{2} \right)$$

c = class interval = 1 (Day)

j = number of deaths needed to reach median animal from lower class boundary (J = A minus total deaths prior to day  $D_M$ )

$f_M$  = frequency of class; i.e., total deaths on  $D_M$

# SAMPLE NUMBER (SMPL)

Crude Natural Products – consists of a suffix code and specimen number.

Suffix Code	Description
none	original sample
A	retest, refermentation or extract to complete sequential testing
B	retest, refermentation or re-extraction to confirm activity following status codes 11, 15, 26P, 27P, 28P, or 31P, and/or to complete testing
D	fermentation research (media, time, temperature studies in flasks), plant collection studies (collection for isolation) or re-collection of plant products
E	fermentation research (jars or tanks); not applicable in plant extracts.

F	fractionation or isolation studies
J	pilot plant production studies
K	purified or crystalline products
T	plant cell fermentation research

Synthetics and Isolated Natural Products – identifies different samples of a compound.

First Digit:	ALPHABETIC M, N, P, or Q – Bulk Drug R – Drug in Clinical Dose Formulation V – Vehicle or Clinical Dose Formulation
Second Digit:	A – Original Material or Lot Number Received by NCI (Including Subsequent Shipments of The Original) B, C, D, etc. and 1-8 – Subsequent Receipts by NCI Not Identified as "A". 9 = Sample number is unknown.
Special:	M999 is used for old compounds or compounds for which the sample number is unknown.

# PARAMETER<sup>1</sup>

- 1 – Mean tumor weight
- 2 – Mean survival time
- 3 – Median survival time
- \*4 – Survival time, mean or median not specified
- 5 – ED<sub>50</sub> (concentration causing 50% inhibition of growth, enzyme activity, etc.)
- 6 – Alkaloid content
- 7 – Median tumor weight estimated from tumor diameter
- 8 – Mean tumor weight estimated from tumor diameter
- 9 – Mean tumor packed cell volume
- A – Tumor Volume
- B – Percent Inhibition
- \*C – ED<sub>50</sub> reported in molar units
- D – Delay in days of tumor growth (T-C) at a point of tumor recovery post-therapy. (Denoted in inoculum level field, see page 21.)
- E – Median Survival Time excluding tumor-free animals
- F – Median Survival Time; survivors are listed for end of Rx not Toxicity Evaluation Day

- G – Mean Tumor Weight change (mean wt $\Delta$ ) between day zero and final evaluation day. Mean wt $\Delta$  = mean final tumor weight – mean initial tumor weight.
- H – Optimum mean tumor weight change (mean wt $\Delta$ ) between day zero and any one of several possible final evaluation days (FED). Mean wt $\Delta$  = final tumor weight minus initial tumor weight. Optimum mean wt $\Delta$  is the calculated test mean wt $\Delta$  that when divided by the control mean wt $\Delta$  yields the most optimum T/C%. For each experiment, only mean wt $\Delta$  values occurring during a specific predefined range of days are considered for selecting an optimum.
- J – Median tumor weight change (median wt $\Delta$ ) is determined by subtracting the group median initial tumor weight from the group median final tumor weight. Median wt $\Delta$  = Group median final tumor weight minus group median initial tumor weight.
- K – Degree of reversal of cyclic AMP- induced change.
- L – Strength of induction reaction
- N – Degree of inhibition of growth (zone)

<sup>1</sup>The parameter defines the method of evaluating the test.

\*Discontinued Parameter

# VEHICLE (VEH)

NOTE: This list of vehicles and codes is provided exclusively for the purpose of interpreting the screening data summary (SDS) report. IT IS NOT TO BE CONSTRUED as a list of potential vehicles for use with new experiments. Consult Protocol 3 for experiment vehicle selection and procedures.

00 - None	0D - Alcohol
01 - Methylcellulose (MC)	0E - Dimethylformamide
02 - Saline	0F - Dioxane
03 - Acid diluted with saline	0G - Dextrose
04 - Steroid suspending solution	0H - Acid diluted with CMC
05 - Alkali diluted with saline	0J - Alkali diluted with water
06 - Olive oil, sesame oil, peanut oil	0K - Lactate
07 - Other	0L - Clinical formulation
08 - Carboxymethylcellulose (CMC)	0M - Klucel (Hydroxypropylcellulose) (HPC)
09 - Water	0N - Suspension in Saline
10 - Single (1X) Strength Eagles MEM (serumless)	0P - PVP
11 - 1% Dimethylsulfoxide (DMSO)	0Q - Citric acid
12 - 1% Ethanol	0R - Lactic acid
13 - 5% Dimethylformamide	0S - Saline sonified
14 - 0.1% Dioxane	0T - Saline with Tween-80
15 - 0.5% 1N HCL	0U - Gum acacia
16 - 0.5% 1N NaOH	0V - Sodium bicarbonate
17 - Distilled Water	0W - Saline + Tween 80 + alkali
18 - Single Strength 10% Hanks bal. Salt Sol.	0X - DMSO
19 - 50% DMSO	0Y - Alkali diluted with CMC
20 - 100% DMSO	0Z - Saline + alcohol
21 - Chloroform	0+ - Distilled water + Tween 80
22 - 10% 1N NaOH	0* - Distilled water + alcohol
0A - Normal media	0= - Distilled water + Tween 80 + alcohol
0B - Propylene glycol	0% - Saline + Tween 80 + alcohol
0C - Acetone	0S - Klucel + Tween 80

## DETAIL TEST COMMENTS

Detail test comments, supplied by the screener, are provided for each individual test if appropriate. Each such comment follows the test line to which it applies. If the control data have an associated comment, this comment will immediately follow the control group data line(s).

