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Chronic Dermal Toxicity of Epoxy Resins I. Skin Carcinogenic Potency and General Toxicity

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CHRONIC DERMAL TOXICITY OF EPOXY RESINS
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EXECUTIVE SUMMARY

This report describes and quantifies the cutaneous and systemic response of male and female C3H mice to skin application of selected commercial epoxy resins and amine curing agents, at the maximum tolerated dermal dose (MTDD). Relevant findings were:

(1) At 75 mg per week, diglycidyl ether of bisphenol A (DGEBA) (CAS no. 1675-54-3), obtained from three separate manufacturers, accelerated mortality in female but not in male mice, had no effect on body weight in either sex, and had no effect on hematological or clinical chemical parameters. Skin exposed to this material exhibited hyperkeratosis, alopecia, depigmentation and sporadic focal inflammation. Treatment-related skin neoplasms were not observed under the prevailing test conditions.

(2) Equal-parts mixtures of the same resins with bis(2,3-epoxycyclopentyl) ether (CAS no. 2386-90-5), a resin shown previously to be a weak skin carcinogen in strain C3H, resulted in positive synergism; the activity of the combination exceeded, by a substantial margin, the activity of either component applied separately. Elevated white cell counts were noted but were considered secondary to cutaneous neoplasms. Skin carcinogenic potencies, relative to benzo(a)pyrene [B(a)P], were similar for all three DGEBA combinations and varied with dose rate,

from approximately 1/5,000th to 1/20,000th the activity of an equivalent surface dose of B(a)P.

(3) A DGEBA manufactured by Union Carbide Corporation (Material E, Appendix A) in the mid-1970's and assayed for skin carcinogenicity previously was chemically characterized. The results of this analysis are included with the present data for comparison purposes.

(4) The corrosiveness of diglycidyl ether of resorcinol (CAS no. 101-90-6) limited the MTDD to 1.8 mg/week. At this dose, systemic toxicity was noted which included weight loss, early and accelerated mortality, and dose-related reduction in white cell count and blood glucose relative to age- and sex-matched vehicle controls. Skin changes included mild hyperkeratosis, depigmentation, and follicle depletion. Treatment-related skin neoplasms were not observed at any dose.

(5) N,N'-diglycidyl-5,5-dimethylhydantoin (CAS no. 15336-81-9) was also a potent direct skin irritant which limited the MTDD to 3.75 mg/week. At this dose level there was accelerated mortality in female but not in male mice and no effect on body weight or clinical parameters. This material was found to be a moderately potent skin carcinogen with an activity approximately 1/200th that of B(a)P.

(6) The diglycidyl ether of neopentyl glycol (CAS no. 17557-23-2) was a potent skin irritant which limited the MTDD to 3.75 mg/week. At this dose level there was no effect on average body weight in either sex. An increased mortality at a single intermediate dose level in female mice was noted. The material was carcinogenic in skin of both sexes with a potency approximately 1/700th that of B(a)P.

(7) A 70:30 mixture of the hydantoin and neopentyl gylycol base resins, respectively, applied at the MTDD of 3.75 mg/week reflected the same pattern of systemic toxicity and skin carcinogenicity observed with each component separately, thus there was no indication of synergesim between these materials. The skin tumorigenic potency of the combination was approximately 1/200th that of B(a)P, which is similar to the activity of the hydantoin base resin alone.

(8) The amine curing agent menthane diamine (CAS no. 80-52-4) was a potent skin irritant. In mice exposed at the MTDD of 3 mg/week, body weight, overall mortality, blood count, and blood chemistry values were not significantly different from those in age- and sex-matched vehicle controls. This material induced mild thickening and scaling of the skin and depletion of hair follicles. Treatment-related skin tumors were not induced.

(9) A second curing agent consisting of an eutectic mixture of meta-phenylenediamine (CAS no. 108-45-2) and DGEBA was systemically toxic via percutaneous absorption. This limited the MTDD to 9 mg/week. At this dose level there was a significantly increased mortality in mice of both sexes. Blood counts, blood chemistry, and body weights were not affected. This material induced mild scaling of the epidermis. Treatment-related skin tumors were not observed.

(10) The commercial materials were characterized by gas and liquid chromatography, spectrometry, potentiometric titration, and vapor pressure as osmometry. The findings are summarized in Appendix A.

(11) Statistical methods have been developed that permit quantitation of skin tumorigenicity. Background information on the special statistical methods used is presented in Appendix C.

INTRODUCTION

Epoxy resins are a diverse class of chemicals that differ in structure, physical properties, and, presumably, biological activity. The purpose of these experiments was to compare the chronic dermal toxicity and carcinogenicity of selected commercial epoxy resins and to determine the potential for positive synergistic carcinogenic interactions between different resins.

This work is an extension and continuation of a Department of Energy sponsored program to evaluate epoxy resins for potential occupational health risks. The materials examined were chosen on the basis of their interest to the U.S. government. They are representative of the manufacturer's production at the time, and therefore the data are completely valid only for the specific production period.

Results of the experimental exposures will be reported in two parts. This report describes the test materials, their chemical and physical characteristics and the experimental design. General (systemic) toxicity will be evaluated and the skin carcinogenicity of the materials compared. A subsequent report will provide morphological descriptions of skin and significant internal pathology induced by the various treatments.

MATERIALS AND METHODS

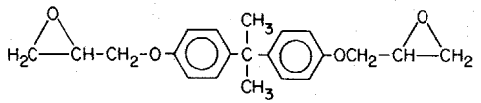
Test Materials

Figure 1 provides the structure, systematic name and Chemical Abstracts (CAS) registry number for the main component of five named epoxy resins (I-VII), two amine curing agents (VIII, IX), and B(a)P (X) which was used as a standard reference skin carcinogen. The commercial sources of the materials are given in Table 1. It is important to realize that the test materials are commercial/proprietary products rather than individual chemical compounds. Thus, materials I, II, and III are similar insofar as

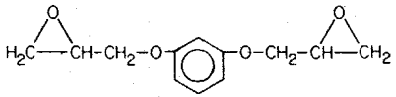
Table 1. Source, identity and purity of test materials

Material	Manufacturer	Trade name	Batch No.	Purity (wt %)
I	Celanese Coatings	Epi-Rez 508	MC8684	97
II	Shell Chemical	Epon 828	8WHJ17	89
III	Ciba Geigy	Araldite 6010	BAP-427	87
IV	Ciba Geigy	ERE 1359	P6602	88
V	Ciba Geigy	XB 2793	BAR90786	89
VI	Wilmington Chemical	Heloxy WC68	GGG1367	70
VII	Union Carbide	ERR 4205	-	97
VIII	Applied Plastics	Apco 2330	J7-017	93
IX	Rohm and Haas	Menthane diamine	G5783	85
X	Aldrich Chemical	Benzo(a)pyrene	031777	99

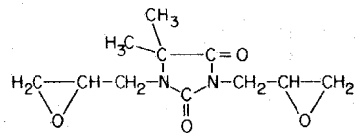
I, II, III 2,2'-[(1-methylethylidene) bis(4,1-phenyleneoxymethylene)] bisOxirane 1675-54-3



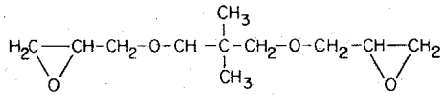
IV 2,2'-[1, 3 phenylenebis (oxymethylene)] bisOxirane 101-90-6



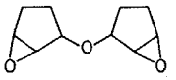
V 5,5-Dimethyl-1, 3-bis (oxiranylmethyl)-2, 4-Imidazolidinedione 15336-81-9



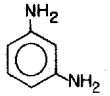
VI 2,2'-[(2, 2-dimethyl-1, 3-propanediyl) bis (oxymethylene)] bisOxirane 17557-23-2



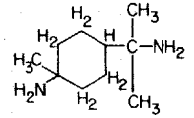
VII Bis(2, 3-epoxycyclopentyl) ether 2386-90-5



VIII 1,3-Benzenediamine 108-45-2



IX 4-amino-α, α, 4-trimethylcyclohexanemethamine 80-52-4



X Benzo[a] pyrene 50-32-8

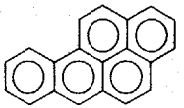


Fig. 1. Structures for the named principal component of commercial epoxy resins and amine curing agents. A roman numeral identifier, systematic name, and Chemical Abstracts registry number is given above each structure.

their main component is DGEBA (see Fig. 1) and oligomers derived from it. However, they also contain small quantities of impurities. Further details concerning the chemical characterization of these materials can be found in Appendix A. In Table 1, purity refers to the amount, by weight, of the named chemical (plus oligomers for I, II, and III) in the commercial product.

All the materials in Table 1, with the exception of VII, were applied separately. Material VII had been tested previously (1,2) and therefore was not retested singly; in the current study it was tested in an equal parts (by volume) mixture with materials I, II, and III. Materials V and VI were also tested in combination but at 70:30 (by volume). Letter codes are used in the text and tables to identify each mixture: (A) 50:50 mixture of III and VII; (B) 70:30 mixture of V and VI; (C) 50:50 mixture of I and VII; and (D) 50:50 mixture of II and VII.

Animal Exposures

Inbred, male and female C3Hf/Bd mice were produced under pathogen-free barrier conditions and held under these conditions for the 24-month duration of the experiment. Mice were weaned at 3–4 weeks of age. At 10 weeks of age the hair was removed from the back with electric clippers and the animals were randomly assigned in groups of five to each treatment dose combination. Mice were housed in polycarbonate shoebox cages with hardwood chip bedding. Food (Purina 5010-C) and water were constantly available.

The dose levels for each material were selected on the basis of a 2-week, five times weekly application of the test materials dissolved in spectro-grade acetone (Matheson-Coleman-Bell). The highest dose for the

2-year exposure was one which could be tolerated without irreversible local skin toxicity or systemic toxicity as reflected by suppression of weight gain or mortality. In some instances (materials I–III), when no significant local or systemic toxicity was observed, the viscosity of the material determined the concentration which could be reproducibly applied to the animals. The concentrations, number of mice per sex, and dose are given in Table 2. For mixtures A–D, the highest dose was set equal to the most toxic component. B(a)P (X) was diluted so that the level of response and distribution of times to skin tumor appearance would be similar to that of a weak skin carcinogen.

At the start of the experiment all materials, except IX and X, were weighed into glass scintillation vials in an amount sufficient to yield the highest concentration after the addition of an appropriate volume of acetone. The vials were kept in the dark at 4°C until used. Because material IX was so unstable that it could not be distributed, it was kept in a dessicator under nitrogen and weighed into vials immediately before solvent dilution. Material X was made from a concentrated stock solution kept at room temperature in a foil-wrapped container.

The material was applied with a 50-µl micropipette on Monday, Wednesday, and Friday, excluding holidays. Mice were reshaved as required. The time of neoplasm appearance was taken as the day on which a raised, circumscribed lesion appeared in the treated area of skin that persisted for the duration of the experiment or until death. The time of initial appearance as the basis for comparison of different materials is preferred to other indices, such as time to reach some arbitrary diameter, because tumor volumes can vary

greatly as a consequence of secondary infection, amount and accumulation of keratin produced, and growth behavior of individual neoplasms.

Table 2. Experimental design

Material	No. of mice		Material concentration (wt/vol %)	Dose (mg/week)[a]
	Female	Male		
I	40	40	50	75
II	40	40	50	75
III	40	40	50	75
IV	25	25	1.25,0.63,0.32	1.8,0.9,0.45
V	25	25	2.5,1.25,0.63	3.75,1.87,0.94
VI	25	25	2.5,1.25,0.63	3.75,1.87,0.94
VII[b]	40	40	50,10	75,15
VIII	25	25	6,3,1.5	9,4.5,2.25
IX	25	25	2,1,0.5	3,1.5,0.75
X	50	50	0.01,0.005,0.0025, 0.00125	0.015,0.0075,0.00375, 0.001875
A	25	25	50,25,12.5	75,37.5,18.75
B	25	25	2.5,1.25,0.63	3.75,1.87,0.94
C	25	25	50,25,12.5	75,37.5,18.75
D	25	25	50,25,12.5	75,37.5,18.75
Acetone	150	150	100	150

[a]Unit density assumed for all materials.

[b]Data obtained previously and included for comparison with the current materials.

Parameters of Chronic Dermal Toxicity

At intervals throughout the experiment body weight was determined, by cage group, at the highest concentration of each material. Cumulative mortality was noted. Heparinized blood samples taken from a random sample of mice surviving the full 24-month exposure were submitted to the clinical laboratory of the ORNL Health Division. For each sample total red and white cell counts, hematocrit, and hemoglobin were determined before the sample was centrifuged to recover the plasma. The plasma was subjected to analysis for total protein, albumin, glutamic-oxalacetic transaminase, alkaline phosphatase, urea nitrogen, glucose and triglycerides. Procedures used and other methodological details can be found in Appendix B. Time to skin tumor observation was, as previously noted, the primary criterion used for comparison of different material–dose groups. The viscera were examined in animals that either died or were killed at the end of the study. Lesions noted were recorded on a standard form for each animal, and tissues were taken for histology only when the gross diagnosis was questionable.

Statistical Analysis

Body weight was evaluated by the t-test for comparison of treated group means with those of the vehicle control. Group means and standard errors were calculated for clinical hematologic and chemical parameters. The effect of treatment on systemic mortality and the effect of the presence of skin tumor on mortality were evaluated by means of the Mantel-Haenszel test on the force of mortality. The "force of mortality" for an animal alive at the beginning of a small time interval is the

probability of death in the interval divided by the length of the interval. Here each interval is taken to be 1 day. The degree of skin carcinogenicity was determined from parameters of the Weibull distribution fitted to the times to tumor for each animal. Potencies relative to material X were obtained for each of the test materials shown to elicit skin neoplasms. Details concerning the statistical theory and methods used can be found in Appendix C.

RESULTS

Acute Toxicity

Mortality was induced after daily dermal application of materials V, VIII, and IX for 2 weeks at concentrations of 20, 12, and 50%, respectively. None of the remaining materials was lethal. Maximum tolerated exposure was limited more by skin inflammation and necrosis than by acute lethality. Acute necrosis with sloughing was observed after one or two applications of materials IV, V, VI, and IX at concentrations greater than 10%. This irritant effect was also noted at lower concentrations, but with lesser degrees of cytotoxicity. Eventually a concentration was reached that could be tolerated without skin ulceration. Materials I, II, III, and VII, after a transient inflammatory response, were tolerated at the maximum concentrations permitted by viscosity. Material VIII was not a primary skin irritant but was systemically toxic. The observed acute toxic potential of these materials is summarized in Table 3. B(a)P (X) and acetone did not cause

Table 3. Concentration at which acute toxic effects were noted when epoxy resins and amine curing agents were applied to the intact skin

Material	Concentration at which effect was noted		
	Body weight loss	Mortality	Skin irritation
I,II,III,VII	none at 50%	none at 50%	mild and transient at 50%
IV	10%	none at 50%	severe above 1.25%
V	20%	20%	severe above 2.5%
VI	none at 50%	none at 50%	severe above 2.5%
VIII	12%	12%	none at tolerated levels
IX	10%	50%	severe above 2%

acute skin irritation, weight loss, or mortality at the concentration and volume applied. Mixtures A–D induced acute toxicity in proportion to the additive effect of each component.

Chronic Toxicity

Evaluation of chronic toxicity was based upon changes in body weight at the highest dose of each material, changes in force of non-skin tumor mortality and blood hematologic and chemical alterations at the highest dose level of each material, relative to the vehicle control.

Body Weight

Average body weights at different times during the experiment are given in Table 4. Body weight was significantly ($P < 0.001$) suppressed at 24 months in male and female mice exposed to materials IV and VII. In all other groups average weight did not differ significantly ($P > 0.05$) from that of the vehicle control.

Mortality

As a summary measure of overall mortality, we used 750-day survival (percent) as shown in Table 5A for female and 5B for male mice. Animals that were killed before 750 days were ignored in this calculation. Except for a few groups, which are indicated in the table, there were at most two such animals in each group.

Table 4. Body weight in male and female C3H mice exposed dermally at the highest dosage

Material	Sex	Average body weight (g ± SE) at		
		6 months	12 months	24 months
I	F	26.7 (0.8)	26.7 (0.6)	26.9 (0.9)
	M	34.2 (0.5)	33.4 (0.5)	31.8 (0.8)
II	F	27.9 (0.5)	27.5 (0.4)	27.7 (0.7)
	M	32.5 (0.2)	31.8 (0.3)	30.9 (0.4)
III	F	28.2 (0.5)	27.8 (0.6)	27.6 (0.4)
	M	32.8 (0.2)	31.8 (0.3)	30.6 (0.7)
IV	F	25.9 (0.3)	25.5 (0.2)	18 (1)[a]
	M	31.3 (0.5)	30 (0.3)	22 (0.7)[a]
V	F	26.6 (0.3)	26.4 (0.6)	26.2 (0.9)
	M	31.8 (0.6)	30.9 (0.4)	29.5 (0.6)
VI	F	27.6 (0.4)	27.4 (0.5)	27.5 (0.5)
	M	32.2 (0.6)	31.6 (0.7)	30.7 (0.4)
VII	F	n.d.[b]	n.d.	21.3 (0.7)[a]
	M	n.d.	n.d.	23.8 (0.8)[a]
VIII	F	27.1 (0.5)	26.3 (0.2)	25.7 (1.3)
	M	32.2 (1)	30.9 (1.1)	28.6 (0.5)
IX	F	29.2 (0.6)	27.8 (0.4)	28.3 (0.4)
	M	34.4 (1.2)	32.6 (1.1)	30.3 (1.2)
X	F	27.2 (0.4)	n.d.	n.d.
	M	32.3 (0.8)	n.d.	n.d.
A	F	27.2 (0.4)	27 (0.5)	26.8 (0.5)
	M	30.8 (0.2)	30.6 (0.4)	28.6 (0.4)
B	F	28.8 (0.8)	27.9 (0.8)	26 (0.8)
	M	32.8 (1)	32.9 (0.6)	30 (0.3)
C	F	27.2 (0.5)	27 (0.4)	26.5 (0.9)
	M	31.1 (0.4)	30.5 (0.3)	29.7 (0.6)
D	F	26.8 (0.4)	26.6 (0.5)	27.5 (0.5)
	M	30.6 (0.4)	30 (0.5)	30.2 (0.5)
Acetone	F	28.2 (0.5)	27.2 (0.3)	27.4 (0.3)
	M	33.4 (0.5)	31.8 (0.5)	30 (0.6)

[a] Mean body weight significantly different from that of vehicle control; $P < 0.001$.

[b] n.d. = not done.

Mortality differences can occur as a result of either systemic toxicity or skin tumors. To investigate systemic toxicity, we compared the force of non-skin tumor mortality in each treated group with that in the acetone controls. A summary chi-squared statistic based on the log-rank test (3) was computed in each case and is presented in Table 5A and B for females and males respectively. The validity of this test depends on the assumption that skin tumor incidence does not select either for or against animals that would otherwise have died later of another cause. In the absence of data on the cause of death, this assumption is not statistically testable. Significant ($P < 0.05$) systemic mortality was noted at the higher doses, especially in female mice. Positive evidence of accelerated mortality in some, but not all treated groups indicates that the doses selected on the basis of a 2-week acute test do not accurately predict systemic toxicity.

Skin tumor-related mortality was assessed within each group by comparing the effect of presence of tumor on force of mortality. Statistical evidence ($P < 0.05$) of skin-tumor related mortality was found for the B(a)P groups at dose = 0.0075 (males and females) and for the B(a)P treated females at dose = 0.0037. At the highest B(a)P dose (0.015) early sacrifice after tumor induction precluded assessment of tumor related mortality. The only other group to show skin-tumor related mortality was the high dose female group treated with material A. In many of the remaining groups, there were not enough animals at risk for natural death in the tumor-bearing and tumor-free states to permit a reasonably powerful statistical test. Lack of statistical significance should therefore not be interpreted as evidence that skin tumors had no effect on mortality.

