CORNING Hazleton

MUTAGENICITY TEST ON

T-6342

MEASURING CHROMOSOME ABERRATIONS IN HUMAN WHOLE BLOOD LYMPHOCYTES WITH A CONFIRMATORY ASSAY WITH MULTIPLE HARVESTS

FINAL REPORT

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LABORATORY PROJECT IDENTIFICATION

CHV Study No.: 17073-0-449CO

SUBMITTED TO

3M Corporation
Building 220-2E-02
3M Center
St. Paul, Minnesota 55144-1000

STUDY COMPLETION DATE

November 1, 1996

QUALITY ASSURANCE STATEMENT

Project Title: Chromosome Aberrations in Human Whole Blood Lymphocytes With a Confirmatory Assay With Multiple Harvests

Project No.: 20990 Assay No.: 17073

Protocol No.: 449CO Edition No.: 2, Modified for 3M Corporation

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the Standard Operating Procedures of the Quality Assurance Unit and according to the general requirements of the appropriate Good Laboratory Practice regulations. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspection/Date	Findings Reported	Auditor
Addition of Colcemid/08/15/1996	08/15/1996	C. Orantes
Draft Report Review/09/18-20/1996	09/20/1996	C. Orantes
Final Report Review/11/01/1996	11/01/1996	C. Smith

Quality Assurance Unit — Date Released: 11/1/96

STUDY COMPLIANCE AND CERTIFICATION

The described study was conducted in compliance with the Organization for Economic Cooperation and Development Principles of Good Laboratory Practice C(81)30 (Final) Annex 2, issued 1979-1980 (effective 1981) with any applicable amendments. There were no significant deviations from the aforementioned regulations or the signed protocol that would affect the integrity of the study or the interpretation of the test results. The raw data have been reviewed by the Study Director, who certifies that the evaluation of the test article as presented herein represents an appropriate conclusion within the context of the study design and evaluation criteria.

All test and control results in this report are supported by an experimental data record and this record has been reviewed by the Study Director. All raw data, documentation, records, protocol and a copy of the final report generated as a result of this study will be archived in the storage facilities of Corning Hazleton Inc. for at least one year following submission of the final report to the Sponsor. After the one year period, the Sponsor may elect to have the aforementioned materials retained in the storage facilities of Corning Hazleton Inc. for an additional period of time, or sent to a storage facility designated by the Sponsor.

Submitted By:

Study Director:

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11/1/96
Study Completion Date

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ABSTRACT

The objective of this in vitro assay was to evaluate the ability of T-6342 to induce chromosomal aberrations in cultured whole blood human lymphocytes with and without metabolic activation.

The test article was dissolved in deionized water at a concentration of 500 mg/ml. The test article solutions and the vehicle control, deionized water, were dosed with a dosing volume of 1% (10 µl/ml) for this assay.

For the dose rangefinding assay with and without metabolic activation, concentrations of 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml were tested. Reductions of 35%, 6%, 38%, 15%, 18%, 57%, and 100% were observed in the mitotic indices of the cultures dosed with 0.500, 1.67, 5.00, 16.7, 500, 1670, and 5000 µg/ml without metabolic activation, respectively, as compared with the solvent control culture. Reductions of 8%, 5%, 4%, 1%, and 100% were observed in the mitotic indices of the cultures dosed with 1.67, 50.0, 500, 1670, and 5000 µg/ml with metabolic activation, respectively, as compared with the solvent control culture.

Based on these data, the initial trial of the chromosomal aberrations assay was conducted testing concentrations of 127, 253, 505, 1010, 1510, 2010, and 2510 µg/ml without metabolic activation and of 253, 505, 1010, 1510, 2010, 2510, 3010, and 4010 µg/ml with metabolic activation in 22.0 hour assays. Cultures dosed with 253, 505, 1010, and 1510 µg/ml without metabolic activation and with 505, 1010, 1510 and 2010 µg/ml with metabolic activation were evaluated for chromosomal aberrations. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the confirmatory assay, replicate cultures were incubated with 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml in a 22.1 hour assay and with 62.5, 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml in a 46.0 hour assay under nonactivation conditions. Replicate cultures were incubated with 250, 500, 1000, 1500, 2000, 2500, and 3000 µg/ml in 22.1 and 46.0 hour assays with metabolic activation. Cultures dosed with 125, 250, 500, and 900 µg/ml from the 22.1 and 46.0 hour nonactivation assays, with 250, 500, 1000, and 1500 µg/ml from the 22.1 hour activation assay, and with 500, 1000, 1500, and 2000 µg/ml from the 46.0 hour activation assay were evaluated for chromosomal aberrations. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed, except for a weak increase in endoreduplication at 2000 µg/ml, an extremely toxic dose level, from the 45.9 hour activation assay.

The test article, T-6342, was considered negative for inducing chromosomal aberrations in cultured whole blood human lymphocytes with and without metabolic activation. These results were verified in independently conducted confirmatory trials.

Chromosomal Aberrations in Human Whole Blood Lymphocytes
With a Confirmatory Assay With Multiple Harvests
With T-6342

1.0 SPONSOR: 3M Corporation

2.0 MATERIAL (TEST ARTICLE):

2.1 Client's Identification: T-6342

2.2 Date Received: July 21, 1995

2.3 Physical Description: Clear, colorless liquid

2.4 Genetics Assay No.: 17073

3.0 TYPE OF ASSAY: Chromosomal Aberrations in Human Whole Blood Lymphocytes With a Confirmatory Assay With Multiple Harvests

4.0 PROTOCOL NO.: 449CO, Edition 2, Modified for 3M Corporation

5.0 STUDY DATES:

5.1 Initiation Date: July 9, 1996

5.2 Experimental Start Date: July 31, 1996

5.3 Experimental Termination Date: August 26, 1996

6.0 SUPERVISORY PERSONNEL:

6.1 Study Director: Hemalatha Murli, Ph.D.

6.2 Laboratory Supervisor: Carol S. Spicer, B.S.

7.0 OBJECTIVE:

The objective of this in vitro assay was to evaluate the ability of the test article, T-6342, to induce chromosomal aberrations in cultured human whole blood lymphocytes, with and without metabolic activation.