Test and control comments will be provided for all test results processed by the computer after July 5, 1980, and for any previous control packs/experiments if they are reprocessed for any reason (corrections, special requests, etc.).

# HOST

## HOST CODES IN VIVO (STRAIN)

### HOST GROUP CODES

- 3 - mouse (host strain codes 01-49, 1A, 1B, 1C etc.)
- 5 - rat (host codes 50-69)
- 7 - Hamster (host codes 70-75)
- 8 - egg (host codes 80-85)
- 9 - other than in vivo (host codes 90-99)

NOTE: The host strain specified by the screener is converted to a host group code which frequently appears as the first position of the 5-position test system as on the summary page (1-1).

01 - Swiss	*22 - CAF <sub>1</sub>	*45 - PRI/P1
02 - B <sub>6</sub> D <sub>2</sub> F <sub>1</sub> (BDF <sub>1</sub> )	23 - C57BL/10SC	46 - AL/N
03 - C57BL/6	*24 - NBL (mutation from C57BL/10H2d)	47 - BALB/cfC3H
04 - DBA/2	25 - A/He	48 - DBA/8
*05 - BCF <sub>1</sub>	27 - A/J	49 - CD8F1
06 - CD <sub>2</sub> F <sub>1</sub> (CDF <sub>1</sub> )	28 - BALB/cJ	50 - Random bred albino rat
07 - C3H/He	29 - BALB/c An	51 - Fischer 344 rat
*08 - C <sub>3</sub> AKF <sub>1</sub> (CHKRF <sub>1</sub> )	*30 - NZB	52 - Wistar-Furth rat
1A - B <sub>6</sub> C <sub>3</sub> F <sub>1</sub>	*31 - NZW	53 - Lewis rat
1B - BALB/CM	32 - SJL/J	54 - Buffalo rat
1C - C <sub>3</sub> B <sub>6</sub> F <sub>1</sub>	*33 - SM/J	55 - AC1 rat
1D - CR:NIH(S)-nu	34 - CBA/J	56 - Wistar rat
1E - AKR/J	*35 - CAF <sub>1</sub> /N	57 - Wistar/Lewis
1F - Athymic NCr-nu	*36 - CAF <sub>1</sub> /J	58 - OM/N
1G - RFM/UN	37 - AKD <sub>2</sub> F <sub>1</sub>	59 - M520
1H - BALB/cAnNCr-nu	*38 - D <sub>2</sub> AKF <sub>1</sub>	60 - August 28807
1J - NIH - II	39 - mouse species not specified	61 - ACP (Piebald)
1K - CR:BG/nu (Beige nude mice)	*40 - C <sub>3</sub> D <sub>2</sub> F <sub>1</sub>	62 - Albany
*10 - D <sub>2</sub> B <sub>6</sub> F <sub>1</sub> (DBF <sub>1</sub> )	*41 - ZWZBF <sub>1</sub> (NZW/B1 X NZW/B1)	63 - Copenhagen 2331
11 - CBF <sub>1</sub>	*42 - ZBZWF <sub>1</sub> (NZB/B1 X NZW/B1)	64 - Zimmerman 61
*12 - BAF <sub>1</sub>	*43 - CFW/P1	65 - Yoshida 38366
*13 - ABF <sub>1</sub>	*44 - NIH/P1	66 - NBR/P1
*14 - D <sub>2</sub> CF <sub>1</sub> (DCF <sub>1</sub> )		69 - rat species not specified
*15 - LAF <sub>1</sub>		70 - Syrian hamster
*16 - ALF <sub>1</sub>		80 - Embryonated egg
*17 - KRCHF <sub>1</sub> (AKC3F <sub>1</sub> )		
18 - AKR/Lw		
19 - C57L		
*20 - A/L		
21 - C3Hf/He		

\*Discontinued

### OTHER THAN IN VIVO

- 90 - Cell culture tube assay
- 91 - Chemical analysis
- 93 - Cell culture chromatography
- 94 - Bioautography
- 95 - Cell-free systems
- 98 - Biochemical assay
- 99 - Microbial