Table 5. Overall and systemic mortality in C3H mice

Material	Dose	% Survival at 750 days (95% confidence limits)	χ^2 for systemic mortality[a]
		A. FEMALES	
I	75	58 (41-74)	12.95***
II	75	70 (55-85)	10.21**
III	75	65 (49-81)	13.10***
IV	1.8	17 (6-36)	66.61***
	0.9	64 (43-81)	3.93*
	0.45	84 (66-94)	0.22
V	3.75	24 (13-51)	8.55**
	1.87	60 (38-78)	2.11
	0.94	72 (53-88)	2.91
VI	3.75	80 (62-92)	0.54
	1.87	56 (34-76)	16.35***
	0.94	72 (53-88)	2.33
VII	75	51 (34-68)	4.95*
	15	62 (45-78)	1.53
VIII	9	44 (24-66)	28.07***
	4.5	68 (47-84)	1.37
	2.25	80 (62-92)	0.36
IX	3	84 (66-94)	0.00
	1.5	72 (53-88)	0.71
	0.75	64 (43-81)	0.83
X	0.015	—[b]	0.65
	0.0075	—[b]	0.46
	0.0037	68 (54-82)	0.20
	0.0019	66 (52-80)	4.95*

(Table 5 continued)

Table 5 (continued)

Material	Dose	% Survival at 750 days (95% confidence limits)	χ^2 for systemic mortality[a]
A	75	80 (62-92)	0.07
	37.5	76 (57-89)	0.30
	18.75	72 (53-88)	1.30
B	3.75	68 (47-84)	1.38
	1.87	72 (53-88)	5.03*
	0.94	72 (53-88)	1.25
C	75	60 (38-78)	3.79
	37.5	56 (34-76)	3.66
	18.75	72 (53-88)	0.76
D	75	84 (66-94)	0.11
	37.5	68 (47-84)	2.62
	18.75	64 (43-81)	3.99*
Acetone	-	82 (76-88)	-
		B. MALES	
I	75	83 (69-96)	1.07
II	75	85 (73-97)	0.27
III	75	79 (66-93)	0.83
IV	1.8	72 (44-88)	1.47
	0.9	72 (53-88)	0.76
	0.45	84 (66-94)	0.18
V	3.75	76 (57-89)	0.36
	1.87	84 (66-94)	0.13
	0.94	60 (38-78)	1.30
VI	3.75	88 (70-97)	0.76
	1.87	84 (66-94)	0.27
	0.94	80 (62-92)	0.07
VII	75	75 (60-90)	0.01
	15	68 (52-83)	0.19

(Table 5 continued)

Table 5 (continued)

Material	Dose	% Survival at 750 days (95% confidence limits)	χ^2 for systemic mortality[a]
VIII	9	64 (43-81)	12.74***
	4.5	84 (66-94)	0.07
	2.25	80 (62-92)	0.23
IX	3	84 (66-94)	1.21
	1.5	80 (62-92)	0.02
	0.75	84 (66-94)	0.42
X	0.015	-[b]	0.24
	0.0075	-[b]	1.57
	0.0037	82 (70-95)	0.00
	0.0019	82 (70-94)	0.03
A	75	72 (53-88)	1.96
	37.5	80 (62-92)	0.17
	18.75	68 (47-84)	4.48*
B	3.75	54 (34-75)	0.05
	1.87	84 (66-94)	0.21
	0.94	76 (57-89)	0.00
C	75	71 (50-88)	0.01
	37.5	92 (76-99)	1.37
	18.75	80 (62-92)	0.03
D	75	92 (75-98)	1.93
	37.5	76 (57-89)	1.06
	18.75	92 (76-99)	2.20
Acetone	-	83 (77-90)	-

[a] *P < 0.05, **P < 0.01, ***P < 0.001.

[b] B(a)P groups sacrificed after 100% tumor response, before 750 days.

Clinical Hematologic Evaluation

Toxic suppression of bone marrow and lymphatic tissues was evaluated by examining the cellular composition of peripheral blood in a randomly selected subset of animals which survived to the end of the experiment. Blood was collected by cardiac puncture, under Metofane® (Pitman-Moore) anesthesia, into a syringe which contained heparin to prevent coagulation. The samples were evaluated for total red cell count, total white cell count, hemoglobin, and hematocrit by use of conventional clinical laboratory procedures (refer to Appendix B for details). Treatment-related effects were evaluated by comparison of the data with that from acetone controls, while age- (or acetone-) related changes were evaluated by comparison of vehicle control with 10- to 12-week-old untreated mice (aging control). Only the highest dose of each material was evaluated, with the exception of material IV, for which body weight suppression and mortality provided evidence of systemic toxicity. Hematologic data are presented in Table 6.

The data indicate an age- (or acetone-) related decrease in the number of circulating red cells and a proportionate decrease in hemoglobin and hematocrit in all treated animals. White cell counts fluctuated widely, with leukocytosis noted in groups in which skin tumors were induced (V, VI, X, B, C, D). Higher-than-normal white blood cell counts in these groups most probably are due to inflammation following necrosis and infection of skin neoplasms. Leukopenia was noted with material IV at the two highest dose levels. Because differential counts were not done, it is not possible to determine whether suppression of lymphocytes, granulocytes, or both, contributed to the decrease in white cell numbers. The fact that red cell

Table 6. Blood counts in C3H mice exposed dermally for 24 months to epoxy resins and amine curing agents

Material	Dose (mg/week)	Sex	No. of animals	Average values (SE)			
				Red cell ($X10^{-6}/mm^3$)	White cell ($X10^{-3}/mm^3$)	Hematocrit (%)	Hemoglobin (g/100 ml)
I	75	F	5	7.14 (0.21)	5.74 (0.66)	36.4 (1.2)	13.1 (0.29)
	75	M	5	6.59 (0.84)	7.22 (0.48)	33.6 (0.51)	11.6 (0.28)
II	75	F	5	6.32 (0.28)	6.9 (1.0)	32.4 (1.4)	11.5 (0.62)
	75	M	5	6.64 (0.17)	8.12 (2.55)	32.8 (0.73)	11.7 (0.31)
III	75	F	5	6.51 (0.57)	7.44 (1.25)	34.4 (0.4)	12.1 (0.17)
	75	M	5	6.78 (0.23)	9.88 (1.87)	34.0 (1.4)	12.0 (0.41)
IV	1.8	F	2	no sample			
	1.8	M	13	7.66 (0.19)	4.38 (0.41)	35.0 (0.59)	13.3 (0.33)
	0.9	F	5	6.68 (0.20)	4.14 (0.68)	33.2 (1.25)	12.0 (0.36)
	0.9	M	5	6.26 (0.50)	4.66 (0.50)	32.8 (1.46)	11.3 (0.84)
	0.45	F	5	6.14 (0.25)	5.88 (1.55)	32.0 (0.94)	11.88 (0.44)
	0.45	M	5	6.99 (0.17)	6.5 (0.50)	34.6 (0.75)	12.7 (0.29)
V	3.75	F	5	5.54 (0.39)	8.4 (4.07)	31.4 (2.06)	10.56 (0.75)
	3.75	M	5	6.05 (0.45)	15.4 (5.12)	34.6 (0.6)	12.14 (0.46)
VI	3.75	F	5	5.84 (0.36)	6.22 (1.37)	33.0 (1.64)	11.5 (0.49)
	3.75	M	5	6.34 (0.36)	13.48 (6.4)	32.0 (1.67)	11.2 (0.73)
VIII	6	F	5	6.54 (0.07)	6.16 (0.89)	35.0 (1.05)	11.9 (0.26)
	6	M	5	7.14 (0.16)	7.94 (0.34)	35.8 (1.56)	12.8 (0.37)
IX	3	F	5	6.38 (0.15)	6.88 (1.01)	32.4 (1.12)	11.6 (0.38)
	3	M	5	7.70 (0.68)	7.50 (1.18)	37.6 (3.37)	13.2 (1.08)
X	0.00375	F	10	5.96 (0.19)	13.32 (6.4)	29.65 (0.84)	10.86 (0.43)
	0.00375	M	10	6.22 (0.33)	12.08 (5.0)	31.5 (1.48)	11.34 (0.57)
A	75	F	5	6.24 (0.26)	5.7 (0.97)	33.0 (0.55)	11.5 (0.38)
	75	M	5	6.82 (0.53)	7.8 (1.17)	35.8 (3.64)	12.5 (1.16)
B	3.75	F	5	5.34 (0.47)	10.5 (3.35)	30.6 (2.58)	10.48 (0.93)
	3.75	M	5	5.06 (0.32)	21.4 (4.91)	32.8 (1.68)	10.08 (0.44)
C	75	F	5	6.44 (0.20)	6.06 (1.53)	35.0 (1.0)	11.96 (0.35)
	75	M	5	6.43 (0.14)	13.64 (8.92)	33.2 (0.49)	11.56 (0.16)
D	75	F	5	5.69 (0.48)	8.5 (1.96)	29.0 (1.52)	10.04 (0.54)
	75	M	5	5.96 (0.36)	14.3 (5.23)	30.2 (1.2)	10.6 (0.57)
Acetone control	--	F	20	6.14 (0.18)	5.3 (0.66)	31.65 (0.51)	11.11 (0.32)
		M	20	6.39 (0.26)	7.02 (0.88)	32.15 (0.89)	11.58 (0.49)
Aging control	--	F	10	7.18 (0.07)	4.44 (0.51)	38.0 (0.39)	13.63 (0.11)
		M	10	7.44 (0.07)	5.58 (0.24)	39.9 (0.28)	13.06 (0.11)

numbers were not reduced in animals exposed to material IV makes it least likely that bone marrow toxicity caused the leukopenia. By default, it is more likely that toxicity to lymphatic tissues reduced the cell count. Hematologic data are not available for material VII by itself. However, to the extent that its effects would be observed as a component in the A, B, C, and D mixtures, there appears to be no significant effect of this material on circulating cells.

Clinical Chemical Evaluation

In conjunction with the determination of the cellular composition of blood, the plasma from the same animals was also subjected to a battery of routine assays to detect systemic or organ-specific toxicity. The results of these determinations are summarized in Table 7. The methods and procedures used are described in Appendix B.

Plasma total protein levels were increased as a function of age in both sexes, with occasional high average levels noted in males. Alkaline phosphatase levels varied widely, both within and between groups. It appeared that female C3H mice had significantly higher alkaline phosphatase levels than males, irrespective of age. Glutamic-oxalacetic transaminase levels were relatively uniform across groups and between sexes, but the range of standard errors gives a clear indication of underlying individual heterogeneity. Glucose levels were little affected by sex or age. A clear treatment- and dose-related hypoglycemia was noted in both male and female mice exposed to material IV. Triglyceride levels varied widely, with no clear indication of an effect of treatment or age, although levels were

Table 7. Clinical chemical evaluation of C3H mice exposed dermally for 24 months to epoxy resins and amine curing agents[a]

Material	Dose (mg/week)	Sex	No. of animals	Total protein (g/dl)	Alkaline phosphatase (units/liter at 30°C)	Glutamic-oxalacetic transaminase (units/liter at 30°C)	Glucose (mg/dl)	Triglycerides (mg/dl)	Urea nitrogen (mg/dl)
I	75	F	5	5.0 (0.1)	70 (8)	52 (4)	94 (12)	127 (25)	35 (2)
	75	M	5	5.1 (0.2)	60 (3)	51 (11)	79 (11)	88 (11)	33 (2)
II	75	F	5	5.2 (0.3)	109 (24)	51 (8)	72 (8)	97 (17)	38 (2)
	75	M	5	5.4 (0.1)	53 (4)	31 (1)	104 (6)	128 (20)	27 (1)
III	75	F	5	4.9 (0.1)	135 (25)	82 (37)	96 (6)	92 (17)	30 (2)
	75	M	5	5.3 (0.3)	52 (8)	82 (45)	85 (8)	134 (20)	41 (3)
IV	1.8	F	2	4.8 (0.03)	74 (3)	55 (6)	44 (10)	77 (15)	30 (2)
	1.8	M	13	5.0 (0.1)	62 (3)	71 (6)	55 (5)	79 (10)	35 (2)
	0.9	F	5	5.1 (0.4)	129 (30)	93 (35)	50 (11)	112 (36)	40 (9)
	0.9	M	5	5.2 (0.2)	63 (3)	56 (6)	64 (8)	88 (15)	29 (2)
	0.45	F	5	5.2 (0.1)	126 (17)	40 (2)	98 (10)	94 (14)	27 (2)
	0.45	M	5	5.4 (0.1)	71 (11)	47 (7)	97 (5)	238 (23)	46 (1)
V	3.75	F	5	n.d.	188 (69)	n.d.	80 (6)	75 (7)	34 (3)
	3.75	M	5	5.3 (0.05)	60 (5)	49 (6)	76 (13)	149 (33)	41 (2)
VI	3.75	F	5	5.2 (0.2)	167 (69)	49 (4)	96 (3)	188 (18)	35 (4)
	3.75	M	5	5.7 (0.2)	99 (39)	39 (7)	81 (7)	167 (39)	43 (7)
VIII	6	F	5	n.d.	109 (12)	n.d.	95 (5)	100 (13)	29 (2)
	6	M	5	5.2 (0.2)	55 (2)	48 (6)	107 (6)	115 (24)	38 (4)
IX	3	F	5	5.5 (0.1)	106 (15)	62 (11)	115 (5)	139 (30)	37 (4)
	3	M	5	6.5 (0.2)	100 (31)	79 (15)	107 (16)	151 (23)	45 (2)

(Table 7 continued)

Table 7 (continued)

Material	Dose (mg/week)	Sex	No. of animals	Total protein (g/dl)	Alkaline phosphatase (units/liter at 30°C)	Glutamic-oxalacetic transaminase (units/liter at 30°C)	Glucose (mg/dl)	Triglycerides (mg/dl)	Urea nitrogen (mg/dl)
X	0.00375	F	10	5 (0.5)	103 (19)	70 (26)	82 (11)	96 (27)	34 (3)
	0.00375	M	10	5 (0.1)	59 (6)	46 (5)	92 (6)	118 (32)	35 (2)
A	75	F	5	5.6 (0.2)	73 (10)	41 (2)	104 (7)	128 (20)	31 (3)
	75	M	5	5.3 (0.1)	52 (3)	40 (4)	85 (13)	194 (34)	45 (2)
B	3.75	F	5	5.2 (0.07)	97 (12)	97 (46)	82 (8)	95 (25)	40 (4)
	3.75	M	5	5.4 (0.1)	55 (8)	51 (11)	90 (11)	165 (35)	42 (5)
C	75	F	5	5.5 (0.3)	83 (20)	41 (3)	112 (5)	98 (15)	26 (1)
	75	M	5	5.8 (0.1)	51 (3)	44 (8)	100 (13)	103 (12)	27 (1)
D	75	F	5	5.3 (0.2)	84 (18)	44 (9)	111 (12)	77 (16)	40 (8)
	75	M	5	6.4 (0.3)	39 (4)	60 (6)	120 (6)	123 (12)	38 (1)
Acetone control	-	F	20	5.4 (0.1)	148 (34)	70 (16)	88 (6)	95 (18)	32 (3)
	-	M	20	5.5 (0.3)	57 (9)	112 (28)	78 (9)	119 (25)	40 (4)
Aging control	-	F	10	4.9 (0.07)	74 (2)	58 (18)	112 (5)	126 (16)	24 (2)
	-	M	10	4.9 (0.06)	51 (2)	82 (22)	98 (4)	216 (14)	30 (1)

[a]Values given are mean (SE).

consistently higher in males than in females. Urea nitrogen levels were higher in males than females and also increased as a function of age. Treatment-related differences were not apparent, although standard errors again suggested considerable variation among individual animals.

Taken together, these data amplify and confirm the evidence that material IV is a systemic toxin at dose levels that fail to induce either skin irritation or neoplasia. Since clinical hematologic and chemical analyses were conducted on individual animals and each animal was also subjected to gross and microscopic evaluation, it eventually will be possible to correlate clinical findings with gross and microscopic pathologic changes. This information will be included in a subsequent report.

Skin Neoplastic Changes

Treatment-related skin neoplasms that were persistent, grew progressively, and contributed to mortality were induced with materials V, VI, VII, and X and with all the resin mixtures (A–D). For interpretation of the tumorigenic properties of each material, independent of natural or treatment-related mortality, the proportion of animals with skin tumors was corrected for deaths in animals before tumor occurrence by the Kaplan-Meier procedure (5). The resulting step curves, relating duration of exposure and probability of surviving without a skin neoplasm, are given in Fig. 2A and B for females and males, respectively. Differences between the distributions for males and females were tested by use of the log-rank test (3) and found to be significant ($P < 0.05$) in many cases; therefore the results are presented separately for each sex.

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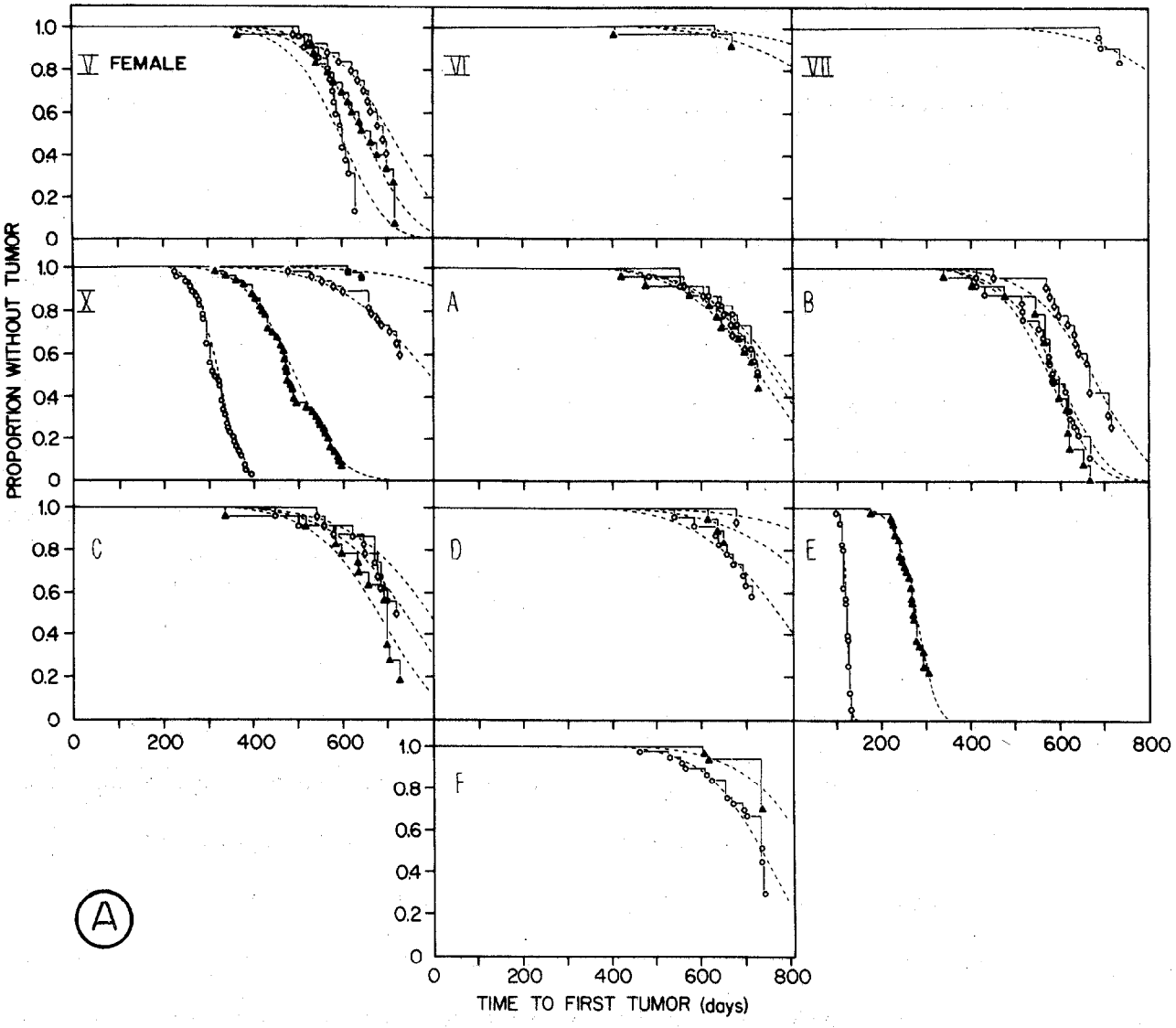