8.0 RATIONALE:

The assay is designed to establish whether the test article or its metabolites can interact with cells to induce chromosome breaks. Chemically induced lesions may result in breaks in chromatin that are either repaired by the cell in such a way as to be undetectable or result in visible damage. Aberrations are a consequence of failure or mistakes in repair processes such that breaks do not rejoin or rejoin in abnormal configurations (Evans, 1962).

In order to detect chromosomal aberrations, cells must be in metaphase so that chromosomes are visible. The lymphocytes in blood do not usually divide and are stimulated to divide in culture by phytohemagglutinin (PHA). The cells are later arrested at the appropriate stage (metaphase) by Colcemid®.

9.0 EXPERIMENTAL DESIGN:

Results from the dose rangefinding assay were used to determine the dose range to be used in the chromosomal aberrations assay. In the dose rangefinding assay, the cultures were harvested 20.1 hours after initiation of treatment. Mitotic indices of the cultures were evaluated for evidence of toxicity. A summary of the treatment schedule for the preliminary test is given below.

Summary of Dose Rangefinding Assay Treatment Schedule in Hours

Test	Test Article	Wash	Colcemid®	Fixation
- S9	0	19.5	20.1	22.1
+ S9	0	3	20.1	22.1

In the chromosomal aberrations assays, replicate cultures were used at each dose level, and negative, solvent controls, and for each dose of the positive control. The aberrations assays were conducted with a 22.0 hour harvest time in the initial trial and with 22.1 and 46.0 hour harvest times in the confirmatory trials. Chromosomal aberrations were analyzed from the cultures treated at four dose levels and from one of the positive control doses. A summary of the treatment schedule for the chromosomal aberrations assays is given below.

Summary of Chromosomal Aberrations Assay Treatment Schedule in Hours

Test	Culture Initiation	Chemical	Wash	Colcemid®	Fixation
Initial Trial					
- S9	-48	0	19.2	20.0	22.0
+ S9	-48	0	3.0	20.0	22.0
Confirmatory Trial					
- S9	-48	0	19.3	20.1	22.1
+ S9	-48	0	3.0	20.1	22.1
- S9	-48	0	43.3	44.0	46.0
+ S9	-48	0	3.0	44.0	46.0

10.0 MATERIALS AND METHODS:

10.1 Cells Used:

Human venous blood from a single, normal, healthy male donor was drawn into sterile, heparinized Vacutainers. Cultures were initiated with 0.3 ml of blood per 5 ml culture for the dose rangefinding assay and 0.6 ml of blood per 10.0 ml culture for the chromosomal aberrations assays in 15 ml centrifuge tubes.

10.2 Cell Culture Medium:

The cells were incubated at about 37°C on a slope, with loose caps, in an atmosphere of about 5 % CO_2 in air. The culture medium used was RPMI 1640 (JRH Biosciences) supplemented with 15% fetal bovine serum (FBS; Biochemed, Lot#E5331, dose rangefinding assay; Lot No.:T06024, chromosomal aberrations assay), 1% phytohemagglutinin (PHA-M; Gibco), penicillin (100 units/ml; Quality Biologicals) and streptomycin (100 µg/ml; Quality Biologicals), and 2mM L-glutamine (Quality Biologicals).

10.3 Negative and Solvent Controls:

In the nonactivation assays, negative controls were cultures which contain only cells and culture medium. Solvent controls were cultures containing deionized water at the highest concentration used in test cultures (1% or 10.0 µl/ml). In the

activation assays, the negative and solvent controls were the same as described in the nonactivation assays but with the S9 activation mix included.

10.4 Positive Control Agents:

The positive control agents which were used in the assays were mitomycin C (MMC) for the nonactivation series and cyclophosphamide (CP) in the metabolic activation series. Mitomycin C (CAS# 50-07-7, Sigma, Lot # 40H2508) is a clastogen that does not require metabolic activation. Cyclophosphamide (CAS # 6055-19-2, Sigma, Lot # 43H0269) does not act directly but must be converted to active intermediates by microsomal enzymes. In the chromosomal aberrations assays, three concentrations of MMC (0.1, 0.2, and 0.3 µg/ml) and CP (20, 30, and 50 µg/ml) were used to induce chromosomal aberrations. One of the dose levels was analyzed in each of the aberration assays. Both MMC and CP were dissolved in water.

10.5 Dose Rangefinding Assay:

In these tests, cultures were initiated with 0.3 ml of blood per 5 ml culture and were incubated for two days prior to treatment.

10.5.1 Test Without Metabolic Activation:

The lymphocytes were incubated with the test article for 19.5 hours at ≈37°C. Then, the test article was washed from the cells with phosphate buffered saline and fresh complete medium containing Colcemid® (final concentration 0.1 µg/ml) was added. The cultures were then harvested 2.0 hours later. (See Sections on Harvest and Slide Preparation and Staining).