### SEX

- M = Male
- F = Female
- X = Mixed

# ACCREDITED ANIMAL SUPPLIERS

Supplier	Symbol	Code	Host	Supplier	Symbol	Code	Host
*Blue Spruce Farms	BSF	01	Mice, Rats	Engle's Laboratory Animal	EH	58	Hamsters, Mice
*Carworth, Inc.	CAR	02	Mice, Rats	*Marshall Research Animals, Inc.	GM	59	Beagles
Sasco Inc.	SAS	03	Mice	*Neamand's White Eagle Farms	WEF	60	Dogs
*Flow Research Animals	DUB	04	Mice, Rats, Dogs	*Primate Imports Corporation	PIC	63	Monkeys
Camm Research Institute	CRI	06	Rats	*Hazleton Research Animals	HRC	69	Dogs
*ARS/Sprague-Dawley, East-Millerton	SCHE	09	Mice	*Woodard Asiatic Corporation	WAC	73	Monkeys
*Rawley Farms	RAW	11	Mice	*Institute for Cancer Research (non comm)	ICR	80	Mice
Harlen/Sprague-Dawley, Madison	SCH	14	Mice, Rats, Hamsters	*Bar Wan Rabbitry & Kennels, Inc.	BAR	81	Dogs
Simonsen Laboratories, California	SIM	17	Mice, Rats	*Argonne National Laboratory (non comm)	ANL	84	Lab. Animals
*Cumberland View Farms	CUM	19	Mice	*Indian Cancer Research Center	ICRC	86	Mice
The Jackson Laboratory	JAX	20	Mice	*Central Drug Research Institute	CDRL	87	Mice
*Bellaire Acres	BEL	24	Mice	*Telaco, Inc.	BIO	88	Hamsters
*University of Kansas (non comm)	UK	25	Mice	*Laboratory Research Enterprises	LRE	89	Beagles
*Battelle Memorial Institute (non comm)	BMI	26	Mice, Rats	*Ridglan Farms	RDG	91	Beagles
Laboratory Supply Company	LSC	28	Mice, Rats	*Gulf South Research Institute (non comm)	GSR	93	Mice, Rats
Microbiological Associates, Inc.	MAI	29	Mice, Rats	*Stanford Research Institute (non comm)	STR	94	Mice, Rats
Charles River, Kingston	CRK	32	Mice, Rats	*Horton Laboratories, Inc.	HLI	95	Mice, Rats
Charles River, Portage	CRP	33	Mice, Rats	Murphy Breeding Laboratories, Inc.	MUF	96	Mice
Taconic Farms	TAC	34	Mice, Rats	*Shamrock Farms	SHA	97	Monkeys
Charles River, Wilmington	CRW	35	Mice, Rats	*H-Bar-B Beagles, Inc.	HHB	99	Beagles
Harlen/Sprague-Dawley, Indianapolis	HAI	36	Mice	*Tulane University (non comm)	TUL	A1	Rats
*Zucca Hamstery	ZUC	38	Hamsters	*Washington State University (non comm)	WSU	A2	Mice
King Animal Laboratories	KNG	39	Mice	*Spartan Research Animals, Inc.	SPB	A3	Mice, Rats
*Lakeview Hamstery	LH	40	Hamsters	Leo Goodwin Institute for Cancer Research (non comm)	GLC	A4	Mice
*ARS/Sprague-Dawley	SD	43	Rats	*Charles River—Italy	CRY	A5	Mice
Southern Animal Farms	SAF	46	Mice	*National Laboratory Animals	NAT	A6	Mice, Rats
*Dennen Animal Industries	DA	47	Hamsters	*Weizman Institute	WN	A7	Mice, Rats
*Russel Miller Farms	RMF	48	Rats	Fredrick Cancer Research Facility	FCRC	A8	Mice, Rats
*Texas Inbred Mice Company	TIM	50	Mice, Rats	*Catholic Medical Center	CMC	A9	Mice
National Institutes of Health (non comm)	NIH	54	Mice, Rats, Hamsters	*Stehlin Foundation	STF	A0	Mice
*Health Research, Inc.	RP	55	Mice	Charles River North Carolina	CRN	B1	Mice

\*Discontinued

## NATURAL PRODUCTS NUMBER RANGE CLASSIFICATION

B000,001 Thru B 69,999 - Fermentation Products  
 B 70,000 Thru B 70,999 - Plant Products  
 B 71,000 Thru B 72,500 - Fermentation Products  
 B 72,501 Thru B 72,999 - Plant  
 B 73,000 Thru B 96,100 - Fermentation  
 B 96,101 Thru B 96,600 - Plant  
 B 96,601 Thru B 98,999 - Fermentation

B 99,000 Thru B 99,999 - Plant  
 B100,000 Thru B 599,999 - Fermentation  
 B600,000 Thru B 699,999 - Plants  
 B700,000 Thru B 799,999 - Animals  
 B800,000 Thru B 899,999 - Plants  
 B900,000 Thru B 999,999 - Fermentation

# INOCULUM

## SITE

- \* -- Not specified
- 1 -- IP (Intraperitoneal)
- 2 -- SC (Subcutaneous)
- 3 -- Spontaneous
- 4 -- Induced
- 5 -- Intrarenal inoculation (IR)  
or Subrenal capsule (SRC)
- 6 -- IM (Intramuscular)
- 7 -- IC (Intracerebral)
- 8 -- Vascular area of the  
chorioallantoic membrane
- 9 -- IV (Intravenous)
- A -- Not applicable
- B -- Inthoracic
- E -- Ear
- F -- Foot Pad
- S -- Intrasplenic
- Blank -- Not Applicable
- C --- Orthotopic -- in control line exp
- OT --- Orthotopic -- site

## TISSUE (TIS)

- \* -- Not specified
- 1 -- Ascitic fluid
- 2 -- Homogenate (or brei), tumor
- 3 -- Homogenate (or brei), spleen
- 4 -- Homogenate (or brei), brain
- 5 -- Homogenate (or brei), other
- 6 -- Fragment, tumor
- 7 -- Fragment, other
- 8 -- Blood
- 9 -- Thymus
- A -- Not applicable
- B -- Normal tissue, not specified

Blank -- Not Applicable

## LEVEL (LVL)

Level is a two position field where the right most field is used as a multiplier and the left most position contains a coded value as follows:

- \* -- Not specified/other
- 1-9 -- Log of cells, e.g. 5 =  $10^5$  cells
- A -- Not applicable
- B -- Dilution 1-2
- C -- Dilution 1-3
- D -- Dilution 1-4
- E -- Dilution 1-5
- F -- Dilution 1-6
- G -- Dilution 1-10
- H -- Dilution 1-20
- \*Note 1
- J -- Log of cells  $5 \times 10^6$
- K -- Dilution 1-100
- \*Note 1
- L -- Log of cells  $5 \times 10^5$
- M -- Tumor diameter between 9 and 12 OMU
- N -- Dilution 1-30
- P -- Dilution 1-7
- R -- Dilution 1-700
- S -- Dilution 1-70
- T -- Dilution 1-7,000

## LEVEL (LVL) FOR PARAMETER D (TUMOR SIZE)

- = -- 100-500 mg (equal sign)
  - \* -- 500-1000 mg (averaged)
  - 1 -- 1000 mg
  - 2 -- 2000 mg
  - 3 -- 3000 mg etc.
- (Size coded in inoculum level field)

\*Note 1: The Codes J and L are being retained because of SDS documents already in existence. Future use of  $5 \times 10^5$  and  $5 \times 10^6$  should be coded 55 and 65 respectively. The codes 1-9 indicate the log of 10 and assume a multiplier of 1, e.g., 5 =  $1 \times 10^5$ .

# BIOCHEMICAL TESTING

ED<sub>50</sub> CALCULATION – Reported in molar concentrations.

L = less than;

M = more than. The number in ( ) is the power of 10.

STRENGTH (STR)

S = Strong =  $10^{-8}$  M or less

M = Moderate =  $10^{-7}$  –  $10^{-6}$  M

W = Weak =  $10^{-5}$  or greater.

Percent Inhibition (% I)

S = Strong\* = 76 – 100%

M = Moderate\* = 51 – 75%

W = Weak\* = 26 – 50%

I = Inactive\* = 0 – 25%

E = Enhancement\* = Negative%

A = Follow-up Testing

\*rate at 1 mM

Metabolic Pathway or Enzyme

00	Purine Synthesis <u>de novo</u>	Purine
10	Adenine Phosphoribosyltransferase	APT
20	Adenosine Kinase	AK
30	Inosine Synthesis	INOS
50	Hypoxanthine – Guanine Phosphoribosyltransferase	HGPT
60	Dihydrofolate Reductase	DHFR

# PUB (PUBLICATION CODE)

0 or (BLANK) – NOT PUBLISHED

8 Literature surveillance natural product

# TEST/CONTROL DEATH PATTERNS

To the left of each dose response is the death pattern (day of death/death count) associated with each test in the dose response. The absence of data means that the data were processed prior to implementation of the new system and the death pattern data are not available other than on microfilm.

Immediately following the dose response is a line of control death pattern data preceded by "CTRL" which depicts the control group death pattern associated with that test. The total number of control group animals is printed to the right of the control death pattern under the heading "TOXD SURV." Again the absence of data means that the data were processed prior to the implementation of the new system and the death pattern data are not available other than on microfilm.

The term "no deaths recorded" indicates the death pattern has been reviewed but no deaths were recorded.

# PRODUCT TYPE/PARTIAL INDICATION

Each Screening Data Summary (SDS) is labeled as to its type as either a synthetic product, Selected Agent Compound (SAC) or a natural product.

The term partial print occurs whenever the SDS is not a total replacement for all previous versions of the SDS.

For a Synthetic Product - Total Replacement.

For a natural product – partial print, the user should retain both the previous and most current reports.

For a selected agent compound – partial print, the user should totally replace the printout for this test system only and the summary page.

## TEST SYSTEM EVAL. CODE – NATURAL PRODUCTS

(Blank) – Has not been evaluated

- C – A material which has passed DTP confirmation protocols in the test system designated
- D – A former “C” which is no longer of interest and has been dropped from further testing in the confirmed system. (WS 23 received)
- F – A material which has failed confirmation testing in the test system designated
- N – A material which has failed confirmation with testing completed in all scheduled test systems
- T – An additional active system; previously confirmed in another system and/or authorized for fractionation in vitro
- S – To be isolated in system listed although previously confirmed in another system
- U – A material in fractionation testing even though it has not passed confirmation in test system designated
- V – A dropped “U”
- X – Instruction to discontinue testing was received before routine testing was completed

## TEST SYSTEM EVAL. CODE

(Blank) – Has not been evaluated

- A – Basis for assignment to 2A
- B – Basis for assignment to 2B
- N – Failed (MC Code 1) criteria
- E – Results equivocal or testing inadequate
- 1 – Meets (MC Code 1) criteria
- 2 – Meets DN-2 criteria

## DATE

- MC – Date Material Classification Code assigned, year, month, day
- EVAL. – Date Evaluation Code assigned, year, month
- YR – Last two digits of calendar year
- MO – 1 thru 12
- DAY – 1 thru 31

## CHEMICAL ANALYSIS DATA (ALKALOID SYSTEM) EVALUATION

Approximate weight of dried plant in kilograms to yield 1 gram of alkaloid.