(A)

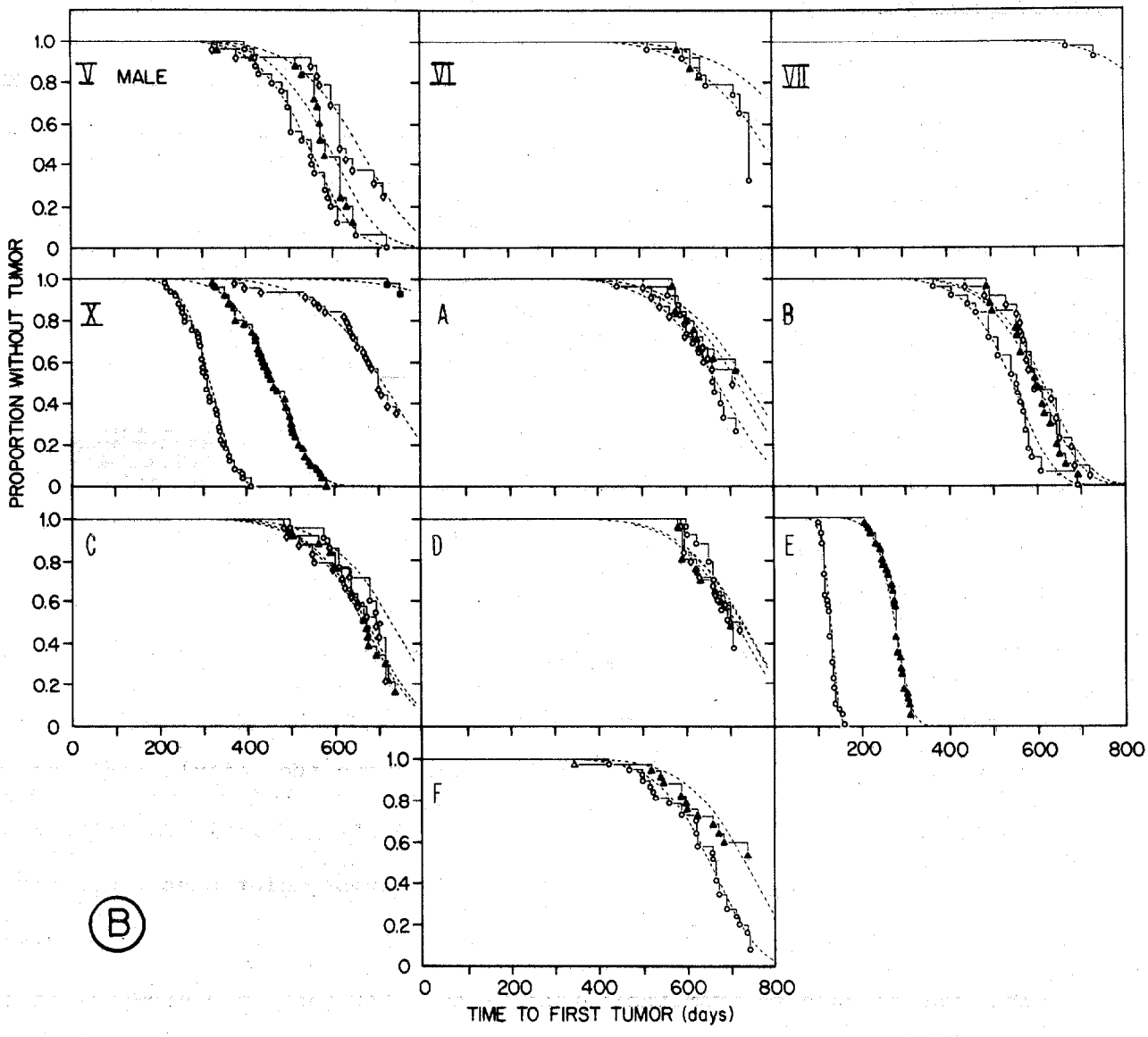


Fig. 2. Distribution of times to skin tumor for female (A) and male (B) C3H mice. Solid lines, Kaplan-Meier proportions; dashed lines, fitted Weibull. When dose responses are either absent or very shallow (Panels A–D) the lines cannot be distinguished. Each panel is identified with the material symbols used in the text. Panel E is the B(a)P control, and panel F the mixture of material VII and the Union Carbide DGEBA tested previously. The data in Panels E and F are included for comparison with the current materials. Symbols correspond to the dosages applied (mg/week) and, in order of decreasing dose, were ○, ▲, ◇, ■ for one or more dosages of each material shown to induce skin neoplasms under the prevailing test conditions.

The log-rank test was used again to test for dose-dependent differences among the distributions for each material–sex combination. Differences were not observed ($P > 0.05$) for material VI in females, for material VII and mix D in males, or for mixes A and C in either sex. All other positive treatment groups demonstrated significant differences due to dose.

The Kaplan-Meier procedure is a useful means of displaying the distribution of times to tumor, requiring minimal assumptions. However, for quantification of the dose-response relationships, further assumptions need to be made. One usual assumption is that the distribution of time to tumor belongs to some parametric family of distributions. Past experiences (6–8) indicate that the Weibull distribution is frequently a good model in continuous skin carcinogenesis experiments. Accordingly, a restricted three-parameter Weibull distribution was fit for each treatment combination. (The restrictions on the Weibull fits concern assumptions needed for dose-response quantification. Details concerning the Weibull model and the fitting may be found in Appendix C.) The resulting Weibull fits are shown as dashed lines in Fig. 2, superimposed on the Kaplan-Meier step functions. As a summary and comparison measure, the expected median time to tumor response, (T50) was calculated from the fitted Weibull for each dose group eliciting at least one skin tumor, together with an approximate standard error (Table 8).

Comparison of different treatment groups on the basis of T50 reveals substantial differences among the materials. Males were more susceptible than females for all materials in which the response was adequate. Just as was observed in previous experiments, materials I, II, and III proved to be synergistic with material VII, on the basis of higher incidence and more

Table 8. Incidence and estimated time to median skin tumor response for materials in which one or more persistent skin tumors were observed

Material	Dose (mg/week)	Sex	No. at start	No. with tumor	T50 (SE) (days)
V	3.75	F	25	16	593 (19)
	3.75	M	25	24	542 (16)
	1.87	F	25	18	646 (20)
	1.87	M	25	22	587 (18)
	0.94	F	25	12	706 (27)
	0.94	M	25	15	654 (24)
VI	3.75	F	25	1	1183 (236)
	3.75	M	25	9	781 (38)
	1.87	F	25	2	991 (136)
	1.87	M	25	4	879 (67)
VII	75	F	40	3	922 (84)
	75	M	40	2	931 (82)
A	75	F	25	10	752 (37)
	75	M	25	15	671 (24)
	37.5	F	25	11	726 (33)
	37.5	M	25	10	738 (33)
	18.75	F	25	8	771 (43)
	18.75	M	25	10	716 (32)
B	3.75	F	25	20	592 (18)
	3.75	M	25	22	542 (15)
	1.87	F	25	20	573 (17)
	1.87	M	25	22	597 (17)
	0.94	F	25	18	671 (23)
	0.94	M	25	21	612 (18)
C	75	F	25	6	796 (50)
	75	M	25	10	729 (30)
	37.5	F	25	14	682 (26)
	37.5	M	25	20	664 (20)
	18.75	F	25	10	743 (35)
	18.75	M	25	17	672 (21)
D	75	F	25	9	776 (41)
	75	M	25	14	711 (24)
	37.5	F	25	3	912 (90)
	37.5	M	25	10	724 (30)
	18.75	F	25	1	1110 (197)
	18.75	M	25	13	727 (26)
X	0.015	F	45	44	322 (6)
	0.015	M	50	48	317 (7)
	0.0075	F	50	45	493 (12)
	0.0075	M	50	50	464 (10)
	0.0038	F	50	16	792 (35)
	0.0038	M	45	26	710 (20)
	0.0019	F	50	2	1164 (170)
	0.0019	M	50	2	1123 (139)

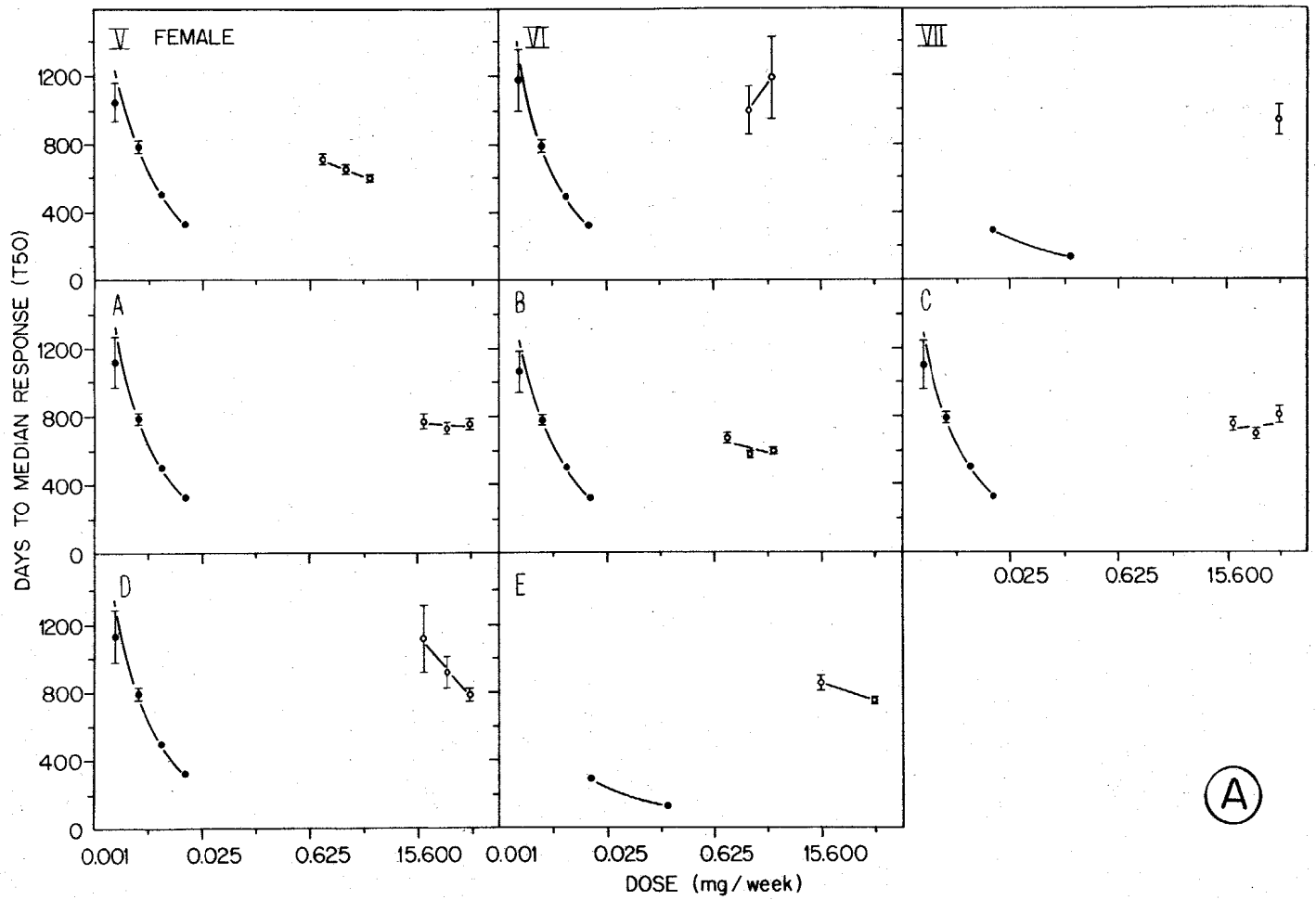
rapid rate of tumor occurrence observed for resin mixtures A, C, and D than observed for either component alone. Mixture B does not exhibit synergism but rather the additive effects of the individual components, i.e., the activity of the combined treatment does not exceed that of either component tested separately.

Determination of Carcinogenic Potency

For comparison of different treatments within a single experiment as well as experiments done at different times but in the same sex and strain, a potency index has been calculated for each treatment–dose combination relative to that obtained for the reference carcinogen (X). The potency index is the ratio of the dose of the reference carcinogen to that of the test material at an equivalent effect level. Here the "effect" was defined to be estimated median time to skin tumor, based upon a three-parameter Weibull fit to each material–dose combination with the shape (k) and location (w) parameters of the model held constant for all doses of the reference carcinogen and test material. In several cases there was evidence that the assumption of common k and w was not valid. However, an alternative computation of potency index in these cases had little effect on the conclusions. (See Appendix C for details concerning the potency calculations and the evaluation of the assumptions on which they were based).

In Fig. 3 the dose-effect observed for the reference carcinogen is compared with that obtained for each dose level of the unknown. Over the experimental dose range two features are apparent: (a) the effect changes more rapidly as a function of dose with the reference carcinogen (X) than

with any of the test materials; (b) for several materials, a change in effect with increasing dose is either very slight or absent. In view of these observations we have evaluated relative potency for each dose; values are given in Table 9 for each sex. Note that the systematic differences between sexes largely disappear when the potency is evaluated on a relative basis. Diminishing potency with increasing dose occurs because the median time to tumor for the reference carcinogen decreases much more rapidly with increasing log dose than does the median time to tumor for the test materials. An arbitrary, but perhaps valid, means of comparing the different materials would be to contrast the relative potencies at the highest exposure level permitted by local or systemic toxicity. By this convention the potencies of materials V and VI are an order of magnitude greater than those observed at the highest permissible doses of either material VII alone or material VII in combination with materials I, II, or III. Material VII exhibits positive synergistic interaction with materials I, II, and III (groups A, C, and D). The combination of materials V and VI (group B) induces a response comparable to that of material V, with no indication of synergism. By way of comparison the data shown in panel E is a previously tested Union Carbide DGEBA base resin together with the contemporary B(a)P reference standard. The response observed is comparable to that observed for the other combinations of DGEBA with material VII (groups A, C, and D).


V FEMALE
VI
VII
A
B
C
D
E
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800
1200
0.001
0.025
0.625
15.600
DOSE (mg/week)
A

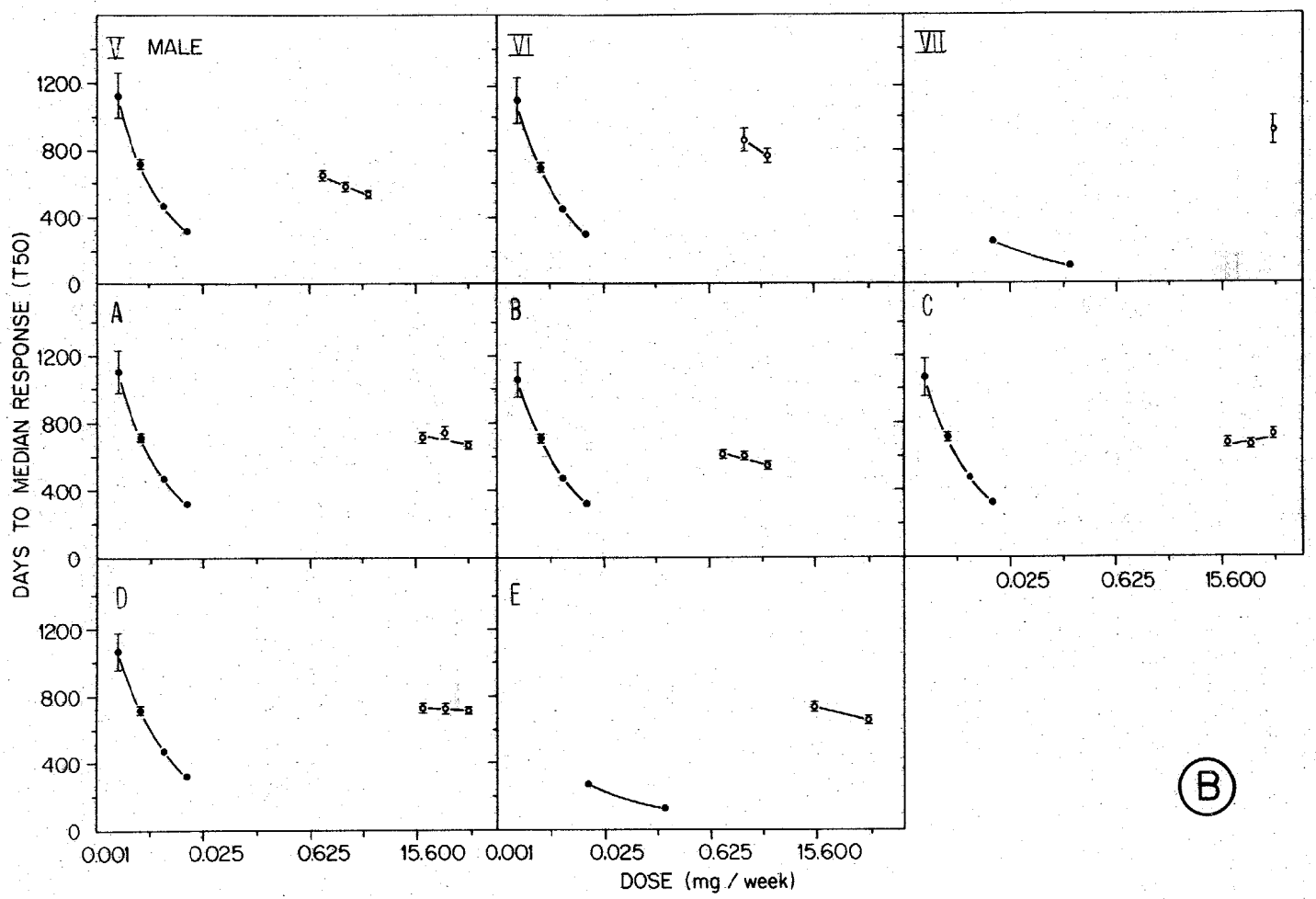

Fig. 3. Comparison of the dose effect obtained for B(a)P (●) with that of each unknown (○) for female (A) and male (B) C3H mice. The points on the ordinate are the maximum likelihood estimates of T50 and on the abscissa are dose on a logarithmic scale. One standard error is shown for each estimate of T50. The solid line connecting the points for each material is the weighted, least-squares best fit to the observed data. Panels are identified for each unknown compared with the concurrent B(a)P positive control. The data in Panels VII and E were obtained previously and are included for comparison with current materials.

Table 9. Skin carcinogenicity of B(a)P relative to that of epoxy resins and resin combinations

Material	Dose (mg/week)	Relative potency^{-1} (lower 95% confidence limit)	
		Female	Male
V	0.94	218 (186)	218 (207)
	1.87	380 (341)	373 (360)
	3.75	667 (578)	640 (614)
VI	1.87	660 (386)	713 (617)
	3.75	1,640 (774)	1,180 (1,070)
VII[a]	75	55,400	206,000
A	18.75	4,740 (3,890)	5,300 (4,650)
	37.5	9,350 (8,140)	9,980 (9,100)
	75	18,400 (15,300)	18,800 (16,800)
B	0.94	190 (152)	200 (184)
	1.87	347 (297)	359 (337)
	3.75	638 (519)	647 (595)
C	18.75	4,380 (3,390)	4,470 (3,970)
	37.5	9,000 (7,450)	9,480 (8,640)
	75	18,500 (13,700)	20,100 (17,500)
D	18.75	7,730 (5,110)	5,280 (4,960)
	37.5	12,300 (9,840)	10,400 (9,890)
	75	19,600 (16,300)	20,300 (19,100)

[a]Data obtained previously and included for comparison with current materials; confidence limit not calculated due to insufficient dose-effect data.