10.5.2 Test With Metabolic Activation:

In this test, the lymphocytes were incubated to the test article for three hours at ≈37°C in the presence of a rat liver S9 reaction mixture (S9 15 µl/ml, NADP 1.5 mg/ml, and isocitric acid 2.7 mg/ml). The S9 fraction (Molecular Toxicology, Inc., Lot #0667) was derived from the liver of male Sprague-Dawley rats which had been previously treated with Aroclor 1254 to induce the mixed function oxidase enzymes which are capable of metabolizing chemicals to more active forms. The three hour incubation time was used because prolonged exposure to the S9 mixture might be toxic to the cells and the enzyme activity of S9 is lost rapidly at

about 37°C. The medium did not have FBS during the exposure period to avoid possible inactivation of short lived and highly reactive intermediates produced by the S9 enzymes by binding to serum proteins.

After the exposure period the cells were washed twice with buffered saline. Complete RPMI culture medium was added to the cultures which were then incubated for 18.5 hours with Colcemid® (final concentration 0.1 µg/ml) added for the last 2.0 hours to collect metaphase cells. The cultures were then harvested, fixed, and slides were prepared and stained as was described for the nonactivation dose rangefinding assay .

10.5.3 Assay Evaluation:

Mitotic index was analyzed from the surviving dose levels by analyzing the number of metaphases present in 1000 consecutive cells.

10.6 Aberrations Assay Without Metabolic Activation:

Cultures were initiated two days prior to treatment with 0.6 ml of whole blood per 10.0 ml culture in 15 ml centrifuge tubes. Two days after culture initiation, the cells were treated with the test article at predetermined concentrations for about 19.3 and 43.3 hours. The cultures were then washed with buffered saline and complete RPMI 1640 medium containing 0.1 µg/ml Colcemid® was placed back onto the cells. Two hours later, the cells were harvested and air dried slides were made. The slides were then stained in 5 % Giemsa solution for the analysis of chromosomal aberrations.

10.7 Aberrations Assay With Metabolic Activation:

Cultures were initiated two days prior to treatment with 0.6 ml of whole blood per 10.0 ml culture in 15 ml centrifuge tubes. Two days after culture initiation, the cultures were incubated at ≈37°C for three hours in the presence of the test article and the S9 reaction mixture. After the three hour exposure period, the cells were washed twice with buffered saline and the cells were refed with complete RPMI 1640 medium. The cells were incubated for the rest of the culture period up to the time of harvest with 0.1 µg/ml Colcemid® present during the last 2.0 hours of incubation. The metaphase cells were then harvested and prepared for cytogenetic analysis.

10.8 Harvest Procedure:

The cell suspension was centrifuged, the supernatant was discarded and cells were treated with hypotonic KCl (0.075 M) for approximately 10 minutes. This treatment helps to swell the cells and thus disperse the chromosomes. After centrifugation and removal of the KCl, the cells were washed three times with freshly prepared fixative (absolute methanol:glacial acetic acid, 3:1, v:v). Air-dried slides were prepared from the harvested cells.

10.9 Slide Preparation and Staining:

Slides were prepared by dropping the harvested cultures on clean slides. The slides were stained with 5% Giemsa solution for the analysis of mitotic index and chromosomal aberrations. All slides were then air-dried and cover slipped.

10.10 Aberrations Analysis and Assay Evaluation:

Cells were selected for good morphology and only cells with the number of centromeres equal to the modal number 46 were analyzed.

One hundred cells, if available, from each replicate culture at four dose levels of the test article, the negative, solvent, and positive control cultures were analyzed for the different types of chromosomal aberrations (Evans, 1962; See Section 15.0). At least 25 cells were analyzed for chromosomal aberrations from those cultures with >25% cells with chromosomal aberrations. For control of bias, all slides were coded prior to analysis. Cells with aberrations were recorded on the data sheets by the microscope stage location. Mitotic index was assessed by analyzing the number of mitotic cells in 1000 cells and the ratio was expressed as a percentage of mitotic cells.

The following factors were taken into account in the evaluation of the chromosomal aberrations data:

1. The percentage of cells with any aberrations.
2. The percentage of cells with more than one aberration.
3. Any evidence for increasing amounts of damage with increasing dose, i.e., a positive dose response.

Chromatid and isochromatid gaps, if observed, were noted in the raw data and were tabulated. They were not, however, considered in the evaluation of the ability of the test article to induce chromosomal aberrations since they may not represent true chromosomal breaks and may possibly be induced by toxicity. Percent polyploidy and endoreduplication were analyzed and results were tabulated. Historical control data are presented in Table 8.

A cell classified as "GT" is considered to contain 10 aberrations for statistical purposes but a ">" is also included in the tables for this classification to indicate that it is a minimum number.

Statistical analysis employed a Cochran-Armitage test for linear trend and Fisher's Exact Test (Thakur *et al.*, 1985) to compare the percentage of cells with aberrations (and, if applicable, the percentage of cells with more than one aberration), polyploidy, and endoreduplication in treated cells with results from vehicle controls. Test article significance was established where $p<0.01$. All factors as stated previously were taken into account and the final evaluation of the test article was based upon scientific judgement.

11.0 RESULTS:

11.1 Solubility and Dose Determination

Deionized water (Prepared at CHV, Lot # 20) was the solvent of choice for this assay. T-6342 was dissolved in deionized water at a concentration of 500 mg/ml for the dose rangefinding assay . The test article solutions and the vehicle control, deionized water, were dosed with a dosing volume of 1% (10 µl/ml) for this assay. Concentrations of 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml were tested in the dose rangefinding assay with and without metabolic activation. The stability of the test article under the preparation and dosing conditions used in this assay is the responsibility of the sponsor.