Code •

- 0 – negative or trace of alkaloid
- 1 – 10 Kg      3 – 1 Kg
- 2 – 3 Kg      4 – <1 Kg



## QNS (QUANTITY NOT SUFFICIENT)

- D – Refill not available; Drug Synthesis and Chemistry Branch Decision
- J – No more compound available from original supplier
- K – Refill requested
- L – On Prepare Lab List
- Q – Compound no longer available from original supplier; activity does not warrant procuring an additional supply
- S – Quantity sufficient for Cell Culture testing only
- T – Quantity sufficient for one schedule only in vivo
- Z – Former QNS; subsequently received by NCI

## OTHER (TESTING)

- AT – Plant and Animal Materials formerly assigned Synthetic Numbers (Test data moved to Natural Products File)
- ET – Endocrine testing
- NS – Never shipped
- NT – No test processed
- RP – Radiation Protector
- ST – Special testing
- RS – Radiosensitizer

## MC (MATERIAL CLASSIFICATION)

### NATURAL PRODUCTS

- C – A material which has passed DTP confirmation protocols in one or more tumor systems
- CC – A "C" from which a purified active material has been isolated
- D – A former "C" which is no longer of interest and has been dropped from further testing in the confirmed system. (WS 23 received)
- DA – Deferred due to inability to recover active principle
- DD – Work on all collections of this genus and species considered complete
- DK – Deferred for presence of known compound
- DL – Deferred because culture of fermentation product was lost or re-collection of plant or animal not available
- DM – Deferred due to absence of activity in L-1210, P-388, or W-256
- DN – Deferred for insufficient activity
- DR – Deferred for failure to reconfirm
- DS – Deferred due to instability of active principle
- DT – Deferred due to excessive toxicity
- D1 – First re-collection inactive
- D2 – Second re-collection inactive
- F – A material which has failed confirmation testing in one or more test systems
- N – A material which has failed confirmation with testing completed in all scheduled test systems
- U – A material in fractionation testing even though it has not passed confirmation
- UC – A "U" from which a purified active material has been isolated
- V – A dropped "U"
- VK – A "V" from which a known purified active material has been isolated
- X – Worksheet 23 to discontinue testing has been received prior to completion of routine testing

# MC (MATERIAL CLASSIFICATION)

## SYNTHETIC

\* Formerly listed as Selected Agent

X No additional testing in test system contemplated.  
No folder available.

Ø Special Interest or folder available

D - Active in pre-screen and does not meet MC 1 activity criteria, or testing incomplete.

H - Active in pre-screen only-3 mice/test

P - Active in P388 pre-screen (1976 or later)

S - Active in pre-screen only (1975)-6 mice/test

1 Reproducible Minimal Activity:

See Screener Instruction 271

D - Deferred: Does not meet DN-2 activity criteria

F - Dropped: See Folder, (usually impurity of compound or resupply not feasible).

K - Cell Culture Confirmed; negative or unconfirmed activity as tested in vivo. No folder available.

W - Committee referral

X - Cell Culture Confirmed; not tested in vivo. No folder available.

2 Decision Network (DN) 2A

A - Passed: DTP Test System

B - Dropped: Not superior to parent compound or Drug Evaluation Committee/Prescreen Subcommittee (DEC/PSS) decision point (DN-2A)

C - Passed: "Other" Systems

D - Dropped. Failed Activity Criteria (DN 2A).

E - Passed: Endocrine compound

F - Dropped: Production or Usable Formulation not feasible (DN 2B)

G - Dropped from 2A. Insufficient Program Interest

H - Rejected at Pre-DN or DN. Insufficient Program Interest

I - Dropped due to impurity in compound

L - DN Special for Limited Studies/Development

M - Referred to Biological Response Modifier Program (BRMP)

P - Passed (DN 2B): Go to 3

R - Recycle (DN 2A or DN 2B)

S - Dropped: Insufficient Activity in route or Schedule Dependency Study (DN 2B)

T - Dropped due to toxicity prior to DN-3

U - Assigned to EORTC (European Organization for Research on Treatment of Cancer)

X - Passed 2A. Further development to be done by Industry.

Z - Pre-Clinical PROD (Project to Review Older Drugs) Compound

3 DN-3 - Toxicology

A - Passed: File INDA (Investigational New Drug Application to FDA - Food and Drug Administration), go to DN-4

D - Dropped Before INDA Filed: Not 3F or 3T

F - Dropped: Formulation not feasible

R - Recycle

T - Dropped: Toxicology

4 DN-4 - IND Filed

A - Passed Phase I Clinical Trials: Go to DN-5

B - Passed 4. Bypass DN-5, go to DN-6

C - Dropped: Insufficient clinical interest

D - Dropped: Irreversible toxicity in man

R - Recycle

5 DN-5

A - Passed: Effective in man, go to DN-6

D - Dropped: INDA withdrawn

T - Dropped: INDA withdrawn due to toxicity in man

Z - Clinical PROD (Project to Review Older Drugs) Compound

6 DN-6

A - Passed: Effective in man, go to DN-7

D - Dropped: Not effective in man (INDA withdrawn - negative - Clinical Trial)

R - Recycle

7 DN-7 NDA

A NCI Development

B Not NCI Development

E Endocrine Compound

# TEST STATUS CODE (TSC)

## Code

- 1, 3, 5, 7 – Toxic Test (In Vivo); Cytotoxic Test (In Vitro)
- 2, 4, 6, 8 – Non-Toxic Inactive (In Vivo); Non-Cytotoxic Inactive (In Vitro)
- 11, 13 – Passed Stage 1 of Sequential Screen
- 15 – Passed Stage 2 of Sequential Screen
- 17 – Passed Stage 3 of Sequential Screen
- 20 – Confirmation Testing
- 21 – Single test assay (Natural Products)
- 22 – Multiple dose assay (Synthetic); all regimens not covered by TSC 25 and 24; all Special Study Code B, E and J testing.
- 23 – Single test assay (Synthetics)
- 24 – Multiple dose assay (Synthetic) Single Day Treatment
- 25 – Multiple dose assay (Synthetic); every 4th Day Treatment (Q4D)
- 26 – Multiple dose assay (Natural Products); every 4th Day Treatment (Q4D)
- 27 – Multiple dose assay (Natural Products); Single Day Treatment
- 28 – Multiple dose assay (Natural Products); all regimens not covered by TSC 26 or 27.
- 29 – Positive Control
- 30 – 3 Mouse multiple dose assay (Synthetic) any regimen (except QD 1-9)
- 31 – 3 Mouse multiple dose assay (Natural Products) any regimen
- 32 – 3 Mouse multiple dose assay (Synthetic) daily treatment, QD 1-9