DISCUSSION

The present data demonstrate the chronic toxicity and skin carcinogenicity of selected commercial epoxy resin formulations applied as dilute acetone solution to the skin of C3H mice. An order of magnitude or greater difference in potency was noted. In general, male mice were more sensitive to skin tumor induction than female mice, whereas females were more sensitive to systemic toxicity. The potential for synergistic interaction between different materials was evaluated by application of resin mixtures. It had been noted previously (2) that material VII interacted synergistically with a Union Carbide product generically similar to I, II and III. Since this previously tested Carbide material was later found to contain appreciable amounts of epichlorohydrin and other nontypical components (see Appendix A), it was possible that synergism was due to these contaminants and not to the resin monomers as had been originally suspected. The present demonstration of an equivalent degree of synergism between VII and each of three separate resins obtained from different sources each with low but different levels of epichlorhydrin suggests strongly that synergism is between the principal components.

Skin neoplasms were not induced by materials I, II, III, IV, VIII, and IX at the dosage levels applied to C3H mice. Materials IV and IX are noteworthy in that both are corrosive on mouse skin and thus must be applied at low concentration. Material IV also attracts attention as a potential systemic toxicant at levels of exposure that do not induce local irritation. Additional long-term feeding studies to determine the toxic and carcinogenic

potential of material IV are in progress, sponsored by the National Toxicology Program (1980). Previously published animal carcinogenicity studies of material IV reveal that it is capable of eliciting skin neoplasms in C57BL (9) but not in Swiss ICR (10) mice following chronic skin exposure. This is consistent with the present data in which skin tumors were not induced in C3H mice, which have previously been shown to be less sensitive to chemical skin carcinogenesis than C57BL/6 (2,11). In our opinion, the most significant occupational risk for material IV would be primary skin irritation and potential systemic toxicity associated with skin absorption. It is unlikely that chronic dermal exposures at concentrations above those used in the present experiment would be unnoticed by workers due to the irritant properties of this material.

The significance of the synergistic interaction between materials I, II, III, and VII, as it bears on potential occupational hazard, will depend upon a better understanding of mechanism. Studies are in progress in this and other laboratories to examine the hypothesis that material VII is a competitive inhibitor of epoxide hydrolase, the principal detoxification enzyme for DGEBA, the major component of materials I, II, and III (12). If material VII inhibits epoxide hydrolase, then reactive intermediates may accumulate as well as persist longer within the cell. In either case, the probability is increased that critical targets will be affected. The importance of this to the question of human risk can be investigated directly by comparing the levels of metabolites generated in parallel cultures of human and mouse skin following application of radiolabeled resins either singly or in combination. Assuming the original hypothesis is valid, then it

should be possible to compare both species in terms of whether risks are either comparable or substantially different, and, if different, the direction of the difference and its magnitude. The current observation of no or a very shallow dose response with the combined resin exposures is interpreted as a saturation phenomenon and thus is consistent with the enzymatic interaction hypothesis. An amount of material VII sufficient to achieve maximal steady-state levels of a reactive intermediate within epidermal cells may have been achieved at the lowest concentration in the current study. This raises the possibility that the absence of a carcinogenic effect of materials similar to I, II, and III applied singly is due to their slow rate of percutaneous absorption and their rapid detoxification. If this is true, then any modification that either increases penetration of the stratum corneum or decreases metabolism, e.g., by epoxide hydrolase, would presumably increase the potential carcinogenicity of these materials.

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Appendix A

CHEMICAL ANALYSES OF TEST MATERIALS

G. F. Dorsey, Development Division

The compositions and properties of the test materials were examined by liquid and gas chromatography, and gas chromatography/mass spectrometry, potentiometric titration, and vapor pressure osmometry.

Liquid and gas chromatography were the major chemical identification and quantification methods. Chromatographic procedures and techniques used were the result of consultation with, and a visit to, the analytical laboratories of Shell Development Company (Houston, Texas) and Dow Chemical Company (Freeport, Texas).

MATERIAL I

Diglycidyl ether of bisphenol A (DGEBA)

Celanese Coatings Epi-Rez 508

Lot MC8684

CAS no. 1675-54-3

Oligomer distribution: N = 0, 96%; N = 1, 1%; N = 2, 0

Impurities:

diol of DGEBA*	2%	epichlorohydrin	4 ppm
unidentified	1%	toluene	26 ppm
total chlorine	0.3%	methyl ethyl ketone	<50 ppm
		phenyl glycidyl ether	220 ppm

additional very low-concentration impurities were noted but not identified

Chemical/physical character:

av. mol. wt.	362	epoxy equiv. wt.	168.0 g/equiv.
viscosity @ 25°C	4930 cps	density @ 25°C	1.16 g/cm^3

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*2-[4-(2,3-dihydroxypropoxy)phenyl]-2-[4-(2,3-epoxypropoxy)phenyl]propane.

MATERIAL II

DGEBA

Shell Chemical Co. Epon 828

Lot 8WHJ17

CAS no. 1675-54-3

Oligomer distribution: N = 0, 78%; N = 1, 9%; N = 2, 2%

Impurities:

diol of DGEBA	4%	toluene	40 ppm
total chlorine	0.2%	methyl isobutyl ketone	40 ppm
epichlorohydrin	29 ppm	1,3-dichlorohydrin	15 ppm

additional low-concentration impurities were noted but not identified

Chemical/physical character:

av. mol. wt.	388	epoxy equiv. wt.	184.8 g/equiv.
viscosity @ 25°C	13,300 cps	density @ 25°C	1.16 g/cm^3

MATERIAL III

DGEBA

Ciba-Geigy Araldite 6010

Lot BAP-427

CAS no. 1675-54-3

Oligomer distribution: N = 0, 78%; N = 1, 7%; N = 2, 2%

Impurities:

diol of DGEBA	4%	epichlorohydrin	3 ppm
total chlorine	0.3%	toluene	13 ppm
		1,3-dichlorohydrin	10 ppm

additional low-concentration impurities were noted but not identified

Chemical/physical character:

av. mol. wt.	390	epoxy equiv. wt.	184.6 g/equiv.
viscosity @ 25°C	13,320 cps	density @ 25°C	1.17 g/cm^3

MATERIAL IV

Diglycidyl ether of resorcinol

Ciba-Geigy ERE 1359

Lot P6602

CAS no. 101-90-6

Oligomer/isomer total: estimated at 88%

Impurities:

total chlorine	1%	phenyl glycidyl ether	406 ppm
toluene	6000 ppm	toluene glycidyl ether	present
epichlorohydrin	845 ppm	monochlorohydrin	<10 ppm

several aromatic species containing oxygen were present

Chemical/physical character:

av. mol. wt.	257	epoxy equiv. wt.	124 g/eqiv.
viscosity @ 25°C	250 cps	density @ 25°C	1.21 g/cm^3

MATERIAL V

N,N'-diglycidyl-5,5-dimethylhydantoin

Ciba-Geigy XB 2793

Lot BAR90786

CAS no. 15336-81-9

Oligomer/isomer total: estimated 89%

Impurities:

total chlorine	2.7%	toluene	<100 ppm
epichlorohydrin	1725 ppm	phenyl glycidyl ether	500 ppm

several aromatic species containing oxygen were present

Chemical/physical character:

av. mol. wt.	265	epoxy equiv. wt.	140.2 g/equiv.
viscosity @ 25°C	177 cps	density @ 25°C	1.21 gm/cm^3

MATERIAL VI

Diglycidyl ether of neopentyl glycol

Wilmington Chemicals Heloxy WC68

Lot GGG1367

CAS no. 17557-23-2

Oligomer/isomer total: estimated 70%

Impurities:

toluene	1%	total chlorine	4.6%
epichlorohydrin	none detected		

Pentyl moieties containing oxygen with molecular weights of 290, 310, 346, 402, and 440 were present

numerous unidentified low-boiling impurities were present in low concentrations

Chemical/physical character:

av. mol. wt.	250	epoxy equiv. wt.	136.6 g/equiv.
viscosity @ 25°C	16.1 cps	density @ 25°C	1.07 g/cm^3

MATERIAL VII

Bis(2,3-epoxycyclopentyl) ether

Union Carbide Chemicals and Plastics ERR 4205

CAS no. 2386-90-5

Oligomer/isomer total: ~97% (includes several isomeric forms)

Impurities:

low concentrations of structurally similar components such as 1-cyclopentene-3-one present, as well as other material containing carbonyl groups

Chemical/physical character:

av. mol. wt.	192	epoxy equiv. wt.	96.0 g/equiv.
viscosity @ 25°C	35 cps	density @ 25°C	1.17 g/cm^3

MATERIAL VIII

Liquified meta-phenylenediamine

Applied Plastics Company Apco 2330

Lot J7-017

CAS no. 108-45-2

Oligomer distribution: N = 0, 68%; N = 1 + N = 2, ~25%

Impurities:

oxygen	0.3%	sodium formate	400 ppm

several small unidentified peaks observed in chromatographic analysis

Chemical/physical character:

av. mol. wt.	157	amine equiv. wt.	67.2 g/equiv.
viscosity @ 38°C	3250 cps	density @ 25°C	1.17 g/cm^3

MATERIAL IX

Menthane diamine

Rohm and Haas

Lot G5783

CAS no. 80-52-4

Oligomer/isomer total: estimated 85%

Impurities:

All structurally similar: t-butylbenzene, hydroxy derivative of t-butylbenzene moiety, with 2-aminopropyl ion present; molecular weights of 182, 195, 333, respectively. Aromatic compounds with molecular weights of 272.

Chemical/physical character:

av. mol. wt.	172	amine equiv. wt.	93.3 g/equiv.
viscosity @ 25°C	13 cps	density @ 25°C	0.92 g/cm^3

MATERIAL E[a]

DGEBA

Union Carbide Corporation

Lot 1742

Oligomer distribution:[b] N = 0, 85%; N = 1, 7%; N = 2, 1%

Impurities:[b]

diol of DGEBA	1%	mesityl oxide	46 ppm
unidentified	1%	glycidol	30 ppm
epichlorohydrin	1476 ppm	2,3 dichlorohydrin	180 ppm
toluene	14 ppm	phenyl glycidyl ether	369 ppm

Chemical/physical character:[c]

av. mol. wt.	374	epoxy equiv. wt.	199 g/equiv.
viscosity @ 25°C	13,800 cps	density @ 25°C	1.16 g/cm^3

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[a]Material tested previously in experiments begun in 1975 and reported in ORNL 5375, where analysis indicated significant amounts (~10%) of an epoxidized polyglycol. Later analysis at Shell Development Company (Houston, Texas) indicated <5% 1,4-butanediol glycidyl ester was present in the resin. Analysis by Union Carbide Nuclear Division at the end of this test series did not show these materials to be present.

[b]1981 analysis.

[c]1978 analysis.

Appendix B

HEMATOLOGY AND BLOOD CHEMISTRY ANALYSES

C. A. Burtis, S. Garrett, E. M. Hall, E. L. Hurst, C. J. McDowell, J. M. Morton, and D. B. North, Health Division

Hematologic and blood chemistry analyses described in the text were performed in the clinical laboratory of the Health Division of the Oak Ridge National Laboratory.

Hematology

Cell counting — Total red cell count and white cell count were determined for each specimen with a Model FN Coulter Counter (Coulter Electronics, Inc., Hialeah, Florida).

Hemoglobin analysis — The hemoglobin content of each sample was measured with a Coulter Hemoglobinometer (Coulter Electronics, Inc., Hialeah, Florida).

Blood Chemistry

Total protein (TP), alkaline phosphatase (ALP), glutamic-oxalacetic transaminase (SGOT), glucose (GLU), triglycerides (TRIG), and blood urea nitrogen (BUN) were measured for each specimen with the miniature centrifugal analyzer that at the time of these studies was routinely operated in the clinical laboratory of the ORNL Health Division.

Analytical system — The centrifugal analyzer system used in these studies was developed and fabricated at the Oak Ridge National Laboratory and is a computer-controlled, multicuvet spectrophotometer (1,2) which utilizes a centrifugal field to simultaneously transfer and initiate several

individual reactions. These reactions subsequently proceed under identical conditions of time and temperature and are repetitively monitored as the cuvets spin through the analyzer's optical system. As a result, centrifugal analyzers generate a large quantity of time-absorbance data that may be either acquired, processed, and reduced in "real time" or stored for later processing by means of an integrated data system (3). In addition, a wide variety of computational algorithms are available (3) to calculate analytical results.

Reagents — Standard clinical chemical methods for determining BUN, GLU, TRIG, TP, ALP, and SGOT have been scaled down and adapted for use with the miniature analyzer. When available, commercial reagent kits were used in these studies.

For five of the assays Stat-Pak reagent kits were obtained from Calbiochem (San Diego, California). The two-vial kits were reconstituted by dissolving the contents of one vial with 2 ml of water or buffer, which was then added to and mixed with the contents of the second vial.

For the total protein assay, biuret reagent was prepared by dissolving 18 g $CuSO_4 \cdot 5H_2O$, 9 g potassium-sodium tartrate, and 5 g potassium iodide in 700 ml of distilled water; 80-ml of 50% NaOH was then added, and the volume was adjusted to 1 liter.

Procedures — The procedures for the individual determinations have been described previously (2). The pertinent analytical parameters are summarized in Table B-1. For each rotor analyzed, three quality control samples were assayed, and their results were evaluated statistically to validate the results.

Table B-1. Analytical parameters for clinical methods adapted for use with the centrifugal analyzer

Procedure	Volume (µl)		Wavelength (nm)	Reaction type	Reference
	Sample	Total			
Enzyme					
ALP	10	130	405	rate	4
SGOT	20	130	340	rate	5
Metabolites					
BUN	2	122	340	rate ratiometric	6
GLU	2	122	340	equilibrium	7
TP	3	123	540	equilibrium	8
TRIG	4	124	340	equilibrium	9

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Appendix C

Statistical Analysis of Mortality and Relative Skin Carcinogenicity

D. A. Wolf and T. J. Mitchell, Computer Sciences Division

Systemic Mortality

For the statistical test of systemic mortality (text Table 5), the event of interest was time to death from causes other than skin tumor. Since cause of death was not routinely recorded, we treated the occurrence of a skin tumor as a censoring mechanism, i.e., the only information drawn from skin tumor-bearing animals was that the event of interest occurred (or would have occurred but for sacrifice or death related to skin tumor) later than the appearance of the skin tumor. To avoid bias, it was also necessary to assume that the censoring was "nonprognostic" (1) in that skin tumor incidence did not select either for or against animals that would otherwise have died of another cause at a given later time.

Under these assumptions, we used the standard log-rank test (2) to compare the force of non-skin tumor mortality in each treated group with that of the acetone control. (This test can also be viewed as a special case of the Mantel-Haenszel (3) test familiar to many biologists.) The test statistic, approximately distributed as a chi-squared under the hypothesis of identical time-dependent force of non-skin tumor mortality in both groups, is given in text Table 5A and B.

Tumor-Related Mortality

To investigate the effect of the presence of skin tumor on the force of mortality in each group, we again used a variation of the Mantel-Haenszel

test. Just prior to the ith "natural" death (i.e., excluding sacrifices), there are TF_i skin tumor-free animals and TB_i skin tumor-bearing animals. ("Tied" deaths were ordered arbitrarily. Deaths precede sacrifices in case of ties.) Under the null hypothesis that presence of skin tumor has no effect on the force of mortality, the probability that the ith natural death comes from the tumor-bearing group is $p_i = TB_i/(TB_i + TF_i)$. Let $X_i = 1$ if this event is observed and $X_i = 0$ otherwise; then X_i is a Bernoulli random variable with mean p_i and variance $v_i = p_i(1 - p_i)$. For the purpose of making inferences about the force of mortality, it is appropriate to consider TB_i and TF_i as fixed for each i, so the X_i are treated as independent random variables. The sum $X = \Sigma X_i$, summed over the deaths when there were animals at risk with and without tumors, has mean $p = \Sigma p_i$ and variance $v = \Sigma v_i$. Because of the central limit effect of summing several variables, the statistic $\phi = (X - p)^2/v$ is approximately distributed under the null hypothesis as chi-squared with one degree of freedom. In cases where fewer than 9 X_i's contributed to the sum or where $P < 2$, we found this approximation to be poor, so we ignored the chi-squared values.

It should be noted that the power of this test (and the test for systemic mortality described above) depends on the number and classification of the animals at risk prior to each death and also on the behavior of the relative forces of mortality. If, for example, the presence of a tumor decreases the force of mortality early in life and increases it later, ϕ will likely be too small to be declared "significant." The correct interpretation for a non-significant test is therefore "inconclusive" rather than "no difference."

Relative Potency

The potency of a test material relative to a standard is defined as the ratio of doses, standard/test, that elicit equivalent effects (4). The standard was B(a)P and the test materials were the epoxy resins. Median time to tumor, T50, was the effect. Each relative potency calculation used only data from a single test material (at several doses) and from the appropriate B(a)P dose groups. Males and females were considered separately because of the noticeably greater tumor incidence in males. The χ^2 for the log-rank test (with 1 degree of freedom) of the hypothesis of no sex difference with respect to tumor response (2) are given in Table C-1. The inverses of the estimated relative potencies and their confidence limits are reported in text Table 9.

To estimate T50, the distribution of time (T) from first treatment to first skin tumor was modelled by use of a Weibull distribution with shape, location, and scale parameters k, w, and b, respectively. The three-parameter Weibull distribution can be characterized by the cumulative distribution function $F(t) = 1 - \exp[-b(t - w)^k]$ for $k,b > 0$ and $t > w$. T50 is therefore given by

$$T50 = w + (0.69315/b)^{1/k}. \qquad (1)$$

If k and w are the same for the standard and test materials, then any two doses that are equivalent in terms of T50 are also equivalent in terms of b by Eq. (1). Relative potency in terms of T50 can therefore be calculated equivalently in terms of b. The subsequent estimate of the standard error of

Table C-1. Sex effect on time to tumor distribution

Material	Dose (mg/week)	Observed/Expected[a]		χ^2 for log-rank test[b]
		Females	Males	
V	3.75	16/23.05	24/16.95	5.09*
	1.87	18/24.10	22/15.90	3.88*
	0.94	12/15.7	15/11.30	2.08
VI	3.75	1/5.01	9/4.99	6.43*
	1.87	2/2.85	4/3.15	0.49
VII	75	3/1.97	2/3.03	0.88
X	0.0150	44/45.33	48/46.67	0.08
	0.0075	45/54.99	50/40.01	4.31*
	0.0038	16/23.10	26/18.09	4.85*
	0.0019	2/1.71	2/2.29	0.09
XI[c]	0.150	40/32.97	40/47.03	2.55
	0.015	31/35.63	38/33.37	1.25
A	75	10/15.12	15/9.98	4.21*
	37.5	11/10.09	10/10.91	0.16
	18.75	8/10.00	10/8.00	0.90
B	3.75	20/27.00	22/15.00	5.09*
	1.87	20/17.10	22/24.90	0.83
	0.94	16/22.99	21/14.01	5.62*
C	75	6/8.17	10/7.83	1.18
	37.5	14/15.23	20/18.77	0.18
	18.75	10/14.76	17/12.24	3.38
D	75	9/12.03	14/10.97	1.6
	37.5	3/7.11	10/5.89	5.24*
	18.75	1/7.16	13/6.84	10.84**
E[d]	75	17/28.33	28/16.67	12.24**
	15	6/11.11	13/7.89	5.65*

[a](Observed number of tumors)/(expected number of tumors if no differences in time-to-tumor distributions).

[b]*P < 0.05; **P < 0.001.

[c]B(a)P from an earlier experiment tested concurrently with materials VII and E.