11.2 Dose Rangefinding Assay Without Metabolic Activation

Hemolysis was observed prior to wash in the cultures dosed with 5000 µg/ml. Mitotic indices were analyzed from the cultures dosed with 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml (Table 1). Reductions of 35%, 6%, 38%, 15%, 18%, 57%, and 100% were observed in the mitotic indices of the cultures dosed with 0.500, 1.67, 5.00, 16.7, 500, 1670, and 5000 µg/ml. Based on these results, the initial trial of the aberrations assay without metabolic activation

was conducted with a 22.0 hour harvest testing concentrations of 127, 253, 505, 1010, 1510, 2010, and 2510 µg/ml.

11.3 Dose Rangefinding Assay With Metabolic Activation

Hemolysis was observed prior to wash in the cultures dosed with 5000 µg/ml. Mitotic indices were analyzed from the cultures dosed with 0.167, 0.500, 1.67, 5.00, 16.7, 50.0, 167, 500, 1670, and 5000 µg/ml (Table 1). Reductions of 8%, 5%, 4%, 1%, and 100% were observed in the mitotic indices of the cultures dosed with 1.67, 50.0, 500, 1670, and 5000 µg/ml, as compared with the solvent control culture. Based on these results, the initial trial of the aberrations assay with metabolic activation was conducted with a 22.0 hour harvest testing concentrations of 253, 505, 1010, 1510, 2010, 2510, 3010, and 4010 µg/ml.

11.4 Chromosomal Aberrations Assay Without Metabolic Activation

INITIAL TRIAL

Hemolysis was observed prior to wash in the cultures dosed with 2510 µg/ml. Reductions of 38%, 18%, 18%, 50%, 55%, and 95% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 127, 253, 505, 1010, 1510, and 2010 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 253, 505, 1010, and 1510 µg/ml (Table 2). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

Based on these results, the confirmatory trial under nonactivation conditions were conducted testing dose levels of 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml with a 22.1 harvest and 62.5, 125, 250, 500, 900, 1200, 1600, and 2000 µg/ml with a 46.0 harvest.

CONFIRMATORY TRIAL

In the 22.1-hour confirmatory trial, hemolysis was observed prior to wash of the cultures dosed with 1600 and 2000 µg/ml, and a slight evidence of hemolysis was evident at harvest of the cultures dosed with 1600 µg/ml. Reductions of 2%, 14%, 64%, 74%, 93%, and 93% in the mitotic indices as compared with the solvent control cultures were observed in the cultures dosed with 125, 500, 900, 1200, 1600, and 2000 µg/ml, respectively. Chromosomal aberrations were ana-

lyzed from the cultures treated with 125, 250, 500, and 900 µg/ml (Table 3). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the 46.0-hour confirmatory trial, hemolysis was observed prior to wash of the cultures dosed with 1600 and 2000 µg/ml. Reductions of 59%, 93%, 98%, and 98% in the mitotic indices as compared with the solvent control cultures were observed in the cultures dosed with 900, 1200, 1600, and 2000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 125, 250, 500, and 900 µg/ml (Table 4). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

The sensitivity of the cell culture for induction of chromosomal aberrations is shown by the increased frequency of aberrations in the cells exposed to MMC, the positive control agent. The test article is considered negative for inducing chromosomal aberrations, polyploidy, and endoreduplication under nonactivation conditions.

11.5 Chromosomal Aberrations Assay With Metabolic Activation

INITIAL TRIAL

Hemolysis was observed prior to wash in the cultures dosed with 2010, 2510, 3010, and 4010 µg/ml. No cells were visible prior to the addition of Colcemid® to the cultures dosed with 4010 µg/ml, and hemolysis was observed prior to the addition of Colcemid® in the cultures dosed with 3010 µg/ml. Reductions of 15%, 20%, 15%, 43%, 77%, and 95% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 253, 505, 1010, 1510, 2010, and 2510 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 505, 1010, 1510, and 2010 µg/ml (Table 5). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

Based on these results, the confirmatory trial under activation conditions were conducted testing dose levels of 250, 500, 1000, 1500, 2000, 2500, and 3000 µg/ml with 22.1 and 46.0 hour harvests.

CONFIRMATORY TRIAL

In the 22.1-hour confirmatory trial, hemolysis was observed prior to wash and prior to harvest of the cultures dosed with 2000, 2500, and 3000 µg/ml. Reductions of 15%, 5%, 69%, 82%, 97%, and 100% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 500, 1000, 1500, 2000, 2500, and 3000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 250, 500, 1000, and 1500 µg/ml (Table 6). No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed.

In the 46.0-hour confirmatory trial, hemolysis was observed prior to wash and prior to harvest of the cultures dosed with 2000, 2500, and 3000 µg/ml. Reductions of 15%, 80%, 100%, and 100% in the mitotic indices as compared with the solvent control cultures were observed in the cultures treated with 1500, 2000, 2500, and 3000 µg/ml, respectively. Chromosomal aberrations were analyzed from the cultures treated with 500, 1000, 1500 and 2000 µg/ml (Table 7). Due to toxicity, only 52 metaphases were available for analysis in one of the cultures dosed with 2000 µg/ml. No significant increase in cells with chromosomal aberrations, polyploidy, or endoreduplication was observed at the concentrations analyzed, except for a weak increase in endoreduplication at 2000 µg/ml, an extremely toxic dose level.

The successful activation of the metabolic system is illustrated by the increased incidence of cells with chromosomal aberrations in the cultures induced with cyclophosphamide, the positive control agent. The test article is considered negative for inducing chromosomal aberrations, polyploidy, and endoreduplication under conditions of metabolic activation, except for a weak increase in endoreduplication at an extremely toxic dose level in the 46.0 hour assay.