- 33 – Test to be repeated
- 34 – Test to be repeated – absence of ascitic fluid
- 35 – Published negative data
- 38 – Non-Injectable Compound
- 39 – Negative Control
- 83 – Test to be repeated, solid tumor-screener assigned
- 84 – Test to be repeated, solid tumor-computer assigned
- 85 – Test processed in the solid tumor system
- 89 – Positive Control in the solid tumor system

## Suffix

- A – Preliminary confirmation - in vitro only
- C – Activity confirmed - in vitro only
- E – Exception to routine testing procedure - in vitro only
- F – Activity failed criteria
- N – Activity not confirmed - in vitro only
- P – Activity passed criteria
- \*Q – Machine-assigned code 20
- R – Erratic dose response
- T – Cytotoxic Dose Response – Test to be repeated
- X – Published negative data (partial data)

\*discontinued

# CELL CULTURE FIELDS

**Fold Growth** – Multiple of day final control increase over baseline value.

**Slope** – Change of response for each one-log change of dose.

**Duration (DUR)** – Number of hours the compound was under test.

**W/D** – Indication of dosage as a weight (W) or dilution (D).

**ED<sub>50</sub>** – The dose that inhibits growth to 50% of control growth. For materials tested by weight (W in W/D column), ED<sub>50</sub> expressed in micrograms per ml. For materials tested by dilution (D in W/D column), ED<sub>50</sub> expressed as a dilution; e.g. 2.2 ×

10(3) equals a dilution of 1:2,200. L = less than; M = more than. Using log notation the number in ( ) is the power of 10.

**Number Doses** – The number of doses field indicates the number of different dose levels utilized in the calculation for the compound.

**Log Dose** – The log of the dose actually being tested.

Example:

<u>DOSE</u>	<u>LOG</u>
100 MCG/ML	2.00
75	1.86
50	1.70

## SURVIVORS (SURVS)

C NT TS

These columns identify the number of cures (C), no-takes (NT) and/or tumored survivors (TS) associated with each test group of animals.

Tumored survivors are defined as survivors that cannot be classified as either cures or no-takes. Animals alive, in a survival system, that have visible tumor on final evaluation day.

While the numbers are self explanatory; the cures field may contain the following special symbols. These symbols were employed prior to keeping track of all three items independently.

### Symbol Definition

- \* Tumored Survivors only
- + Tumored Survivors + Cures
- # Tumored Survivors + No-Takes
- \$ Cures + No-Takes
- ? Tumored Survivors + Cures + No-Takes
- % No-Takes only
- = See microfilm for actual cures

## DAY OF EVALUATION (EVAL)

001-999 = Day experiment is terminated  
Z - Until death

## TEST WEIGH DAYS (WD1/ WD2)

The days when animal body weights were recorded in order to calculate the test animal body weight change (weigh day 2 minus weigh day 1). The final body weight is adjusted by subtracting the tumor weight recorded on the same day for tumor inhibition systems. This is accomplished prior to calculating the test body weight change.

## NO. OF INJECTIONS (TOT INJ)

01 - 99 - total number of injections  
A - Ad libitum  
Z - Until death

## CONTROL BODY WEIGHT CHANGE (CNTL BODY CHNG)

Average weight change of control animals in grams (weigh day 2 minus weigh day 1); tumor inhibition systems will have the average tumor weight subtracted from the second weigh day weight (average) before the control body weight change is calculated. Control body weight change is only displayed when recorded on the weigh day 1 and weigh day 2 depicted for the test.

## WEIGHT DIFF. (T-C)\*

### FOR SURVIVAL TEST SYSTEMS

Average animal body weight change of test group minus that of control animals in grams.

\*This value is not calculated when the control group and the test group are not weighed on the same days. Instead, an N.A. (not applicable) appears.

### FOR TUMOR INHIBITION SYSTEMS

Average net animal body weight change\* of test group minus that of control animals in grams.

\*Net weight change = gross weight change minus tumor weight. Exceptions are test systems 3EA11, 3CD12, 3CD13, and any Subrenal Xenograft.

### FOR EGG HOST SYSTEM

Average weight of test embryos minus that of control embryos in grams.

# SOLUBILITY (SOL)

## Solubility (SOL)

### Codes

- \*Ø = Not specified
- 1 = Soluble - No visible particles
- \*4 = Suspension - No further definition
- 7 = Radiation
- 9 = Not applicable

### Suspension Categories

- A = Clear, except for a few fine particles
- B = Cloudy
- C = Smooth suspension - homogeneous
- D = *Barely acceptable suspension - settles rapidly*
- F = Very poor suspension - settles rapidly with large particles

\*Discontinued

# SPECIAL SYSTEM MESSAGES

The following special messages appearing on the summary page all refer to data on a special offline solid tumor data base accessible through the Information Technology Branch:

SEE ROS DATA BASE  
SEE CORBETT DATA BASE  
SEE LL DATA BASE  
SEE B16 DATA BASE  
SEE CD8F1 SOLID TUMOR DATA BASE  
SEE C3H SOLID TUMOR DATA BASE  
SEE XENOGRAFT DATA BASE

The following special messages appearing on the summary page all refer to data on special data bases accessible through the Information Technology Branch:

SEE AKR DATA BASE  
SEE ANTIVIRAL DATA BASE  
SEE COMBINATION CHEMOTHERAPY

The message "scheduled" means that the compound has been shipped for testing in the indicated test system but no results have been reported to date.