[d]Mixture of material VII and Union Carbide DGEBA tested in an earlier experiment.

relative potency is not only simpler but requires fewer dubious approximations than would be needed if k and w were allowed to differ between materials. The assumption of common k and w is therefore a standard part of our estimation procedure. A statistical check on the validity of this assumption is indicated below. For further commentary on the practice of "fixing" k and w, see Peto and Lee (5) or Peto et al. (6).

The method of maximum likelihood was used to estimate the Weibull parameters. Common k and w but individual b's were estimated for each dose of test material and standard. In calculating the likelihood, all observations were used, including the times to death of animals that die before tumor occurrence. In such cases, the time to tumor is considered to be "right-censored" in that it can only be inferred that the time to tumor exceeds the time to death. The censoring mechanism (death) is assumed to be "nonprognostic" (1), i.e., death does not select either for or against animals which would otherwise be "destined" to get a tumor at a given subsequent time.

The maximum likelihood calculations were made with a computer program kindly provided by Dr. D. G. Thomas of the National Cancer Institute. This program was also used to calculate T50 and its standard error, based on the Weibull fit. The results are summarized in Table C-2A and B. The estimates of the Weibull parameters have large variances and are highly correlated, so their individual values are difficult to interpret, whereas the T50 values and their approximate standard errors are fairly stable. Note that the estimates of T50 for the standard treatment [B(a)P] groups differ slightly

Table C-2. Summary of Weibull fits

Parameters and material	Dose (mg/week)	No. of animals	Tumor-bearing animals	b (Weibull)	T50 (SE)
		A. FEMALES			
k = 6.862					
w = 76.068					
X	0.015	45	44	2.64420E-17	323 (6.0)
	0.0075	50	45	6.27310E-19	502 (10.0)
	0.0038	50	16	2.04230E-20	778 (26.1)
	0.0019	50	2	2.23850E-21	1044 (109.0)
V	3.75	25	16	1.65170E-19	593 (18.9)
	1.87	25	18	8.54700E-20	646 (19.8)
	0.94	25	12	4.25680E-20	706 (26.5)
k = 4.645					
w = 157.417					
X	0.015	45	44	3.54600E-11	322 (5.8)
	0.0075	50	45	1.30000E-12	492 (11.8)
	0.0038	50	16	6.56690E-14	794 (35.6)
	0.0019	50	2	7.32790E-15	1178 (175.6)
VI	3.75	25	1	7.18390E-15	1183 (236.3)
	1.87	25	2	1.87920E-14	991 (135.6)
k = 6.927					
w = 66.011					
VI[a]	0.15	40	40	4.61890E-13	123 (1.5)
	0.015	40	31	4.84760E-17	281 (5.9)
VII	75	40	3	3.37810E-21	922 (84.0)
k = 5.381					
w = 131.718					
X	0.015	45	44	3.72710E-13	322 (5.8)
	0.0075	50	45	1.14120E-14	496 (10.9)
	0.0038	50	16	4.87350E-16	787 (31.3)
	0.0019	50	2	5.40160E-17	1117 (142.7)
A	75	25	10	6.53400E-16	752 (36.8)
	37.5	25	11	8.25540E-16	726 (33.3)
	18.75	25	8	5.56200E-16	771 (42.7)

(Table C-2 continued)

Table C-2 (continued)

Parameters and material	Dose (mg/week)	No. of animals	Tumor-bearing animals	b (Weibull)	T50 (SE)
k = 6.296					
w = 97.996					
X	0.015	45	44	1.07630E-15	323 (5.9)
	0.0075	50	45	2.77170E-17	500 (10.2)
	0.0038	50	16	9.91220E-19	780 (27.7)
	0.0019	50	2	1.09070E-19	1067 (118.2)
B	3.75	25	20	7.55850E-18	592 (17.9)
	1.87	25	20	9.74110E-18	573 (17.0)
	0.94	25	16	2.99020E-18	671 (22.8)
k = 5.72					
w = 116.513					
X	0.015	45	44	4.05190E-14	322 (5.9)
	0.0075	50	45	1.19490E-15	497 (10.8)
	0.0038	50	16	4.81490E-17	784 (30.0)
	0.0019	50	2	5.32340E-18	1098 (134.3)
C	75	25	6	4.34580E-17	796 (49.8)
	37.5	25	14	1.24620E-16	682 (26.4)
	18.75	25	10	6.92920E-17	743 (35.0)
k = 5.233					
w = 137.471					
X	0.015	45	44	9.53300E-13	322 (5.8)
	0.0075	50	45	3.00000E-14	496 (11.2)
	0.0038	50	16	1.32010E-15	788 (32.1)
	0.0019	50	2	1.46490E-16	1128 (149.8)
D	75	25	9	1.44920E-15	776 (41.4)
	37.5	25	3	5.30410E-16	912 (90.3)
	18.75	25	1	1.61250E-16	1110 (197.4)
k = 7.69					
w = 59.274					
X[a]	0.15	40	40	8.91250E-15	123 (1.5)
	0.015	40	31	6.11800E-19	282 (5.4)
E[b]	75	40	17	1.13780E-22	740 (21.7)
	15	39	6	3.71330E-23	846 (45.7)

(Table C-2 continued)

Table C-2 (continued)

Parameters and material	Dose (mg/week)	No. of animals	Tumor-bearing animals	b (Weibull)	T50 (SE)
			B. MALES		
k = 6.262					
w = 64.339					
X	0.015	50	48	6.20320E-16	317 (6.3)
	0.0075	50	50	3.55700E-17	464 (9.5)
	0.0038	45	26	1.76160E-18	710 (20.2)
	0.0019	50	2	7.96000E-20	1123 (129.3)
V	3.75	25	24	1.15900E-17	542 (16.2)
	1.87	25	22	6.60070E-18	587 (18.2)
	0.94	25	15	3.09470E-18	654 (24.4)
k = 6.601					
w = 46.567					
X	0.015	50	48	6.10470E-17	317 (6.5)
	0.0075	50	50	3.46500E-18	465 (9.8)
	0.0038	45	26	1.63920E-19	710 (19.7)
	0.0019	50	2	7.35120E-21	1109 (129.4)
VI	3.75	25	9	8.38980E-20	781 (37.8)
	1.87	25	4	3.68580E-20	879 (66.7)
k = 9.909					
w = 0.635					
XI[a]	0.15	40	40	9.24870E-22	128 (2.3)
	0.015	40	38	5.01140E-25	274 (5.0)
VII	75	40	2	2.67190E-30	931 (81.5)
k = 6.699					
w = 45.103					
X	0.015	50	48	3.35920E-17	318 (6.4)
	0.0075	50	50	1.84860E-18	465 (9.6)
	0.0038	45	26	8.49830E-20	710 (19.5)
	0.0019	50	2	3.79670E-21	1103 (123.5)
A	75	25	15	1.27840E-19	671 (24.1)
	37.5	25	10	6.47210E-20	738 (32.9)
	18.75	25	10	8.00940E-20	716 (31.7)

(Table C-2 continued)

Table C-2 (continued)

Parameters and material	Dose (mg/week)	No. of animals	Tumor-bearing animals	b (Weibull)	T50 (SE)
k = 7.857					
w = 0.584					
X	0.015	50	48	1.51280E-20	318 (6.5)
	0.0075	50	50	7.24660E-22	468 (8.9)
	0.0038	45	26	2.72260E-23	711 (17.8)
	0.0019	50	2	1.18150E-24	1060 (103.3)
B	3.75	25	22	2.30290E-22	542 (15.1)
	1.87	25	22	1.07420E-22	597 (16.5)
	0.94	25	21	8.86690E-23	612 (17.5)
k = 7.678					
w = 3.148					
X	0.015	50	48	4.58950E-20	318 (6.5)
	0.0075	50	50	2.31300E-21	468 (9.2)
	0.0038	45	26	9.11450E-23	711 (18.1)
	0.0019	50	2	3.97960E-24	1067 (107.1)
C	75	25	10	7.49580E-23	729 (30.0)
	37.5	25	20	1.54260E-22	664 (19.5)
	18.75	25	17	1.40360E-22	672 (21.3)
k = 7.782					
w = 0.191					
X	0.015	50	48	2.32900E-20	318 (6.4)
	0.0075	50	50	1.15140E-21	468 (9.2)
	0.0038	45	26	4.43990E-23	711 (17.9)
	0.0019	50	2	1.93290E-24	1063 (105.9)
D	75	25	14	4.43820E-23	711 (24.4)
	37.5	25	10	3.86160E-23	724 (29.5)
	18.75	25	13	3.74190E-23	727 (25.9)
k = 8.054					
w = 22.244					
XI[a]	0.15	40	40	3.45550E-17	128 (2.4)
	0.015	40	38	3.45080E-20	272 (5.2)
E[b]	75	40	28	1.98870E-23	652 (15.2)
	15	40	13	7.55790E-24	732 (24.7)

[a] B(a)P from an earlier experiment tested concurrently with materials VII and E.

[b] Mixture of material VII and Union Carbide DGEBA tested in an earlier experiment.

from one comparison to another. This occurs because the comparison with B(a)P was made independently for each test material, and a different k and w were estimated each time.

The next step in the relative potency calculations involved fitting the following equation to the logarithm of the b's:

$$\log_{10} b = a_i + c_i \log_{10} \text{dose}, \qquad (2)$$

where i = test or std. This was done by the method of least squares, applied to the b's; the maximum likelihood estimates of the b's were obtained as described above. The weight used for each b was the number of tumors observed in that treatment group. These weights were derived by noting that, for fixed k and w, the variance of the common logarithm of b is approximately the same as 0.189 times the inverse of the number of tumors. Actually, k and w (though common to all groups within an assay) are not fixed; however, the differences among the logarithms of the b's are fairly stable with respect to variations of k and w (5). The effect of such variations would therefore be to raise or lower a_i in Eq. (2) by roughly a constant amount; this would have little or no effect on the relative potency in Eq. (3) below. [In the future, we plan to estimate the coefficients in Eq. (2) directly by maximum likelihood, thus avoiding the weighted least-squares approach altogether.]

The least-squares results are given in Table C-3.

Table C-3. Weighted least-squares results, $\log_{10} b = a_i + c_i \log_{10}$ dose

Material	Sex	a_{test}	c_{test}	a_{std}	c_{std}	SSE[a]	DF[a]
V, X	F	-19.34	0.9780	- 7.380	5.065	0.8289	3
	M	-17.464	0.9414	- 7.474	4.233	0.0707	3
VI, X	F	-13.35	-1.3820	- 2.3184	4.4780	0.4902	2
	M	-19.75	1.182	- 8.412	4.270	0.0589	2
VII, XI[b]	F	-20.47	-	- 9.06	3.979	-	0
	M	-29.57	-	-18.343	3.266	-	0
A, X	F	-15.32	0.0969	- 3.871	4.713	0.7534	3
	M	-19.64	0.3752	- 8.597	4.311	0.3203	3
B, X	F	-17.38	0.6264	- 5.984	4.948	2.015	3
	M	-22.08	0.6938	-11.52	4.541	0.3003	3
C, X	F	-15.78	-0.1937	- 4.721	4.775	1.560	3
	M	-21.30	-0.385	-11.16	4.474	0.4356	3
D, X	F	-17.71	1.535	- 3.533	4.675	0.6106	3
	M	-22.59	0.1239	-11.41	4.502	0.0900	3
E,[c] XI[b]	F	-23.25	0.6957	-10.62	4.163	-	0
	M	-23.83	0.6011	-13.99	3.001	-	0

[a] SSE is the weighted residual sum of squares. If the fitted model is adequate, SSE/0.189 is approximately distributed as chi-squared with DF degrees of freedom.

[b] B(a)P from an earlier experiment tested concurrently with materials VII and E.

[c] Mixture of material VII and Union Carbide DGEBA tested in an earlier experiment.

Upon completion of the least-squares estimation of Eq. (2), the relative potency at the dosage of the test material, d_{test}, can be calculated by solving for the dosage of the standard, d_{std}, which is predicted to yield the same b as d_{test}. The ratio d_{std}/d_{test} is the relative potency. The common logarithm of this ratio is given by:

$$\log_{10} (\text{relative potency at } d_{test}) = \frac{(a_{test} - a_{std}) + (c_{test} - c_{std})\log_{10} d_{test}}{c_{std}} \qquad (3)$$

It can be seen from Eq. (3) that relative potency does depend upon d_{test} when $c_{test} \neq c_{std}$. It was quite clear that this was the case for the data presented in this report. An upper 95% confidence limit for the ratio of Eq. (3) was obtained by applying Fieller's theorem (4). Taking antilogs of Eq. (3) and of this confidence limit gives the relative potency estimate and its confidence limit, the inverses of which are given in text Table 9 for each assay.

It is evident that the relative potency calculations rest on a series of statistical assumptions:

(i) the adequacy of the Weibull model,

(ii) the assumption of nonprognostic censoring,

(iii) the assumption of common (k,w) in each assay,

(iv) the appropriateness of the weighted least-squares procedure, particularly the rule for assigning weights,

(v) the adequacy of the regression model, Eq. (2).

Statistical tests were made for (iii) and (v). In the case of assumption (iii), the NCI program was used to maximize the likelihood when this assumption is dropped. The ratio ψ of this maximum likelihood to that obtained when the assumption is enforced provides a likelihood ratio test for the validity of the assumption. Twice the natural logarithm of ψ is approximately distributed as chi-squared with $2(n_G - 1)$ degrees of freedom, where n_G is the number of groups in the assay. The results are given in the third column of Table C-4. It is disturbing that in four cases (all male) there is strong statistical evidence that assumption (iii) does not hold. However, (k,w) did not differ significantly among the dose groups of the standard [B(a)P]. We therefore used the following alternative procedure to estimate relative potency for the four cases in which assumption (iii) was rejected. Assuming that (k,w) is constant within the standard dose groups, we used Eq. (1) and (2) (for i = std only) to obtain T50 as a function of dose for the standard. For each dose of the test material, T50 was obtained from the Weibull parameters based on data from that dose group only. We were then able to calculate the equivalent dose of the standard, from which the relative potency followed. This alternative calculation yielded relative potencies that were within the one-sided confidence intervals given in text Table 9 in all cases except Material VII, for which no confidence interval was calculated. We tentatively conclude that although violations of assumption (iii) may occur, they do not seriously affect the results given here.

Assumption (v) was tested by comparison of the weighted SSE from the least-squares analysis with the theoretical variance (0.189). The chi-squared statistic and its degrees of freedom are given in the fourth

Table C-4. Test of assumptions

Material	Sex	χ^2 (DF) for log-rank test,[a] common k and w	χ^2 (DF) for adequacy of linear model[a]
V	F	22.640 (12)*	4.39 (3)
	M	10.816 (12)	0.37 (3)
VI	F[b,c]	10.198 (10)	2.60 (2)
	M[b,c]	14.878 (10)	0.31 (2)
VII	F[b]	7.134 (4)	no test
	M[b]	13.734 (4)**	no test
A	F	11.624 (12)	3.99 (3)
	M	29.992 (12)**	1.70 (3)
B	F	14.956 (12)	10.68 (3)*
	M	15.687 (12)	1.59 (8)
C	F	13.125 (12)	8.27 (3)*
	M	12.358 (12)	2.31 (3)
D	F[a,b]	16.622 (12)	3.24 (3)
	M	45.107 (12)***	0.48 (3)

[a]*P < 0.05; **P < 0.01; ***P < 0.001.

[b]Dose group(s) with 0 and/or 1 tumor.

[c]Average number of tumors per dose fewer than five.

column of Table C-4. In column 2 of the same table are indicated those test materials with an average of fewer than five tumors per dose group or fewer than two tumors in any single dose group. These can be considered warning "flags" that assumption (iv) may be shaky.

The validity of assumption (i) can be evaluated visually in text Fig. 2. [Note that the Weibull curves there are also based on assumption (iii).] We have made no attempt to use statistical models other than the Weibull for time-to-tumor distributions.

Assumption (ii) is intuitively reasonable, but is not statistically testable.

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Appendix D

Animal Data

Key for data on following pages:

1st line - Material, sex, dose

2nd line - Identification no. (ID), age at first painting (AFP), time to first tumor (T), removal code (D), age at death (AAD)

I F 75

ID	AFP	T	D	AAD
1105	71	.	D	199
0304	71	.	D	436
0203	71	.	D	465
0305	71	.	D	582
0101	73	.	D	595
1201	71	.	D	611
0504	71	.	D	617
1103	71	.	D	652
1302	71	.	D	655
0505	71	.	D	690
0401	71	.	D	698
0403	71	.	D	702
0104	73	.	D	705
1202	71	.	D	717
0102	73	.	D	735
1303	71	.	D	736
0302	71	.	D	750
1101	71	.	D	757
0202	71	.	D	761
0201	71	.	D	766
0105	73	.	D	770
0402	71	.	D	773
0501	71	.	D	780
0405	71	.	D	801
1203	71	.	S	803
1204	71	.	S	803
1205	71	.	S	803
1301	71	.	S	803
1304	71	.	S	803
1305	71	.	S	803
0404	71	.	S	807
0502	71	.	S	807
0503	71	.	S	807
0103	73	.	S	810
1102	71	.	S	813
1104	71	.	S	813
0204	71	.	S	814
0205	71	.	S	814
0301	71	.	S	814
0303	71	.	S	814

I M 75

ID	AFP	T	D	AAD
1003	71	.	D	568
0901	71	.	D	607
0601	66	.	D	621
0701	78	.	D	703
0604	66	.	D	717
0903	70	.	D	739
0901	70	.	D	750
1401	71	.	D	751
1001	71	.	D	768
0805	71	.	D	771
0804	71	.	D	778
0902	70	.	D	784
0602	66	.	D	783
1405	71	.	D	793
1402	71	.	D	794
0603	66	.	S	803
0605	72	.	S	809
1403	71	.	S	810
1404	71	.	S	810
1501	71	.	S	810
1502	71	.	S	810
1503	71	.	S	810
1504	71	.	S	810
1505	71	.	S	810
1002	71	.	S	816
1004	71	.	S	816
1005	71	.	S	816
1601	71	.	S	820
1602	71	.	S	820
1603	71	.	S	820
1604	71	.	S	820
1605	71	.	S	820
0802	71	.	S	821
0803	71	.	S	822
0904	70	.	S	822
0905	70	.	S	822
0702	78	.	S	835
0703	78	.	S	835
0704	78	.	S	835
0705	78	.	S	835

II F 75

ID	AFP	T	D	AAD
0101	66	.	D	549
0401	71	.	D	556
1104	71	.	D	596
0304	71	.	D	610
0502	71	.	D	659
1201	71	.	D	661
1301	71	.	D	680
0205	71	.	D	682
0305	71	.	D	708
0403	71	.	D	708
0405	71	.	D	730
1304	71	.	D	747
0303	71	.	D	760
0301	71	.	D	782
1205	71	.	D	782
0402	71	.	D	785
0404	71	.	D	785
1202	71	.	D	785
0102	66	.	D	784
1204	71	.	D	795
1305	71	.	D	795
0203	71	.	D	802
1101	71	.	D	803
1102	71	.	S	803
1103	71	.	S	803
1105	71	.	S	803
1203	71	.	S	803
1302	71	.	S	803
1303	71	.	S	803
0302	71	.	D	806
0103	66	.	S	805
0104	66	.	S	805
0105	66	.	S	805
0501	71	.	S	814
0503	71	.	S	814
0504	71	.	S	814
0505	71	.	S	814
0204	71	.	D	816
0201	71	.	S	828
0202	71	.	S	828

II M 75

ID	AFP	T	D	AAD
0605	70	.	D	528
1604	71	.	D	571
0904	70	.	D	610
0705	71	.	D	626
0905	70	.	D	686
1504	71	.	D	712
0602	70	.	D	756
0902	70	.	D	792
0803	71	.	D	793
1004	71	.	D	793
1603	71	.	D	800
0601	70	.	D	805