12.0 CONCLUSION:

The test article, T-6342, was considered negative for inducing chromosomal aberrations in cultured whole blood human lymphocytes cells with and without metabolic activation. These results were verified in independently conducted confirmatory trials.

13.0 REFERENCES:

Evans, H.J. (1962) Chromosomal aberrations produced by ionizing radiation, International Review of Cytology, 13, 221-321.

Thakur, A.J., Berry, K.J., and Mielke, P.W. Jr (1985) A FORTRAN program for testing trend and homogeneity in proportions, Computer Programs in Biomedicine, 19, 229-233.

14.0 EXPERIMENTAL DATA TABLES

TABLE 1

DOSE RANGEFINDING ASSAY

Assay No.: 17073 Trial No.: I Date: 07/31/96
Compound: T-6342 Lab No.: CY7316

Metabolic Activation: -S9

Treatment			% Mitotic Index
NEGATIVE CONTROL	RPMI 1640		5.9
SOLVENT CONTROL	Water	10.0 µl/ml	6.8
TEST ARTICLE		0.167 µg/ml	7.4
		0.500 µg/ml	4.4
		1.67 µg/ml	6.4
		5.00 µg/ml	4.2
		16.7 µg/ml	5.8
		50.0 µg/ml	7.2
		167 µg/ml	7.1
		500 µg/ml	5.6
		1670 µg/ml	2.9
		5000 µg/ml*	0.0

Metabolic Activation: +S9

Treatment			% Mitotic Index
NEGATIVE CONTROL	RPMI 1640		7.4
SOLVENT CONTROL	Water	10.0 µl/ml	8.3
TEST ARTICLE		0.167 µg/ml	9.4
		0.500 µg/ml	8.6
		1.67 µg/ml	7.6
		5.00 µg/ml	8.3
		16.7 µg/ml	8.4
		50.0 µg/ml	7.9
		167 µg/ml	8.6
		500 µg/ml	8.0
		1670 µg/ml	8.2
		5000 µg/ml*	0.0

*Toxic dose level RPMI 1640 = Culture medium

TABLE 2
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.0 Hours After Treatment

Assay No.: 17073 Trial #: 1 Date: 08/07/96 Lab #: CY8066 Metabolic Activation: -S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
				NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	2	1		1											0.01	1.0	0.0	0.0	0.0	2.0
			B 100	1														0.00	0.0	0.0	0.0	0.0	3.7
			A+B 200	3	1		1											0.01	0.5	0.0	0.0	0.0	2.9
SOLVENT:	Water	10.0 µl/ml	A 100	3														0.00	0.0	0.0	0.0	0.0	4.2
			B 100	3														0.00	0.0	0.0	0.0	0.0	3.8
			A+B 200	6														0.00	0.0	0.0	0.0	0.0	4.0
POSITIVE:	MMC	0.300 µg/ml	A 25	4	2			1	4	3	1							0.36	32.0	4.0	0.0	0.0	3.3
			B 25	7	1		5		2		4							0.44	44.0	0.0	0.0	0.0	2.2
			A+B 50	11	3		5	1	6	3	5							0.40	38.0*	2.0	0.0	0.0	2.8
TEST ARTICLE		127 µg/ml**	A+B 0																				2.5
		253 µg/ml	A 100	7														0.00	0.0	0.0	0.0	0.0	3.5
			B 100	2			1											0.01	1.0	0.0	0.0	0.0	3.0
			A+B 200	9			1											0.01	0.5	0.0	0.0	0.0	3.3
		505 µg/ml	A 100	5			1											0.01	1.0	0.0	0.0	0.0	3.4
			B 100	6														0.00	0.0	0.0	0.0	0.0	3.2
			A+B 200	11			1											0.01	0.5	0.0	0.0	0.0	3.3
		1010 µg/ml	A 100				1	2										0.03	2.0	1.0	0.0	0.0	2.2
			B 100	3	1		1											0.01	1.0	0.0	0.0	0.0	1.7
			A+B 200	3	1		2	2										0.02	1.5	0.5	0.0	0.0	2.0
		1510 µg/ml	A 100	4	3		2											0.02	2.0	0.0	0.0	0.0	2.1
			B 100	2			1			1								0.02	2.0	0.0	0.0	0.0	1.5
			A+B 200	6	3		3			1								0.02	2.0	0.0	0.0	0.0	1.8
		2010 µg/ml***	A+B 0																				0.2

RPMI 1640 = Culture medium MMC = Mitomycin C

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

TABLE 3
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.1 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: -S9

Compound: T-6342

					NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED		TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																								
NEGATIVE:	RPMI 1640		A	100	2														0.00	0.0	0.0	0.0	0.0	4.2
			B	100	1														0.00	0.0	0.0	0.0	0.0	4.4
			A+B	200	3														0.00	0.0	0.0	0.0	0.0	4.3
SOLVENT:	Water	10.0 µl/ml	A	100	2			1											0.01	1.0	0.0	0.0	0.0	4.0
			B	100				1											0.01	1.0	0.0	0.0	0.0	4.3
			A+B	200	2			2											0.01	1.0	0.0	0.0	0.0	4.2
POSITIVE:	MMC	0.300 µg/ml	A	25	5			6	2	4		2	1						0.60	40.0	20.0	0.0	0.0	1.2
			B	25	1	1		3	2	3		1							0.36	32.0	4.0	0.0	0.0	2.2
			A+B	50	6	1		9	4	7		3	1						0.48	36.0*	12.0*	0.0	0.0	1.7
TEST ARTICLE		125 µg/ml	A	100	6														0.00	0.0	0.0	0.0	0.0	3.7
			B	100	3	1													0.00	0.0	0.0	0.0	0.0	4.5
			A+B	200	9	1													0.00	0.0	0.0	0.0	0.0	4.1
		250 µg/ml	A	100															0.00	0.0	0.0	0.0	0.0	4.0
			B	100				1											0.01	1.0	0.0	0.0	0.0	4.4
			A+B	200				1											0.01	0.5	0.0	0.0	0.0	4.2
		500 µg/ml	A	100	6	1													0.00	0.0	0.0	0.0	0.0	4.0
			B	100	3														0.00	0.0	0.0	0.0	0.0	3.1
			A+B	200	9	1													0.00	0.0	0.0	0.0	0.0	3.6
		900 µg/ml	A	100	3	1													0.00	0.0	0.0	0.0	0.0	1.4
			B	100	4				1										0.01	1.0	0.0	0.0	0.0	1.6
			A+B	200	7	1			1										0.01	0.5	0.0	0.0	0.0	1.5
		1200 µg/ml**	A+B	0																				1.1
		1600 µg/ml**	A+B	0																				0.3
		2000 µg/ml**	A+B	0																				0.3