## SELECTION PRIORITY FOR COMPUTED CSC

ASSIGNMENT SEQUENCE	CSC	DEFINITION
1.	5	— Contamination (screener assigned only)
2.	7	— Excessive deaths and mean tumor weight or survival time outside limits (2 + 4)
3.	6	— Excessive deaths and excessive no-takes (2 + 3)
4.	2	— Excessive control deaths by early death day
5.	8	— Excessive no-takes and mean tumor weight or survival time outside limits (3 + 4)
6.	4	— Mean or median tumor weight or survival time outside limits
7.	3	— Excessive control no-takes on control no-take day
8.	A	— Test of positive control compound at standard dose is toxic in otherwise satisfactory control.
9.	9	— T/C of positive control is outside limits at standard dose
10.	1	— Satisfactory control

# GLOSSARY OF TERMINOLOGY

**"AA" TUMOR** – Special code in tumor field indicating toxicity testing in normal animals which received no tumor implant.

**ACQ** – Acquisition Code defining rationale for selection of a compound for testing.

**ACTIVITY** – Status of test determined by comparing calculated T/C to previously established activity threshold for that model. Examples of activity thresholds are a T/C  $\leq$  42 percent for 3CD72, a tumor-inhibition model, and T/C  $\geq$  125 percent for 3LE31, a fast-growing survival model.

**CONFIRMED PLANT AND ANIMAL MATERIALS (CPAM)** – Natural Product Compounds which have passed confirmation.

**CONTROL EVALUATION** – Measurement of a control group according to a parameter; used for comparison to test evaluation.

**CONTROL GROUP** – Group of animals receiving the tumor (and usually the vehicle) but no test drug.

**CONTROL LINE** – A cumulative file containing information concerning In Vivo Control Packs, Cell Culture records, and Plant Constituent Analysis records accepted by the Biological Data Processing System. Used for reports in the Biweekly Production Run.

**CONTROL PACK** – Basic grouping of screening data identified by the same control number, involving a single control group of animals and many test groups. An entire control pack must pass edit validation criteria for data to enter the master files and be reflected on a Screening Experiment Analysis.

**CSC** – Control Status Code, an indication of the validity of the controlled aspects of the screening experiment. (see pg. 10)

**CURES** – Surviving animals which are designated as "cures" on Final Evaluation Day. (see pg. 27)

**DATA ELEMENT** – A unique field in the Input Processing System, identified by a Data Element Number.

**DAY OF FIRST INJECTION** – Day on which treatment begins. (see pg. 9)

**DEATH PATTERN** – Series of entries on Combination Chemotherapy records for a control group or test group. Reflects days on which deaths occur and the number of deaths on those days. Days must appear in ascending sequence (not necessarily consecutive).

**DOSE RESPONSE** – A related series of tests where only the dose amount varies.

**FIRST SCREENER** – Identification of the first testing laboratory authorized to initiate testing.

**IN VITRO** – Cell Culture testing.

**IN VIVO** – Live animal testing.

**INITIAL TREATMENT DAY** – See Day of First Injection. (see pg. 9)

**INQUIRIES** – Transactions which request printed information concerning records on the master file.

**INTERVAL (REGIMEN)** – The frequency of drug administration. (see pg. 9)

**MATERIALS OF INTEREST (MOI)** – Natural Product compounds which have passed or failed confirmation.

**MC CODE** – Material Classification Code, indicates progress of compound testing. (see pg. 24, 25)

**NATURAL PRODUCT COMPOUND** – A drug derived directly from a plant or animal part, designated by a B in NSC Prefix.

**NATURAL PRODUCT SAMPLE NUMBER** – An indication of how many plant or animal samples have been obtained to provide the compound for this test.

**NO-TAKES** – In a survival model, animals which live beyond a predefined day for each test system and their survival is considered to be due to failure of the tumor implant; in a tumor-inhibition model, animals with tumors smaller than the predefined limit considered to be due to failure of the tumor implant. (see pg. 27)

**NUMBER OF INJECTIONS** – Total number of injections administered.

These terms are used in the Biological Data Processing System. A list of acronyms is provided on the last page of this Glossary.

# GLOSSARY OF TERMINOLOGY (Continued)

**PARAMETER** – Identifies the type of evaluation to be used for the control and all tests within a given control pack. (see pg. 17)

**POSITIVE CONTROL** – A single test or dose response utilizing a known active compound where previously experienced results are anticipated (typically designated by a Test Status Code of 29).

**PROTOCOL** – Instructions for the conduct of testing.

**REGIMEN** – See Interval. (see pg. 9)

**SAC (SELECTED AGENT COMPOUNDS)** – Synthetic compounds of special interest.

**SDS (SCREENING DATA SUMMARY)** – A report on the testing of a particular compound.

**SEA (SCREENING EXPERIMENT ANALYSIS)** – A report on all tests in a Control Pack.

**SPECIAL STUDY CODES** – Special test classifications. (see pg. 10)

**SUPPLIERS** – Persons or organizations supplying the compound.

**SURVIVAL SYSTEM** – Tests evaluated on the basis of survival (for example, Parameters 2 and 3).

**SURVIVOR PATTERN** – Series of entries on each dose level for a control group or test group. Reflects days on which the number of survivors changed and survivor count on those days. Days must be in ascending sequence (not necessarily consecutive) and numbers of survivors in descending sequence.