0603	70	.	S	807
0604	70	.	S	807
0701	71	.	S	814
0702	71	.	S	814
0703	71	.	S	814
0704	71	.	S	814
1001	71	.	S	815
1002	71	.	S	815
1003	71	.	S	815
1005	71	.	S	815
1501	71	.	S	815
1502	71	.	S	815
1503	71	.	S	815
1505	71	.	S	815
1601	71	.	S	815
1602	71	.	S	815
1605	71	.	S	815
1401	71	.	S	816
1402	71	.	S	816
1403	71	.	S	816
1404	71	.	S	816
1405	71	.	S	816
0801	71	.	S	821
0901	70	.	D	821
0802	71	.	S	822
0804	71	.	S	822
0805	71	.	S	822
0903	70	.	S	822

III F 75

ID	AFP	T	D	AAD
0401	71	.	D	526
0402	71	.	D	584
0204	78	.	D	605
1201	71	.	D	626
0203	78	.	D	676
0201	78	.	D	722
1204	71	.	D	725
0305	71	.	D	729
0501	71	.	D	730
0205	78	.	D	737
1101	71	.	D	732
1105	71	.	D	740
0505	71	.	D	745
1303	71	.	D	745
0104	80	.	D	769
1301	71	.	D	761
0504	71	.	D	771
0302	71	.	D	775
1302	71	.	D	778
1102	71	.	D	783
1202	71	.	D	787
0303	71	.	D	792
0502	71	.	D	794
1103	71	.	S	800
1104	71	.	S	800
0404	71	.	D	801
0301	71	.	S	807
0304	71	.	S	807
0403	71	.	S	807
0405	71	.	S	807
1203	71	.	S	808
1205	71	.	S	808
0101	80	.	D	818
0102	80	.	S	818
0103	80	.	S	818
0105	80	.	S	818
1304	71	.	S	813
1305	71	.	S	813
0503	71	.	S	814
0202	78	.	D	821

III M 75

ID	AFP	T	D	AAD
1604	71	.	S	124
1403	71	.	D	142
1402	71	.	D	472
0604	70	.	D	627
1605	71	.	D	633
1505	71	.	D	689
0702	69	.	D	689
1002	71	.	D	694
1001	71	.	D	696
0705	69	.	D	777
0801	71	.	D	799
0704	69	.	D	800
1601	71	.	S	807
1602	71	.	S	807
1603	71	.	S	807
0802	71	.	S	808
0803	71	.	S	808
0804	71	.	S	808
0805	71	.	S	808
0701	69	.	S	807
0703	69	.	S	807
1401	71	.	S	810
1404	71	.	S	810
1405	71	.	S	810
1004	71	.	D	811
0601	70	.	D	812
0602	70	.	S	812
0603	70	.	S	812
0605	70	.	S	812
1501	71	.	S	815
1502	71	.	S	815
1503	71	.	S	815
1504	71	.	S	815
1003	71	.	S	822
1005	71	.	S	822
0904	71	.	D	828
0901	71	.	S	835
0902	71	.	S	835
0903	71	.	S	835
0905	71	.	S	835

IV F 1.8

ID	AFP	T	D	AAD
0404	70	.	D	457
0202	78	.	D	472
0403	70	.	D	534
0103	71	.	D	536
0502	71	.	D	579
0505	71	.	D	596
0302	71	.	D	605
0504	71	.	D	662
0204	78	.	D	673
0301	71	.	D	689
0501	71	.	D	695
0102	71	.	D	704
0303	71	.	D	710
0503	71	.	D	718
0405	70	.	D	721
0101	71	.	D	736
0401	70	.	S	743
0402	70	.	S	743
0205	78	.	D	752
0104	71	.	D	746
0105	71	.	D	746
0304	71	.	D	747
0305	71	.	S	751
0201	78	.	D	764
0203	78	.	D	764

IV	F			0.9
ID	AFP	T	D	AAD
1505	71	.	D	540
1503	71	.	D	563
1305	71	.	D	571
1201	78	.	D	627
1101	71	.	D	690
1303	71	.	D	698
1205	78	.	D	712
1405	70	.	D	723
1501	71	.	D	736
1105	71	.	D	771
1302	71	.	D	796
1204	78	.	D	809
1401	70	.	D	805
1102	71	.	S	809
1103	71	.	S	809
1104	71	.	S	809
1202	78	.	S	816
1203	78	.	S	816
1301	71	.	D	810
1502	71	.	S	816
1504	71	.	S	816
1304	71	.	S	827
1402	70	.	S	830
1403	70	.	S	830
1404	70	.	S	830

IV	F			0.45
ID	AFP	T	D	AAD
2304	71	.	D	529
2205	71	.	D	533
2203	71	.	D	592
2204	71	.	D	743
2505	71	.	D	771
2102	71	.	D	778
2305	71	.	D	778
2201	71	.	S	806
2202	71	.	S	806
2301	71	.	S	807
2302	71	.	S	807
2303	71	.	S	807
2401	71	.	S	807
2402	71	.	S	807
2403	71	.	S	807
2404	71	.	S	807
2405	71	.	S	807
2501	71	.	S	816
2502	71	.	S	816
2503	71	.	S	816
2504	71	.	S	816
2101	71	.	S	817
2103	71	.	S	817
2104	71	.	S	817
2105	71	.	S	817

IV	M			1.8
ID	AFP	T	D	AAD
1004	71	.	D	540
0704	78	.	D	591
0902	70	.	D	616
1001	71	.	S	731
1002	71	.	S	731
1003	71	.	S	731
1005	71	.	S	731
0901	70	.	D	732
0703	78	.	D	745
0903	70	.	S	744
0904	70	.	S	744
0905	70	.	S	744
0805	71	.	S	752
0601	71	.	D	757
0801	71	.	S	758
0802	71	.	S	758
0803	71	.	S	758
0804	71	.	S	758
0701	78	.	D	765
0702	78	.	S	766
0705	78	.	S	766
0602	71	.	S	772
0603	71	.	S	772
0604	71	.	S	772
0605	71	.	S	772

IV	M			0.9
ID	AFP	T	D	AAD
1805	71	.	D	477
1605	71	.	D	613
1903	70	.	D	672
1704	71	.	D	701
1603	71	.	D	725
1801	71	.	D	726
1905	70	.	D	737
1802	71	.	D	771
2005	71	.	D	785
2001	71	.	S	803
2002	71	.	S	803
2003	71	.	S	803
2004	71	.	S	803
1701	71	.	S	809
1702	71	.	S	809
1703	71	.	S	809
1705	71	.	S	809
1601	71	.	S	814
1602	71	.	S	814
1604	71	.	S	814
1901	70	.	S	822
1902	70	.	S	822
1904	70	.	S	822
1803	71	.	S	827
1804	71	.	S	827

IV	M			0.45
ID	AFP	T	D	AAD
2805	71	.	D	549
2905	71	.	D	585
2802	71	.	D	610
2604	78	.	D	723
2705	71	.	D	768
3004	71	.	D	771
2701	71	.	D	782
2601	78	.	S	813
2602	78	.	S	813
2603	78	.	S	813
2605	78	.	S	813
2703	71	.	D	807
2702	71	.	S	814
2704	71	.	S	814
2801	71	.	S	814
2803	71	.	S	814
2804	71	.	S	814
2901	71	.	S	820
2902	71	.	S	820
2903	71	.	S	820
2904	71	.	S	820
3001	71	.	S	821
3002	71	.	S	821
3003	71	.	S	821
3005	71	.	S	821

V F 3.75

ID	AFP	T	D	AAD
0305	71	.	D	288
0401	71	.	D	369
0504	71	.	D	495
0103	71	.	D	523
0403	71	.	D	558
0303	71	507	D	698
0104	71	518	D	677
0304	71	550	D	710
0205	71	.	D	625
0101	71	571	D	743
0302	71	574	D	760
0201	71	581	S	815
0105	71	584	D	659
0301	71	588	D	760
0203	71	597	D	717
0502	71	602	S	738
0503	71	602	S	738
0405	71	.	D	675
0102	71	609	D	780
0402	71	616	S	752
0404	71	630	D	724
0202	71	630	D	750
0204	71	630	S	815
0501	71	.	S	738
0505	71	.	S	738

V F 1.87

ID	AFP	T	D	AAD
1404	70	368	S	814
1304	70	.	D	457
1203	71	.	D	561
1102	71	.	D	568
1201	71	534	D	764
1204	71	540	D	724
1403	70	543	D	696
1503	71	571	S	816
1101	71	583	D	738
1401	70	602	D	695
1202	71	616	D	736
1405	70	623	S	814
1501	71	639	S	816
1105	71	.	D	715
1505	71	644	D	793
1103	71	.	D	717
1402	70	665	D	752
1205	71	679	S	806
1303	70	.	D	758
1504	71	700	S	816
1104	71	716	S	808
1301	70	718	S	821
1302	70	718	S	821
1305	70	718	S	821
1502	71	.	D	813

V F 0.94

ID	AFP	T	D	AAD
2302	70	.	D	527
2402	71	493	S	815
2105	71	528	S	807
2502	70	.	D	619
2202	71	570	S	806
2103	71	595	S	807
2503	70	.	D	693
2504	70	623	S	821
2501	70	637	D	801
2205	71	651	S	806
2404	71	.	D	724
2304	70	660	D	759
2405	71	.	D	736
2102	71	665	S	807
2201	71	.	D	745
2505	70	.	D	745
2305	70	681	D	788
2401	71	693	S	815
2203	71	700	S	806
2101	71	.	D	795
2403	71	.	D	804
2204	71	.	S	806
2104	71	.	S	807
2301	70	.	S	821
2303	70	.	S	821

V M 3.75

ID	AFP	T	D	AAD
0604	71	399	D	744
0701	71	422	D	802
0903	71	424	D	725
0804	78	431	D	772
0605	71	462	D	759
0805	78	483	D	792
0904	71	497	D	802
0602	71	497	S	809
0702	71	504	D	767
0703	71	504	S	809
0705	71	504	S	809
1005	71	529	S	803
0901	71	550	S	816
0905	71	550	S	816
0603	71	552	D	694
0803	78	557	D	661
0801	78	581	D	788
0802	78	581	D	792
1001	71	588	S	803
0704	71	595	S	809
1002	71	609	D	736
0902	71	609	S	816
1003	71	.	D	691
0601	71	651	S	809
1004	71	721	S	803

V M 1.87

ID	AFP	T	D	AAD
1903	71	336	D	563
2003	71	420	S	820
1703	71	514	S	807
1602	71	528	D	743
1705	71	557	D	774
1704	71	557	S	807
1802	78	557	S	814
1605	71	564	D	792
1603	71	569	S	807
1804	78	569	S	814
1601	71	571	S	807
1604	71	571	S	807
1701	71	581	S	807
1805	78	581	S	814
1801	78	616	S	814
1803	78	616	S	814
2001	71	616	S	820
2002	71	616	S	820
2005	71	616	S	820
1904	71	630	D	736
1901	71	644	S	806
1902	71	644	S	806
1905	71	.	D	716
2004	71	.	D	779
1702	71	.	S	807

V M 0.94

ID	AFP	T	D	AAD
3003	71	324	D	766
2901	71	380	D	696
3005	71	.	D	575
2802	78	.	D	617
2703	71	550	D	747
2604	71	564	D	682
2701	71	570	D	652
3001	71	.	D	648
2801	78	.	D	655
2702	71	595	S	806
2605	71	595	S	807
2602	71	.	D	684
2803	78	616	D	764
2704	71	616	S	806
2705	71	616	S	806
2805	78	616	S	813
2603	71	630	S	807
2904	71	644	S	806
3004	71	.	D	745
2601	71	693	S	807
2804	78	714	S	813
3002	71	.	S	803
2902	71	.	S	806
2903	71	.	S	806
2905	71	.	S	806

VI F 3.75

ID	AFP	T	D	AAD
0405	71	.	D	652
0503	71	.	D	677
0303	71	.	D	689
0401	71	630	S	821
0305	71	.	D	702
0402	71	.	D	717
0101	71	.	D	757
0404	71	.	D	757
0204	78	.	D	764
0505	71	.	D	764
0502	71	.	D	800
0501	71	.	S	807
0504	71	.	S	807
0201	78	.	S	816
0202	78	.	S	816
0203	78	.	S	816
0205	78	.	S	816
0102	71	.	S	814
0103	71	.	S	814
0104	71	.	S	814
0105	71	.	S	814
0403	71	.	S	821
0301	71	.	S	823
0302	71	.	S	823
0304	71	.	S	823

VI F 1.87

ID	AFP	T	D	AAD
1404	71	406	D	704
1204	78	.	D	593
1505	71	.	D	593
1305	71	.	D	645
1205	78	.	D	673
1103	71	.	D	684
1104	71	.	D	701
1405	71	.	D	729
1503	71	.	D	729
1303	71	669	S	806
1101	71	.	D	743
1402	71	.	D	743
1304	71	.	D	764
1401	71	.	D	766
1502	71	.	D	772
1105	71	.	D	775
1203	78	.	D	782
1403	71	.	D	797
1301	71	.	D	802
1102	71	.	S	803
1302	71	.	S	806
1201	78	.	S	813
1202	78	.	S	813
1501	71	.	S	807
1504	71	.	S	807

VI F 0.94

ID	AFP	T	D	AAD
2402	71	.	D	533
2104	71	.	D	632
2305	71	.	D	659
2504	71	.	D	668
2203	71	.	D	696
2501	71	.	D	736
2405	71	.	D	746
2101	71	.	D	766
2201	71	.	D	768
2102	71	.	D	792
2403	71	.	D	794
2105	71	.	D	796
2103	71	.	S	803
2202	71	.	S	803
2204	71	.	S	803
2205	71	.	S	803
2301	71	.	S	806
2302	71	.	S	806
2303	71	.	S	806
2304	71	.	S	806
2502	71	.	S	807
2503	71	.	S	807
2505	71	.	S	807
2401	71	.	S	809
2404	71	.	S	809

VI M 3.75

ID	AFP	T	D	AAD
0901	70	.	D	560
0902	70	518	D	626
1002	71	597	S	803
0602	71	.	D	708
0703	71	637	S	809
0905	70	637	S	815
1004	71	651	S	803
0801	71	.	D	767
1001	71	714	S	803
0803	71	729	S	823
0805	71	729	S	823
0604	71	.	D	802
1003	71	.	S	803
1005	71	.	S	803
0601	71	.	S	809
0603	71	.	S	809
0605	71	.	S	809
0701	71	.	S	809
0702	71	.	S	809
0704	71	.	S	809
0705	71	.	S	809
0903	70	.	S	815
0904	70	.	S	815
0804	71	751	S	823
0802	71	.	S	823

VI M 1.87

ID	AFP	T	D	AAD
1605	71	.	D	649
1603	71	.	D	652
1702	71	584	S	807
2004	71	616	D	736
2003	71	616	D	789
1901	70	637	D	758
1903	70	.	D	721
1604	71	.	D	775
1601	71	.	S	803
1602	71	.	S	803
1902	70	.	D	805
1801	71	.	S	806
1802	71	.	S	806
1803	71	.	S	806
1804	71	.	S	806
1805	71	.	S	806
1701	71	.	S	807
1703	71	.	S	807
1704	71	.	S	807
1705	71	.	S	807
1904	70	.	S	815
1905	70	.	S	815
2001	71	.	S	816
2002	71	.	S	816
2005	71	.	S	816

VI M 0.94

ID	AFP	T	D	AAD
2705	71	.	D	442
2801	71	.	D	491
3001	71	.	D	645
2601	71	.	D	722
3004	71	.	D	730
2904	70	.	D	795
2701	71	.	S	806
2702	71	.	S	806
2703	71	.	S	806
2704	71	.	S	806
2602	71	.	S	807
2603	71	.	S	807
2604	71	.	S	807
2605	71	.	S	807
2802	71	.	S	808
2803	71	.	S	808
2804	71	.	S	808
2805	71	.	S	808
2901	70	.	S	815
2902	70	.	S	815
2903	70	.	S	815
2905	70	.	S	815
3002	71	.	S	816
3003	71	.	S	816
3005	71	.	S	816

VII F 75

ID	AFP	T	D	AAD
1001	63	.	D	168
1005	63	.	D	504
1402	61	.	D	603
1303	61	.	D	611
0605	70	.	D	641
0205	70	.	D	646
0601	70	.	D	647
0902	63	.	D	687
1404	61	.	D	687
0204	70	.	D	702
0101	70	.	S	703
0905	63	.	D	697
1401	61	.	D	712
0602	70	.	D	723
0502	70	.	D	724
0901	63	.	D	721
0105	70	.	D	728
0201	70	.	D	735
0102	70	.	D	739
1304	61	.	D	737
0604	70	689	S	805
1301	61	.	D	754
0203	70	693	S	805
1305	61	.	D	768
1002	63	.	D	770
1004	63	.	D	779
1403	61	.	D	782
1302	61	.	S	796
1405	61	.	S	796
0103	70	735	S	805
0104	70	.	S	805
0202	70	.	S	805
0501	70	.	S	805
0503	70	.	S	805
0504	70	.	S	805
0505	70	.	S	805
0603	70	.	S	805
0903	63	.	S	800
0904	63	.	S	800
1003	63	.	S	800

VII F 15

ID	AFP	T	D	AAD
0201	70	.	D	102
0902	63	.	D	319
0504	66	.	S	441
0202	70	.	D	513
1404	60	.	D	545
0604	66	.	D	556
0605	66	.	D	616
1405	60	.	D	665
0102	70	.	D	676
0203	70	.	D	707
1403	60	.	D	699
1003	63	.	D	725
0601	66	.	D	732
0205	70	.	D	750
1304	60	.	D	746
1004	63	.	D	749
0101	70	.	D	770
1001	63	.	D	772
0501	66	.	S	775
0903	63	.	D	778
1002	63	.	D	795
0502	66	.	S	801
0503	66	.	S	801
0505	66	.	D	801
0602	66	.	S	801
0603	66	.	S	801
0103	70	.	S	805
0104	70	.	S	805
0105	70	.	S	805
0204	70	.	S	805
1301	60	.	S	797
1302	60	.	S	797
1303	60	.	S	797
1305	60	.	S	797
1401	60	.	S	797
1402	60	.	S	797
0901	63	.	S	800
0904	63	.	S	800
0905	63	.	S	800
1005	63	.	S	801

VII M 75

ID	AFP	T	D	AAD
1603	60	.	D	222
0805	70	.	D	408
0704	70	.	D	449
1204	53	.	D	544
1104	64	.	D	610
1105	64	.	D	654
0403	72	.	D	675
0305	72	.	D	702
1502	60	.	D	719
0301	72	672	S	807
1203	53	.	D	739
1503	60	.	D	762
0702	70	.	D	785
0703	70	.	D	793
0701	70	.	D	794
0803	70	.	D	798
0405	72	.	D	804
1501	60	.	D	794
1505	60	.	D	794
1504	60	.	S	795
0705	70	.	S	805
0801	70	.	S	805
0802	70	.	S	805
0804	70	.	S	805
0302	72	735	S	807
0303	72	.	S	807
0304	72	.	S	807
0401	72	.	S	807
0402	72	.	S	807
0404	72	.	S	807
1601	60	.	S	796
1602	60	.	S	796
1604	60	.	S	796
1605	60	.	S	796
1201	53	.	S	790
1202	53	.	S	790
1205	53	.	S	790
1101	64	.	S	801
1102	64	.	S	801
1103	64	.	S	801

VII M 15

ID	AFP	T	D	AAD
0805	69	.	D	479
1204	63	.	D	522
1104	63	.	D	539
0803	69	.	D	610
0404	70	.	D	693
1201	63	.	D	701
0704	69	.	D	713
1604	59	.	D	706
1505	59	.	D	714
1605	59	.	D	731
1603	59	.	D	735
1203	63	.	D	742
1503	59	.	D	747
1105	63	.	D	756
1601	59	.	D	759
0702	69	.	D	794
0701	69	.	S	804
0703	69	.	S	804
0705	69	.	S	804
0801	69	.	S	804
0802	69	.	S	804
0804	69	.	S	804
0301	70	.	S	805
0302	70	.	S	805
0303	70	.	S	805
0304	70	.	S	805
0305	70	.	S	805
0401	70	.	S	805
0402	70	.	S	805
0403	70	.	S	805
0405	70	.	S	805
1501	59	.	S	796
1502	59	.	S	796
1504	59	.	S	796
1602	59	.	S	796
1101	63	.	S	801
1102	63	.	S	801
1103	63	.	S	801
1202	63	.	S	801
1205	63	.	S	801