RPMI 1640 = Culture medium MMC = Mitomycin C * Significantly greater than the solvent controls, $p<0.01$.
** Chromosome aberrations not analyzed due to excessive toxicity.

TABLE 4
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 46.0 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: -S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	1			3											0.03	2.0	1.0	0.0	0.0	5.3
			B 100	2			1	1										0.02	2.0	0.0	0.0	0.0	4.5
			A+B 200	3			4	1										0.03	2.0	0.5	0.0	0.0	4.9
SOLVENT:	Water	10.0 µl/ml	A 100				2											0.02	2.0	0.0	0.0	0.0	6.0
			B 100	2			1	1										0.02	2.0	0.0	0.0	0.0	4.8
			A+B 200	2			3	1										0.02	2.0	0.0	0.0	0.0	5.4
TEST ARTICLE		62.5 µg/ml*	A+B 0																				5.6
		125 µg/ml	A 100	5			1											0.01	1.0	0.0	0.0	0.0	6.3
			B 100	6														0.00	0.0	0.0	0.0	0.0	6.0
			A+B 200	11			1											0.01	0.5	0.0	0.0	0.0	6.2
		250 µg/ml	A 100	5														0.00	0.0	0.0	0.0	0.0	5.4
			B 100	4														0.00	0.0	0.0	0.0	0.0	7.2
			A+B 200	9														0.00	0.0	0.0	0.0	0.0	6.3
		500 µg/ml	A 100	4			1	1										0.02	2.0	0.0	0.0	0.0	5.9
			B 100	5	1													0.00	0.0	0.0	0.0	0.0	5.6
			A+B 200	9	1		1	1										0.01	1.0	0.0	0.0	0.0	5.8
		900 µg/ml	A 100	4	1		1											0.01	1.0	0.0	0.0	0.0	1.9
			B 100	4														0.00	0.0	0.0	0.0	0.0	2.4
			A+B 200	8	1		1											0.01	0.5	0.0	0.0	0.0	2.2
		1200 µg/ml**	A+B 0																				0.4
		1600 µg/ml**	A+B 0																				0.1
		2000 µg/ml**	A+B 0																				0.1

RPMI 1640 = Culture medium

* Chromosome aberrations not analyzed due to higher doses available for analysis.

** Chromosome aberrations not analyzed due to excessive toxicity.

TABLE 5
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.0 Hours After Treatment

Assay No.: 17073 Trial #: 1 Date: 08/07/96 Lab #: CY8066 Metabolic Activation: +S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																			
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLYPLOID CELLS	% ENDOREDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	1	1													0.00	0.0	0.0	0.0	0.0	4.8
			B 100															0.00	0.0	0.0	0.0	0.0	5.0
			A+B 200	1	1													0.00	0.0	0.0	0.0	0.0	4.9
SOLVENT:	Water	10.0 µl/ml	A 100	3			2											0.02	2.0	0.0	0.0	0.0	6.8
			B 100	3	1													0.00	0.0	0.0	0.0	0.0	5.2
			A+B 200	6	1		2											0.01	1.0	0.0	0.0	0.0	6.0
POSITIVE:	CP	50.0 µg/ml*	A 25	4			7	1		2	3							0.52	44.0	8.0	0.0	0.0	1.7
			B 25	4	5		14	1		2	3	2						0.88	52.0	28.0	0.0	0.0	1.2
			A+B 50	8	5		21	2		4	6	2						0.70	48.0*	18.0*	0.0	0.0	1.5
TEST ARTICLE		253 µg/ml**	A+B 0																				5.1
		505 µg/ml	A 100	2														0.00	0.0	0.0	0.0	0.0	4.7
			B 100	2														0.00	0.0	0.0	0.0	0.0	4.9
			A+B 200	4														0.00	0.0	0.0	0.0	0.0	4.8
		1010 µg/ml	A 100															0.00	0.0	0.0	0.0	0.0	4.2
			B 100	6														0.00	0.0	0.0	0.0	0.0	5.9
			A+B 200	6														0.00	0.0	0.0	0.0	0.0	5.1
		1510 µg/ml	A 100	4	1		3											0.03	2.0	1.0	1.0	0.0	3.1
			B 100	7	1		1											0.01	1.0	0.0	1.0	0.0	3.7
			A+B 200	11	2		4											0.02	1.5	0.5	1.0	0.0	3.4
		2010 µg/ml	A 100	2			1											0.01	1.0	0.0	0.0	0.0	1.1
			B 100	7	2		1											0.01	1.0	0.0	0.0	0.0	1.7
			A+B 200	9	2		2											0.01	1.0	0.0	0.0	0.0	1.4
		2510 µg/ml***	A+B 0																				0.3