**SYNTHETIC COMPOUND** – A material (not a crude natural product) designated by a blank NSC Prefix.

**T/C** – Test evaluation divided by the control evaluation to yield percent evaluation. Used to determine activity of test. (see pg. 10)

**T-C** – Test minus control. Example: test average animal weight change minus control average animal weight change.

**TEST EVALUATION** – Measurement of a test group according to a parameter; used for comparison to control evaluation.

**TEST GROUP** – Group of animals receiving one dose level of the test drug.

**TEST STATUS CODE SUFFIX** – An indication of the meaning of test results (for example, P = Activity passed criteria, F = Activity failed criteria, blank = retest needed). (see pg. 26)

**TEST SYSTEM** – Identification of model by five characters describing key fields in the sequence: Host Group, Tumor (2 characters), Parameter, and Inoculum Site. (see pg. 8)

**TOXICITY DAY (TOXDAY)** – Day on which the number of survivors are checked to determine acute drug toxicity (typically 4 days beyond the day of initial drug injection). (see pg. 12)

**TREATMENT SCHEDULE** – Statement describing drug administration relative to time of tumor implant. Includes the basic number of injections per cycle, interval, day of first injection, time of day of administration of initial treatment, restart days and total treatments. (see pg. 9)

**TSC** – Test Status Code, a code describing the type of test. (see pg. 26)

**TUMOR INHIBITION SYSTEMS** – Test systems in which activity is evaluated on the basis of tumor inhibition (for example, Parameters 1, 7, and 8).

**TUMOR WEIGHT SYSTEMS** – See Tumor Inhibition Systems.

**TUMORED SURVIVORS** – Animals living beyond a predefined day for each test system which can neither be classified as cures nor no-takes.

**UPDATES** – Records which update information already on the Master Files.



## **\*\* ASTROCYTOMA ASSAY — IN VITRO**

The Astrocytoma assay carries a test system identifier of 9ASK. The basis of this assay is that immature AC glioma cells can be induced by N<sup>6</sup>, O<sup>21</sup> — D:butyryl adenosine 3':5' cyclic monophosphoric acid, sodium salt — db-cAMP to change to the morphology of mature, differentiated astrocytes, and that treatment with certain drugs can reverse this astrocyte formation. Distinction between these two types of cells is, therefore, critical. An AC cell ( of the cell line which originated from a rat glioma in 1974) is an immature neuroglial cell that resembles an epithelial cell with an abundance of cytoplasm. The astrocyte-like cell (effect of exposure to db-cAMP) resembles a mature, differentiated neuroglial cell (astrocyte or oligodendrocyte) with very little cytoplasm and with obvious cytoplasmic processes. Each individual test is made up of two identical cultures designated Dish A and Dish B. The results of both dishes are presented. The TSC is assigned on the basis of the best set of dishes. Values for the percent astrocyte reversal columns are not required if the cytotoxicity column (% cell destruction) reflects values in excess of 50%. Percentages displayed are determined as a result of comparing the test dish(es) to a set of control dishes.

**Cytotoxicity:** Cytotoxicity is a measure of the cell destruction of the immature AC Glioma cells accomplished by the test compound. Astrocyte reversal is not measured and the test(s) must be repeated at lower doses whenever cell destruction is 50% or more in either of the duplicate dishes.

**Astrocyte % Reversal:** This item is a measure of the ability of the test compound to reverse the astrocyte formation induced by the db-cAMP addition to immature AC Glioma cells. The higher the percentage, the more active the drug. The success or failure of the compound under test is summarized in the sequential assignment of a test status code which takes into account the compounds' complete history of 9ASK testing.

### **Test Status Code (TSC) Meanings for 9ASK Testing**

The test status code (TSC) and suffix are interpreted in a very similar manner to the 9KB5 test system, as follows:

<u>Code</u>	<u>Meaning</u>
01,03,05	The test is considered cytotoxic; that is, 50% or more of the cells have been destroyed. Repeat testing at lower doses is required.
02, 06	The initial sample is inactive. The compound is considered inactive in 9ASK and sequential testing in test system 9ASK is completed.
11	The initial sample is presumed active (51 — 90% astrocyte reversal, noncytotoxic), but must be repeated.
15	The initial sample is active (91% and above astrocyte reversal, noncytotoxic), or the repeat of the initial sample, following a TSC of 11 is active (51% or more astrocyte reversal, noncytotoxic). Testing of a second sample (B002) is authorized.
20	Note that the TSC 20 is not used for 9ASK.
27A*; 24A	Second sample (B002) is equivocal. Repeat test is required.
27C*; 24C	Second sample (B002) is active. Compound is considered active in 9ASK and sequential testing in test system 9ASK is completed.
27N*; 24N	Second sample (B002) is inactive. Compound is considered inactive in 9ASK and sequential testing in test system 9ASK is completed.
27T*; 24T	Second sample is cytotoxic. Repeat testing at lower doses required.
33, 34	Invalid test; to be repeated.

\*TSC 24 designates Synthetic materials.

TSC 27 designates Natural Products materials.

\*\*Discontinued Assay