VIII F 9

ID	AFP	T	D	AAD
0301	71	.	D	366
0401	71	.	D	491
0103	69	.	D	556
0205	76	.	D	587
0304	71	.	D	659
0405	71	.	D	673
0203	76	.	D	678
0201	76	.	D	709
0505	71	.	D	719
0403	71	.	D	723
0404	71	.	D	729
0502	71	.	D	729
0503	71	.	D	736
0102	69	.	D	748
0101	69	.	D	755
0202	76	.	D	764
0302	71	.	S	766
0303	71	.	S	766
0305	71	.	S	766
0501	71	.	D	766
0104	69	.	D	784
0504	71	.	D	793
0204	76	.	S	799
0105	69	.	S	799
0402	71	.	S	809

VIII F 4.5

ID	AFP	T	D	AAD
1503	71	.	D	387
1404	70	.	D	723
1502	71	.	D	724
1303	71	.	D	738
1401	70	.	D	738
1105	66	.	D	735
1101	66	.	D	739
1203	71	.	D	750
1405	70	.	D	751
1304	71	.	D	760
1403	70	.	D	767
1201	71	.	S	800
1202	71	.	S	800
1204	71	.	S	800
1205	71	.	S	800
1102	66	.	S	801
1103	66	.	S	801
1104	66	.	S	801
1501	71	.	S	806
1504	71	.	S	806
1505	71	.	S	806
1301	71	.	S	808
1302	71	.	S	808
1305	71	.	S	808
1402	70	.	S	809

VIII F 2.25

ID	AFP	T	D	AAD
2404	71	.	D	264
2503	71	.	D	499
2105	66	.	D	622
2401	71	.	D	732
2405	71	.	D	750
2103	66	.	D	759
2504	71	.	D	782
2203	76	.	D	794
2505	71	.	D	799
2102	66	.	D	796
2101	66	.	S	801
2104	66	.	S	801
2501	71	.	S	806
2502	71	.	S	806
2201	76	.	S	811
2202	76	.	S	811
2204	76	.	S	811
2205	76	.	S	811
2402	71	.	S	808
2403	71	.	S	808
2301	71	.	S	809
2302	71	.	S	809
2303	71	.	S	809
2304	71	.	S	809
2305	71	.	S	809

VIII M 9

ID	AFP	T	D	AAD
0902	70	.	D	532
0705	71	.	D	655
0903	70	.	D	672
1001	71	.	D	702
0703	71	.	D	705
0604	73	.	D	713
1005	71	.	D	732
0702	71	.	D	733
1004	71	.	D	750
0603	73	.	D	768
0901	70	.	D	779
0605	73	.	D	788
0805	71	.	D	787
1003	71	.	D	792
1002	71	.	D	800
0804	71	.	D	802
0601	73	.	S	809
0602	73	.	S	809
0701	71	.	S	809
0704	71	.	S	809
0904	70	.	S	809
0905	70	.	S	809
0801	71	.	S	814
0802	71	.	S	814
0803	71	.	S	814

VIII M 4.5

ID	AFP	T	D	AAD
1801	78	.	D	515
1902	70	.	D	700
2003	71	.	D	703
1703	69	.	D	709
1701	69	.	D	778
1802	78	.	S	807
1803	78	.	S	807
1804	78	.	S	807
1805	78	.	S	807
2001	71	.	S	802
2002	71	.	S	802
2004	71	.	S	802
2005	71	.	S	802
1601	70	.	S	802
1602	70	.	S	802
1603	70	.	S	802
1604	70	.	S	802
1605	70	.	S	802
1904	70	.	D	806
1702	69	.	S	806
1704	69	.	S	806
1705	69	.	S	806
1901	70	.	S	807
1903	70	.	S	807
1905	70	.	S	807

VIII M 2.25

ID	AFP	T	D	AAD
2601	70	.	D	448
2605	70	.	D	486
2903	70	.	D	616
3003	71	.	D	711
2603	70	.	D	746
2804	71	.	D	787
3002	71	.	D	800
3001	71	.	D	802
3004	71	.	S	803
3005	71	.	S	803
2602	70	.	S	805
2604	70	.	S	805
2701	71	.	S	806
2702	71	.	S	806
2703	71	.	S	806
2704	71	.	S	806
2705	71	.	S	806
2901	70	.	S	809
2902	70	.	S	809
2904	70	.	S	809
2905	70	.	S	809
2801	71	.	S	814
2802	71	.	S	814
2803	71	.	S	814
2805	71	.	S	814

IX F 3

ID	AFP	T	D	AAD
0203	71	.	D	431
0303	71	.	D	659
0505	71	.	D	673
0104	71	.	D	746
0504	71	.	D	765
0103	71	.	D	766
0502	71	.	D	794
0201	71	.	D	799
0202	71	.	S	802
0204	71	.	S	802
0205	71	.	S	802
0501	71	.	S	803
0503	71	.	S	803
0401	71	.	S	806
0402	71	.	S	806
0403	71	.	S	806
0404	71	.	S	806
0405	71	.	S	806
0101	71	.	S	807
0102	71	.	S	807
0105	71	.	S	807
0301	71	.	S	807
0302	71	.	S	807
0304	71	.	S	807
0305	71	.	S	807

IX F 1.5

ID	AFP	T	D	AAD
1204	71	.	D	578
1501	71	.	D	638
1202	71	.	D	649
1305	71	.	D	705
1101	71	.	D	711
1403	70	.	D	714
1304	71	.	D	719
1504	71	.	D	759
1103	71	.	D	766
1405	70	.	D	780
1201	71	.	S	802
1203	71	.	S	802
1205	71	.	S	802
1401	70	.	S	805
1402	70	.	S	805
1404	70	.	S	805
1102	71	.	S	806
1104	71	.	S	806
1105	71	.	S	806
1502	71	.	S	808
1503	71	.	S	808
1505	71	.	S	808
1301	71	.	S	809
1302	71	.	S	809
1303	71	.	S	809

IX F 0.75

ID	AFP	T	D	AAD
2501	71	.	D	625
2502	71	.	D	634
2302	71	.	D	696
2304	71	.	D	705
2201	71	.	D	708
2505	71	.	D	726
2102	71	.	D	729
2105	71	.	D	729
2101	71	.	D	740
2404	71	.	D	785
2202	71	.	S	802
2203	71	.	S	802
2204	71	.	S	802
2205	71	.	S	802
2301	71	.	S	802
2303	71	.	S	802
2305	71	.	S	802
2103	71	.	S	806
2104	71	.	S	806
2503	71	.	S	806
2504	71	.	S	806
2401	71	.	S	807
2402	71	.	S	807
2403	71	.	S	807
2405	71	.	S	807

IX M 3

ID	AFP	T	D	AAD
0601	71	.	D	614
0905	70	.	D	665
0703	71	.	D	683
0902	70	.	D	746
0901	70	.	S	805
0903	70	.	S	805
0904	70	.	S	805
1001	71	.	S	806
1002	71	.	S	806
1003	71	.	S	806
1004	71	.	S	806
1005	71	.	S	806
0602	71	.	S	807
0603	71	.	S	807
0604	71	.	S	807
0605	71	.	S	807
0701	71	.	S	807
0702	71	.	S	807
0704	71	.	S	807
0705	71	.	S	807
0801	71	.	S	809
0802	71	.	S	809
0803	71	.	S	809
0804	71	.	S	809
0805	71	.	S	809

IX M 1.5

ID	AFP	T	D	AAD
1604	71	.	D	589
1802	78	.	D	596
2005	71	.	D	607
1602	71	.	D	715
2004	71	.	D	736
1801	78	.	D	796
1701	71	.	S	802
1702	71	.	S	802
1703	71	.	S	802
1704	71	.	S	802
1705	71	.	S	802
1803	78	.	S	809
1804	78	.	S	809
1805	78	.	S	809
1901	71	.	S	806
1902	71	.	S	806
1903	71	.	S	806
1904	71	.	S	806
1905	71	.	S	806
1605	71	.	D	807
2001	71	.	S	807
2002	71	.	S	807
2003	71	.	S	807
1601	71	.	S	808
1603	71	.	S	808

IX M 0.75

ID	AFP	T	D	AAD
2803	71	.	D	543
3001	71	.	D	593
2601	71	.	D	638
3005	71	.	D	736
3004	71	.	D	801
2801	71	.	S	802
2802	71	.	S	802
2804	71	.	S	802
2805	71	.	S	802
2701	78	.	S	809
2702	78	.	S	809
2703	78	.	S	809
2704	78	.	S	809
2705	78	.	S	809
2602	71	.	S	803
2603	71	.	S	803
2604	71	.	S	803
2605	71	.	S	803
3002	71	.	S	807
3003	71	.	S	807
2901	71	.	S	808
2902	71	.	S	808
2903	71	.	S	808
2904	71	.	S	808
2905	71	.	S	808

X F 0.015

ID	AFP	T	D	AAD
0203	70	227	S	490
0105	70	231	D	361
0204	70	252	S	490
0205	70	262	S	490
0203	70	266	D	438
0402	71	275	S	479
0501	71	281	S	463
0401	71	283	S	479
0303	70	289	S	492
0304	70	289	S	492
0405	71	290	D	100
0202	70	297	D	455
0102	70	297	S	490
0104	70	297	S	490
0105	70	297	S	490
0201	70	297	S	492
0401	71	304	D	456
0402	71	304	S	470
0403	71	304	S	470
0404	71	304	S	470
0201	70	309	D	479
0103	70	309	S	490
0204	70	315	D	483
0505	71	323	S	463
0101	70	325	S	490
0102	70	329	D	490
0101	70	329	S	492
0104	70	329	S	492
0404	71	332	S	479
0405	71	332	S	479
0305	70	336	S	492
0501	71	340	S	466
0504	71	340	S	466
0505	71	343	S	466
0103	70	346	D	490
0503	71	354	S	463
0403	71	357	S	479
0503	71	361	S	466
0301	70	368	S	492
0502	71	372	S	463
0205	70	379	S	492
0302	70	379	S	492
0504	71	382	S	463
0502	71	.	S	466
0202	70	395	S	492

X F 0.0075

ID	AFP	T	D	AAD
1305	70	317	D	513
1303	71	.	D	396
1404	71	340	D	662
1204	70	364	D	560
1105	70	380	D	662
1203	70	400	D	590
1201	70	400	D	595
1301	70	406	D	637
1205	70	417	D	570
1303	70	417	D	625
1502	71	421	D	631
1304	71	428	D	606
1503	71	434	D	600
1304	70	434	D	638
1202	70	434	D	641
1403	71	444	D	649
1505	71	455	S	682
1201	70	462	D	606
1105	70	462	D	665
1205	70	469	S	694
1405	71	470	D	635
1102	70	470	D	648
1504	71	473	D	634
1502	71	473	D	676
1203	70	476	D	690
1505	71	477	D	674
1504	71	477	S	683
1402	71	.	D	554
1102	70	483	D	626
1405	71	487	D	641
1503	71	490	D	673
1501	71	490	S	682
1202	70	497	S	697
1402	71	518	S	684
1204	70	532	S	697
1401	71	539	D	676
1401	71	546	D	652
1404	71	549	S	684
1302	70	556	D	630
1403	71	560	S	683
1104	70	567	S	694
1101	70	571	S	681
1305	71	571	S	691
1103	70	581	S	681
1101	70	588	S	694
1302	71	589	D	680
1104	70	595	S	681
1301	71	.	D	677
1501	71	.	S	683
1103	70	.	S	694

X F 0.00375

ID	AFP	T	D	AAD
2501	71	.	D	334
2501	71	.	D	424
2403	71	480	D	666
2303	70	.	D	560
2301	70	.	D	562
2405	71	.	D	584
2304	70	532	D	665
2303	71	555	D	667
2503	71	.	D	631
2203	70	.	D	648
2105	70	581	D	681
2402	71	.	D	668
2404	71	602	S	807
2101	70	.	D	716
2302	70	.	D	723
2401	71	.	D	726
2202	70	660	D	772
2201	70	660	S	834
2204	70	660	S	834
2505	71	665	D	794
2305	70	.	D	742
2502	71	679	S	814
2201	70	688	S	820
2204	70	.	D	763
2504	71	707	D	794
2103	70	721	S	834
2304	71	721	S	837
2104	70	728	S	820
2105	70	728	S	834
2301	71	.	D	801
2401	71	.	D	801
2402	71	.	S	807
2502	71	.	S	813
2504	71	.	S	813
2503	71	.	S	814
2505	71	.	S	814
2102	70	.	S	820
2202	70	.	S	820
2205	70	.	S	820
2403	71	.	S	821
2404	71	.	S	821

2405	71	.	S	821
2203	70	.	D	821
2103	70	.	S	821
2101	70	.	S	834
2102	70	.	S	834
2104	70	.	S	834
2205	70	.	S	834
2302	71	.	S	837
2305	71	.	S	837

X F .001875

ID	AFP	T	D	AAD
3503	71	.	D	561
3301	70	.	D	563
3201	70	.	D	569
3301	71	.	D	575
3405	71	.	D	592
3204	70	.	D	592
3502	71	.	D	669
3205	70	.	D	673
3403	71	613	D	715
3101	70	.	D	692
3402	71	.	D	696
3102	70	.	D	709
3103	70	.	D	714
3504	71	644	S	815
3205	70	.	D	721
3302	71	.	D	726
3404	71	.	D	737
3202	70	.	D	738
3501	71	.	D	766
3303	71	.	D	778
3202	70	.	D	784
3401	71	.	D	785
3305	70	.	D	787
3203	70	.	D	794
3105	70	.	D	798
3505	71	.	D	801
3404	71	.	S	807
3405	71	.	S	807
3502	71	.	S	807
3504	71	.	S	807
3505	71	.	S	807
3304	71	.	D	809
3501	71	.	S	815
3503	71	.	S	815
3305	71	.	S	816
3401	71	.	S	822
3402	71	.	S	822
3403	71	.	S	822
3102	70	.	D	822
3101	70	.	D	826
3104	70	.	S	826
3105	70	.	S	826
3203	70	.	S	840
3201	70	.	S	840
3204	70	.	S	840
3103	70	.	S	844
3104	70	.	S	844
3302	70	.	S	844
3303	70	.	S	844
3304	70	.	S	844

X M 0.015

ID	AFP	T	D	AAD
0702	70	214	S	491
0905	71	218	S	485
0703	70	227	S	493
0904	71	239	S	485
0605	70	.	S	316
0704	70	246	D	438
0904	71	246	S	481
0802	71	252	D	436
0903	71	254	D	435
0603	70	259	S	493
0605	70	260	D	436
1005	71	276	S	472
0701	70	276	S	491
0702	70	289	D	392
0901	71	290	D	430
0805	71	291	S	488
0801	71	294	S	488
0802	70	297	D	485
0602	70	297	S	491
0804	70	297	S	492
0901	71	301	S	481
0905	71	301	S	481
0902	71	302	S	485
1001	71	308	S	474
0601	70	309	S	491
0705	70	309	S	491
0801	70	309	S	492
0602	70	315	S	493
0705	70	315	S	493
1002	71	316	S	472
0601	70	329	S	493
0704	70	329	S	493
0902	71	332	S	481
0603	70	337	S	491
0604	70	337	S	491
0805	70	337	S	492
0803	71	339	S	488
1001	71	340	S	472
1003	71	340	S	472
0701	70	346	S	493
0804	71	352	S	488
0903	71	359	S	485
0803	70	359	S	492
1004	71	361	S	472
1004	71	371	S	474
1005	71	371	S	474
0604	70	389	S	493
1002	71	392	S	474
1003	71	.	S	474
0703	70	408	S	491

X M 0.0075

ID	AFP	T	D	AAD
1703	70	323	D	630
1601	70	331	D	583
1704	70	351	D	654
1705	70	351	S	694
1904	71	359	D	442
1603	70	359	D	522
2005	71	371	D	519
1604	70	375	D	541
1901	71	375	D	561
1903	71	375	D	631
1803	70	395	S	682
2002	71	413	D	493
1604	70	413	S	694
1802	71	420	S	691
1801	71	421	D	673
1701	70	427	D	673
1804	70	427	S	682
2004	71	428	D	659
1605	70	435	S	694
1802	70	436	S	682
2003	71	441	S	683
1605	70	448	D	654
2002	71	449	S	683
1803	71	455	S	691
1901	71	462	S	684
1702	70	462	S	694

1905	71	469	S	684
1601	70	487	S	694
1602	70	487	S	694
1701	70	490	S	686
1704	70	490	S	686
1902	71	498	S	691
1905	71	498	S	691
1801	70	501	S	682
1805	70	501	S	682
1903	71	504	S	684
1603	70	505	S	694
2004	71	511	S	683
1904	71	518	S	684
1705	70	518	S	686
1804	71	528	S	691
1602	70	532	D	669
1703	70	532	S	686
2001	71	542	S	683
2005	71	546	S	683
2003	71	560	S	683
1902	71	567	S	684
2001	71	571	S	683
1702	70	581	S	686
1805	71	581	S	691

X M 0.00375

ID	AFP	T	D	AAD
2802	71	373	D	695
2905	71	396	S	836
3003	71	434	D	598
2704	70	535	S	808
2601	70	.	D	610
2703	70	.	D	623
2903	71	555	D	743
2702	70	567	D	801
2805	70	.	D	639
2903	71	581	S	828
2605	70	623	D	801
2904	71	630	D	773
2804	70	634	S	843
2701	70	637	S	820
2605	70	.	D	711
3004	71	644	S	807
2804	71	653	D	743
2801	71	653	S	828
2602	70	667	S	821
2705	70	672	S	808
2702	70	679	S	820

2802	70	.	D	752
2901	71	686	S	836
3001	71	700	S	807
3002	71	700	S	807
2703	70	700	S	808
2704	70	700	S	820
2602	70	707	S	834
3004	71	.	D	790
2603	70	721	S	820
2603	70	721	S	834
3005	71	.	S	807
2701	70	.	S	808
2803	70	742	S	843
2604	70	.	D	813
2705	70	.	S	820
2604	70	.	D	821
3001	71	.	S	823
3002	71	.	S	823
3003	71	.	S	823
3005	71	.	S	823
2601	70	.	D	826
2805	71	.	S	828
2902	71	.	S	836
2801	70	.	S	843

X M .001875

ID	AFP	T	D	AAD
3601	70	.	D	388
4003	71	.	D	577
3702	70	.	D	610
3801	70	.	D	618
3703	70	.	D	683
3704	70	.	D	707
3804	71	.	D	736
3602	70	.	D	739
3802	71	.	D	743
3802	70	.	D	760
4002	71	.	D	792
3904	71	.	D	792
3801	71	721	S	823
3701	70	.	S	805
3702	70	.	S	805
3705	70	.	S	805
4003	71	.	D	806
4001	71	.	S	807
4002	71	.	S	807
4004	71	.	S	807
4005	71	.	S	807

3905	71	.	D	809
3601	70	.	D	815
3603	70	.	S	816
3604	70	.	S	816
3605	70	.	S	816
4001	71	.	S	822
4004	71	.	S	822
4005	71	.	S	822
3604	70	.	D	822
3803	71	752	S	823
3805	71	.	S	823
3901	71	.	S	827
3902	71	.	S	827
3903	71	.	S	827
3901	71	.	S	830
3902	71	.	S	830
3903	71	.	S	830
3904	71	.	S	830
3905	71	.	S	830
3602	70	.	S	842
3603	70	.	S	842
3605	70	.	S	842
3701	70	.	S	844
3703	70	.	S	844
3704	70	.	S	844
3705	70	.	S	844
3803	70	.	S	844
3804	70	.	S	844
3805	70	.	S	844