RPMI 1640 = Culture medium CP = Cyclophosphamide

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

[a] Due to toxicity, only 83 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 6
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 22.1 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: +S9

Compound: T-6342

					NUMBER AND TYPE OF ABERRATION																		
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	T	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	8														0.00	0.0	0.0	0.0	0.0	4.5
			B 100	6				1										0.01	1.0	0.0	0.0	0.0	4.7
			A+B 200	14				1										0.01	0.5	0.0	0.0	0.0	4.6
SOLVENT:	Water	10.0 µl/ml	A 100	3			2									1		0.03	3.0	0.0	0.0	0.0	4.1
			B 100	5	2													0.00	0.0	0.0	0.0	0.0	3.6
			A+B 200	8	2		2									1		0.02	1.5	0.0	0.0	0.0	3.9
POSITIVE:	CP	50.0 µg/ml***	A 25	4	2		7		2		1							0.40	32.0	8.0	0.0	0.0	0.7
			B 25	5	1		6	2			1							0.36	36.0	0.0	0.0	0.0	0.3
			A+B 50	9	3		13	2	2		2							0.38	34.0*	4.0	0.0	0.0	0.5
TEST ARTICLE		250 µg/ml	A 100	5	1	1												0.00	0.0	0.0	0.0	0.0	4.4
			B 100	2	1													0.00	0.0	0.0	0.0	0.0	4.2
			A+B 200	7	2	1												0.00	0.0	0.0	0.0	0.0	4.3
		500 µg/ml	A 100	3			1											0.01	1.0	0.0	0.0	0.0	2.1
			B 100	5	1		2											0.02	2.0	0.0	1.0	0.0	4.4
			A+B 200	8	1		3											0.02	1.5	0.0	0.5	0.0	3.3
		1000 µg/ml	A 100	7			1											0.01	1.0	0.0	0.0	0.0	3.6
			B 100	7			1											0.01	1.0	0.0	0.0	0.0	3.8
			A+B 200	14			2											0.01	1.0	0.0	0.0	0.0	3.7
		1500 µg/ml	A 100	9	2		2	1										0.03	2.0	1.0	0.0	0.0	1.2
			B 100	10			4											0.04	4.0	0.0	1.0	0.0	1.1
			A+B 200	19	2		6	1										0.04	3.0	0.5	0.5	0.0	1.2
		2000 µg/ml**	A+B 0																				0.7
		2500 µg/ml**	A+B 0																				0.1
		3000 µg/ml**	A+B 0																				0.0

RPMI 1640 = Culture medium CP = Cyclophosphamide

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to excessive toxicity.

*** Due to toxicity, only 56 metaphases from the A culture and 36 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 7
CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
Cells Fixed 46.0 Hours After Treatment

Assay No.: 17073 Trial #: 2 Date: 08/14/96 Lab #: CY8166 Metabolic Activation: +S9

Compound: T-6342

				NUMBER AND TYPE OF ABERRATION																	
					NOT COMPUTED			SIMPLE		COMPLEX								OTHER	# OF ABERRATIONS PER CELL	% CELLS WITH ABERRATIONS	% CELLS WITH >1 ABERRATIONS	% POLY-PLOID CELLS	% ENDO-REDUPLICATED CELLS	% MITOTIC INDEX
			CELLS SCORED	TG	SG	UC	TB	SB	ID	TR	QR	CR	D	R	CI	DF	GT						
CONTROLS																							
NEGATIVE:	RPMI 1640		A 100	3														0.00	0.0	0.0	1.0	0.0	8.0
			B 100	2			1											0.01	1.0	0.0	0.0	0.0	8.1
			A+B 200	5			1											0.01	0.5	0.0	0.5	0.0	8.1
SOLVENT:	Water	10.0 µl/ml	A 100	1	1		1											0.01	1.0	0.0	0.0	0.0	6.3
			B 100	3			1											0.01	1.0	0.0	0.0	0.0	6.9
			A+B 200	4	1		2											0.01	1.0	0.0	0.0	0.0	6.6
TEST ARTICLE		250 µg/ml**	A+B 0																				7.7
		500 µg/ml	A 100	3														0.00	0.0	0.0	1.0	0.0	7.8
			B 100	1	1													0.00	0.0	0.0	0.0	0.0	8.1
			A+B 200	4	1													0.00	0.0	0.0	0.5	0.0	8.0
		1000 µg/ml	A 100	3														0.00	0.0	0.0	0.0	0.0	6.4
			B 100	2			1											0.01	1.0	0.0	1.0	0.0	7.7
			A+B 200	5			1											0.01	0.5	0.0	0.5	0.0	7.1
		1500 µg/ml	A 100	4														0.00	0.0	0.0	1.0	1.0	5.6
			B 100	9	1		1											0.01	1.0	0.0	1.0	0.0	5.5
			A+B 200	13	1		1											0.01	0.5	0.0	1.0	0.5	5.6
		2000 µg/ml*	A 52	2	2		1	1										0.04	3.8	0.0	0.0	7.4	0.8
			B 148	2			2			1	1							0.03	2.0	0.7	0.0	5.2	1.8
			A+B 200	4	2		3	1		1	1							0.03	2.5	0.5	0.0	6.3*	1.3
		2500 µg/ml***	A+B 0																				0.0
		3000 µg/ml***	A+B 0																				0.0

RPMI 1640 = Culture medium

* Significantly greater than the solvent controls, $p<0.01$.

** Chromosome aberrations not analyzed due to higher doses available for analysis.

*** Chromosome aberrations not analyzed due to excessive toxicity.

* Due to toxicity, only 54 metaphases from the A culture and 58 metaphases from the B culture were analyzed for polyploidy and endoreduplication.

TABLE 8

CONTROL DATA OF CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES
4-95 THROUGH 12-95

	Activation		# Of Aberrations Per Cell	% Of Cells With Aberrations	% Of Cells With >1 Aberration	% Poly-ploidy	% Endore-duplicated Cells	% Mitotic Index
Negative Control								
	Without	MIN	0.00	0.0	0.0	0.0	0.0	0.4
		MAX	0.06	2.5	0.5	1.0	1.0	7.1
		AVG	0.012	0.72	0.06	0.18	0.03	3.57
		N	18	18	18	17	35	18
Solvent Control								
	Without	MIN	0.00	0.0	0.0	0.0	0.0	0.5
		MAX	0.06	2.5	0.5	1.0	2.0	10.9
		AVG	0.011	0.78	0.05	0.14	0.10	4.52
		N	29	29	29	18	35	29
Positive Control Mitomycin C	Without	MIN	0.02	1.5	0.0	0.0	0.0	0.1
		MAX	0.60	39.5	15.0	0.0	0.0	6.6
		AVG	0.267	22.22	3.63	0.00	0.00	2.46
		N	19	19	19	11	31	19
Negative Control								
	With	MIN	0.00	0.0	0.0	0.0	0.0	0.6
		MAX	0.03	2.0	0.5	1.0	0.5	9.6
		AVG	0.010	0.75	0.06	0.28	0.02	4.68
		N	18	18	18	17	27	18
Solvent Control								
	With	MIN	0.00	0.0	0.0	0.0	0.0	0.5
		MAX	0.02	2.0	0.5	2.0	0.0	10.7
		AVG	0.009	0.66	0.05	0.25	0.00	6.13
		N	28	28	28	17	27	28
Positive Control Cyclophosphamide	With	MIN	0.28	21.7	0.0	0.0	0.0	0.1
		MAX	2.52	40.0	40.0	1.0	0.0	5.9
		AVG	0.647	31.45	12.90	0.22	0.00	1.35
		N	17	17	17	9	25	17

15.0 DEFINITIONS OF CHROMOSOME ABERRATIONS FOR GIEMSA STAINED CELLS

SIMPLE

TB	Chromatid Break:	An achromatic region in one chromatid, larger than the width of a chromatid. The associated fragment may be partially or completely displaced.
SB	Chromosome Break:	Chromosome has a clear break, forming an abnormal (deleted) chromosome with an acentric fragment that is dislocated. This classification now includes the acentric fragment (AF). An AF is different from a SB only in that it can not be related to any specific chromosome.
DM	"Double Minute" Fragment:	These are small double dots, which may represent terminal or interstitial deletions, or even small rings. These possible origins are not distinguishable.

COMPLEX

ID	Interstitial Deletion:	Length of chromatid "cut out" from midregion of a chromatid, resulting in a small fragment or ring lying beside a shortened chromatid or a gap in the chromatid.
TR	Triradial:	An exchange between two chromosomes, or one chromosome and an acentric fragment, which results in a three-armed configuration.
QR	Quadriradial:	An exchange like a triradial, but resulting in a four-armed configuration.
CR	Complex Rearrangement:	An exchange among more than two chromosomes or fragments, caused by the induction of several breaks.
D	Dicentric:	An exchange between two chromosomes which results in a chromosome with two centromeres. This is often associated with an acentric fragment in which case it is classified as DF.
DF		Dicentric with fragment.

COMPLEX (Continued)

TC	Tricentric:	An exchange involving three chromosomes and resulting in a chromosome with three centromeres. Often associated with two to three AF. Such exchanges can involve many chromosomes and are named as follows:
QC	Quadricentric:	four centromeres, up to four AF
PC	Pentacentric:	five centromeres, up to five AF
HC	Hexacentric:	six centromeres, up to six AF
R	Ring:	A chromosome which forms a circle containing a centromere. This is often associated with an acentric fragment, in which case it is classed as RF.
RC	Ring Chromatid:	Single chromatid ring (acentric).
RF		Ring with associated acentric fragment.
CI	Chromosome Intrachange:	Exchange within a chromosome; e.g., a ring that does not include the entire chromosome.
T	Translocation:	Obvious transfer of material between two chromosomes resulting in two abnormal chromosomes. When identifiable, scored as "T" not "2AB".
AB	Abnormal:	Abnormal monocentric chromosome. This is a chromosome whose morphology is abnormal for the karyotype, and often the result of a translocation, pericentric inversion, etc. Classification used if abnormality cannot be ascribed to, e.g., a reciprocal translocation.

OTHER

GT	Greater than Ten:	Greater than 10 aberrations: A cell which contains more than 10 aberrations. Heavily damaged cells will be analyzed to identify the types of aberrations because multiple fragments, such as those found associated with a tricentric, do not count as independent aberrations.
PP	Polyploid Cell:	A cell containing multiple copies of the haploid number (n) of chromosomes.
E	Endoreduplication:	A failure of chromosomes to separate, resulting in a 4n cell.

NOT COMPUTED

TG	Chromatid Gap:	("tid gap"). An achromatic (unstained) region in one chromatid, the size of which is equal to or smaller than the width of a chromatid. These are noted but not usually included in final totals of aberrations as they may not all be true breaks.
SG	Chromosome Gap:	("isochromatid gap, IG"). Same as chromatid gap but at the same locus in both sister chromatids.
UC	Uncoiled Chromosome:	Failure of chromatin packing. Probably not a true aberration.