XI F 0.15

ID	AFP	T	D	AAD
1301	67	96	S	226
0601	60	106	S	211
0602	60	106	S	211
0902	63	111	S	218
1002	63	111	S	218
1003	63	111	S	218
1005	63	111	S	218
0502	60	113	S	211
1302	67	115	S	226
1304	67	115	S	226
1305	67	115	S	226
1401	67	115	S	226
1402	67	115	S	226
1404	67	115	S	226
1405	67	115	S	226
0104	66	120	S	216

0105	66	120	S	216
0504	60	122	S	211
0901	63	126	S	218
0903	63	126	S	218
0904	63	126	S	218
0905	63	126	S	218
1001	63	126	S	218
1004	63	126	S	218
0604	60	128	S	211
0201	66	129	S	216
0202	66	129	S	216
0203	66	129	S	216
0204	66	129	S	216
0205	66	129	S	216
0501	60	132	S	211
0503	60	132	S	211
0505	60	132	S	211
0603	60	132	S	211
0605	60	132	S	211
0101	66	135	S	216
0102	66	135	S	216
0103	66	135	S	216
1303	67	136	S	226
1403	67	136	S	226

XI F 0.015

ID	AFP	T	D	AAD
0101	65	175	S	375
0903	63	220	D	340
0203	65	226	S	375
0505	58	231	S	368
1304	67	231	S	379
0205	65	238	S	375
0501	58	241	S	368
0504	58	241	S	368
0605	58	241	S	368
0901	63	246	S	373
1001	63	252	S	373
1402	67	256	S	379
0603	58	263	S	368
0905	63	267	S	373
1005	63	267	S	373
1301	67	269	S	379
1303	67	269	S	379
0105	65	270	S	375
0503	58	273	S	368
0604	58	273	S	368
0202	65	274	S	375

0103	65	280	S	375
0104	65	280	S	375
0201	65	280	S	375
0204	65	280	S	375
0902	63	287	S	373
0602	58	296	S	368
1401	67	297	S	379
1403	67	297	S	379
1404	67	297	S	379
0601	58	308	S	368
0502	58	.	S	368
0904	63	.	S	373
1002	63	.	S	373
1003	63	.	S	373
1004	63	.	S	373
0102	65	.	S	375
1302	67	.	S	379
1305	67	.	S	379
1405	67	.	S	379

XI M 0.15

ID	AFP	T	D	AAD
1501	66	100	S	225
0701	60	106	S	215
0801	60	106	S	215
0401	66	108	S	217
0402	66	108	S	217
1201	63	111	S	220
0704	60	113	S	215
0301	66	113	S	217
0302	66	113	S	217
0403	66	113	S	217
0404	66	113	S	217
1504	66	115	S	225
1505	66	115	S	225
1601	66	115	S	225
1605	66	115	S	225
0305	66	120	S	217
0804	60	122	S	215
1502	66	123	S	225
1101	63	126	S	220
1103	63	126	S	220
1105	63	126	S	220
1202	63	126	S	220
1205	63	126	S	220
0702	60	132	S	215
0703	60	132	S	215
0802	60	132	S	215

0803	60	132	S	215
0805	60	132	S	215
1102	63	134	S	220
1104	63	134	S	220
1203	63	134	S	220
1503	66	136	S	225
1604	66	136	S	225
0303	66	139	S	217
0304	66	139	S	217
0405	66	139	S	217
1204	63	147	S	220
0705	60	155	S	215
1602	66	159	S	225
1603	66	159	S	225

XI M 0.015

ID	AFP	T	D	AAD
1202	63	205	S	373
0304	66	214	S	376
0305	66	219	S	376
1603	60	231	S	372
0705	63	231	S	373
0703	63	241	S	373
1201	63	246	S	373
1204	63	246	S	373
0302	66	248	S	376
1604	60	256	S	372
0801	64	259	S	374
1103	63	267	S	373
1104	63	267	S	373
0403	66	270	S	376
0701	63	273	S	373
0704	63	273	S	373
1101	63	275	S	373
1501	60	276	S	372
1502	60	276	S	372
1503	60	276	S	372
1504	60	276	S	372
1505	60	276	S	372
1602	60	276	S	372
1102	63	280	S	373
0402	66	280	S	376
0404	66	280	S	376
1105	63	287	S	373
0803	64	288	S	374
0804	64	288	S	374
0301	66	291	S	376
0702	63	296	S	373

1205	63	296	S	373
0802	64	296	S	374
0303	66	303	S	376
1605	60	304	S	372
0805	64	308	S	374
1203	63	.	S	373
0401	66	310	S	376
0405	66	310	S	376
1601	60	.	S	372

A F 75

ID	AFP	T	D	AAD
0405	70	.	D	595
0203	71	.	D	606
0204	71	549	D	757
0303	71	549	D	757
0501	71	612	D	703
0302	71	640	D	778
0304	71	.	D	723
0502	71	665	S	802
0103	69	.	D	738
0105	69	676	S	805
0403	70	.	D	760
0205	71	.	D	768
0404	70	707	S	805
0305	71	707	S	807
0301	71	714	D	795
0104	69	.	D	790
0201	71	721	S	814
0503	71	.	S	802
0504	71	.	S	802
0505	71	.	S	802
0401	70	.	S	805
0402	70	.	S	805
0101	69	.	S	805
0102	69	.	S	805
0202	71	.	S	814

A F 37.5

ID	AFP	T	D	AAD
1302	71	417	D	585
1203	71	.	D	512
1405	71	470	D	785
1303	71	.	D	582
1401	71	.	D	591
1305	71	569	D	782
1501	71	.	D	653
1504	71	.	D	659
1102	80	613	S	817
1104	80	630	S	817
1202	71	640	S	800
1204	71	679	S	800
1402	71	.	D	760
1503	71	693	S	823
1403	71	707	S	803
1101	80	.	D	794
1201	71	721	S	800
1404	71	722	S	803
1205	71	.	S	800
1103	80	.	S	817
1105	80	.	S	817
1301	71	.	S	809
1304	71	.	S	809
1502	71	.	S	823
1505	71	.	S	823

A F 18.75

ID	AFP	T	D	AAD
2104	69	480	D	622
2503	71	.	D	590
2303	71	.	D	592
2405	71	557	D	814
2203	71	602	S	803
2501	71	.	D	683
2302	71	633	S	809
2504	71	647	S	809
2403	71	.	D	726
2201	71	661	D	771
2404	71	665	S	816
2204	71	.	D	740
2103	69	.	D	745
2301	71	.	D	754
2402	71	693	S	816
2101	69	.	D	797
2202	71	.	S	803
2205	71	.	S	803
2102	69	.	D	805
2105	69	.	S	806
2304	71	.	S	809
2305	71	.	S	809
2502	71	.	S	809
2505	71	.	S	809
2401	71	.	S	816

A M 75

ID	AFP	T	D	AAD
0802	78	443	D	684
0602	66	.	D	607
0702	71	.	D	612
1004	71	560	D	733
1002	71	.	D	635
0704	71	584	D	764
0904	70	588	S	806
0605	66	598	S	801
0905	70	602	S	806
0601	66	616	S	801
1003	71	630	S	809
0805	78	640	S	816
0705	71	.	D	732
0703	71	661	D	767
0901	70	661	D	801
0902	70	665	D	756
0701	71	.	D	739
1005	71	679	S	809
0804	78	.	D	758
0903	70	686	S	806
0801	78	714	S	816
0603	66	.	D	787
0604	66	.	S	801
1001	71	.	S	809
0803	78	.	S	816

A M 37.5

ID	AFP	T	D	AAD
1604	70	570	S	802
1705	71	577	D	673
1701	71	577	S	802
1702	71	577	S	802
2005	71	.	D	660
1904	70	.	D	662
1805	71	602	S	803
2003	71	619	D	782
1605	70	.	D	694
1902	70	626	S	805
1703	71	630	S	802
1905	70	665	S	805
2002	71	.	D	740
2004	71	.	D	768
1603	70	714	S	802
1602	70	.	D	798
1704	71	.	S	802

1601	70	.	S	802
1801	71	.	S	803
1802	71	.	S	803
1803	71	.	S	803
1804	71	.	S	803
1901	70	.	S	805
1903	70	.	S	805
2001	71	.	S	806

A M 18.75

ID	AFP	T	D	AAD
2904	70	.	D	500
2801	78	.	D	561
2701	71	.	D	571
2705	71	504	D	775
2704	71	522	D	687
3001	71	542	D	708
3003	71	564	D	808
3005	71	.	D	638
3002	71	.	D	647
2602	73	598	S	808
2603	73	598	S	808
2803	78	640	S	807
2604	73	651	S	808
2703	71	661	S	803
2805	78	.	D	747
2802	78	.	D	764
3004	71	.	D	758
2905	70	707	S	805
2804	78	.	S	807
2702	71	.	S	803
2901	70	.	S	805
2902	70	.	D	805
2903	70	.	S	805
2601	73	.	S	808
2605	73	.	S	808

B F 3.75

ID	AFP	T	D	AAD
0401	71	409	S	802
0504	71	410	D	610
0502	71	428	D	781
0302	71	511	D	806
0103	71	512	D	773
0501	71	514	D	778
0403	71	.	D	620
0102	71	550	S	809
0405	71	560	D	754
0301	71	574	D	757
0304	71	574	S	814
0303	71	575	D	654
0203	71	581	D	732
0201	71	582	S	814
0305	71	609	S	814
0503	71	616	D	797
0205	71	616	S	814
0104	71	620	D	795
0404	71	630	S	802
0204	71	640	D	743
0202	71	.	D	715
0505	71	.	D	715
0105	71	.	D	729
0101	71	665	D	779
0402	71	.	S	802

B F 1.87

ID	AFP	T	D	AAD
1201	71	336	D	556
1203	71	400	D	673
1202	71	.	D	498
1303	78	.	D	522
1403	71	473	S	803
1405	71	542	D	764
1404	71	542	S	803
1204	71	563	D	778
1101	71	563	S	802
1205	71	563	S	807
1502	71	574	D	771
1505	71	574	D	817
1401	71	581	S	774
1301	78	581	S	814
1103	71	595	S	802
1104	71	595	S	802
1102	71	.	D	676
1501	71	.	D	679
1504	71	612	S	817
1304	78	616	D	792
1305	78	616	S	814
1105	71	.	D	689
1402	71	619	D	779
1302	78	651	S	814
1503	71	665	S	817

B F 0.94

ID	AFP	T	D	AAD
2204	71	.	D	375
2502	71	448	D	688
2102	71	.	D	547
2501	71	567	D	661
2301	71	574	D	710
2303	71	585	D	757
2105	71	595	S	802
2203	71	616	D	760
2103	71	630	D	704
2302	71	633	D	782
2504	71	.	D	708
2205	71	640	S	803
2505	71	658	S	806
2401	70	665	S	805
2402	70	665	S	805
2404	70	665	S	805
2503	71	.	D	768
2403	70	707	S	805
2405	70	707	S	805
2305	71	.	D	782
2304	71	714	S	806
2201	71	.	D	793
2101	71	.	D	799
2104	71	.	S	802
2202	71	.	S	803

B M 3.75

ID	AFP	T	D	AAD
0701	78	.	S	109
0905	71	366	D	558
0604	71	407	S	809
0603	71	444	S	809
0705	78	463	D	796
0901	71	491	D	661
0903	71	491	D	704
0803	71	491	D	710
0605	71	512	D	708
0602	71	512	D	773
1001	71	.	D	605
0804	71	542	D	773
0801	71	542	S	814
1005	71	553	S	827
0805	71	556	S	814
0702	78	563	S	821
0904	71	570	D	716

0902	71	574	D	659
0802	71	574	S	814
0704	78	581	D	745
0703	78	581	S	821
1004	71	588	S	827
0601	71	.	D	677
1002	71	609	D	708
1003	71	693	S	827

B M 1.87

ID	AFP	T	D	AAD
1801	71	487	S	806
1705	71	494	D	682
1702	71	494	S	807
1805	71	499	D	775
2004	71	553	D	794
2002	71	553	S	817
1803	71	556	D	757
1604	71	563	S	802
1704	71	563	S	807
1901	70	588	D	714
1905	70	588	S	807
1603	71	595	S	802
1903	70	602	D	777
1902	70	.	D	673
2001	71	612	S	817
2003	71	612	S	817
1701	71	616	D	771
1703	71	.	D	696
1602	71	630	S	802
1802	71	644	S	806
1804	71	644	S	806
2005	71	651	S	817
1605	71	665	D	802
1601	71	693	S	802
1904	70	.	S	807

B M 0.94

ID	AFP	T	D	AAD
2801	71	.	D	424
2904	71	.	D	431
2902	71	438	D	645
2705	71	483	S	803
2603	71	532	S	802
2905	71	556	S	806
2703	71	563	D	761
2802	71	564	D	750
2804	71	571	S	809
2805	71	.	D	645
2604	71	577	S	802
2605	71	577	S	802
2704	71	581	D	729
2602	71	595	D	793
2601	71	595	S	802
2901	71	633	S	806
2903	71	644	D	796
2803	71	644	S	809
3003	71	651	D	806
3004	71	651	S	824
2701	71	679	S	803
3001	71	686	D	804
3005	71	686	S	824
2702	71	721	S	803
3002	71	.	S	824

C F 75

ID	AFP	T	D	AAD
0501	71	449	D	738
0104	69	.	D	528
0201	71	501	D	726
0504	71	.	D	600
0402	70	.	D	617
0503	71	.	D	666
0203	71	623	D	768
0401	70	.	D	702
0301	71	.	D	725
0502	71	.	D	736
0205	71	.	D	740
0303	71	672	S	772
0304	71	672	S	772
0305	71	686	S	772
0302	71	.	S	772
0105	69	.	D	785
0102	69	.	D	792
0204	71	.	D	794
0202	71	.	S	800
0505	71	.	S	806
0101	69	.	S	806
0103	69	.	S	806
0403	70	.	S	809
0404	70	.	S	809
0405	70	.	S	809

C F 37.5

ID	AFP	T	D	AAD
1505	71	337	D	575
1202	71	.	D	498
1204	71	519	S	806
1502	71	.	D	613
1203	71	584	D	708
1101	66	584	S	798
1102	66	598	S	798
1503	71	634	D	743
1304	71	.	D	708
1305	71	.	D	708
1105	66	637	S	798
1104	66	.	D	705
1205	71	.	D	728
1405	71	658	S	806
1302	71	.	D	736
1103	66	.	D	748
1501	71	693	S	808
1402	71	700	D	787
1201	71	700	S	806
1404	71	700	S	806
1301	71	707	S	814
1303	71	.	D	782
1403	71	729	S	806
1401	71	.	S	806
1504	71	.	S	808

C F 18.75

ID	AFP	T	D	AAD
2403	71	542	D	726
2402	71	560	S	802
2302	78	.	D	656
2305	78	581	D	680
2401	71	.	D	689
2501	71	.	D	705
2303	78	648	S	807
2505	71	651	S	796
2104	70	.	D	730
2102	70	.	D	732
2202	78	679	S	814
2205	78	679	S	814
2504	71	686	D	801
2103	70	.	D	759
2304	78	.	D	771
2405	71	700	S	802
2301	78	721	S	807

2502	71	.	D	793
2503	71	.	S	796
2404	71	.	S	802
2101	70	.	S	802
2105	70	.	S	802
2201	78	.	S	814
2203	78	.	S	814
2204	78	.	S	814

C M 75

ID	AFP	T	D	AAD
1002	71	.	D	317
0902	71	.	D	554
0802	71	498	S	779
0901	71	.	D	621
0803	71	.	D	631
0903	71	575	D	750
1005	71	588	D	661
0701	69	.	D	678
0603	69	609	D	791
0702	69	609	S	806
0904	71	633	S	772
1003	71	.	S	718
0805	71	679	S	779
0703	69	679	S	806
0804	71	693	S	779
0705	69	702	S	806
0801	71	.	S	779
0601	69	.	S	806
0602	69	.	S	806
0604	69	.	S	806
0605	69	.	S	806
0704	69	.	S	806
1001	71	.	S	809
1004	71	.	S	809
0905	71	.	S	822

C M 37.5

ID	AFP	T	D	AAD
1904	70	484	D	774
1905	70	504	D	749
1802	71	563	D	771
2003	71	588	S	808
1801	71	602	S	800
1703	71	602	S	806
1705	71	.	D	708
1704	71	637	D	792
1605	70	637	S	806
1902	70	637	S	807
1803	71	651	S	800
1903	70	665	S	807
2002	71	665	S	808
1702	71	672	S	806
1602	70	673	S	806
1603	70	675	S	806
2001	71	693	S	808
1604	70	714	S	806
1804	71	721	S	800
1805	71	721	S	800
1701	71	.	D	801
1601	70	736	S	806
1901	70	.	S	807
2004	71	.	S	808
2005	71	.	S	808

C M 18.75

ID	AFP	T	D	AAD
2902	70	.	D	525
2901	70	484	D	704
3001	71	490	D	761
2804	71	518	D	729
2905	70	549	D	778
3003	71	553	S	806
2703	71	595	S	807
2805	71	616	S	807
3004	71	623	D	772
3002	71	.	D	695
2705	71	637	S	807
2802	71	651	S	807
2803	71	.	D	740
2704	71	672	S	807
2801	71	.	D	764
3005	71	693	S	806
2701	71	700	S	807
2601	66	714	S	802
2603	66	714	S	802
2605	66	714	S	802
2702	71	714	S	807
2602	66	.	S	802
2604	66	.	S	802
2903	70	.	S	806
2904	70	.	S	806

D F 75

ID	AFP	T	D	AAD
0203	71	540	D	799
0504	71	.	D	617
0205	71	585	D	757
0404	71	.	D	675
0301	71	633	S	807
0201	71	640	D	765
0403	71	.	D	722
0405	71	658	S	807
0401	71	.	D	738
0303	71	672	S	807
0101	71	695	D	792
0104	71	700	D	803
0202	71	714	S	814
0302	71	.	D	800
0304	71	.	S	807
0305	71	.	S	807
0402	71	.	S	807
0102	71	.	S	808
0103	71	.	S	808
0105	71	.	D	808
0204	71	.	S	814
0501	71	.	S	820
0502	71	.	S	820
0503	71	.	S	820
0505	71	.	S	820

D F 37.5

ID	AFP	T	D	AAD
1401	71	.	D	233
1403	71	.	D	542
1303	71	.	D	652
1305	71	.	D	659
1302	71	.	D	668
1201	71	616	S	800
1405	71	.	D	698
1104	71	637	S	803
1304	71	.	D	715
1503	71	651	S	809
1504	71	.	D	750
1102	71	.	D	785
1502	71	.	D	799
1202	71	.	S	800
1203	71	.	S	800
1204	71	.	S	800
1205	71	.	S	800

1402	71	.	D	801
1101	71	.	S	803
1103	71	.	S	803
1105	71	.	S	803
1301	71	.	S	806
1404	71	.	S	809
1501	71	.	S	809
1505	71	.	S	809

D F 18.75

ID	AFP	T	D	AAD
2201	71	.	D	430
2105	71	.	D	596
2503	71	.	D	659
2202	71	.	D	688
2402	71	.	D	704
2203	71	.	D	710
2504	71	.	D	726
2302	71	.	D	739
2101	71	.	D	745
2205	71	679	D	778
2301	71	.	D	773
2303	71	.	D	789
2502	71	.	D	793
2204	71	.	S	800
2505	71	.	D	800
2102	71	.	S	806
2103	71	.	S	806
2104	71	.	S	806
2501	71	.	S	806
2401	71	.	S	813
2403	71	.	S	813
2404	71	.	S	813
2405	71	.	S	813
2304	71	.	S	815
2305	71	.	S	815

D M 75

ID	AFP	T	D	AAD
0804	78	.	S	240
0905	71	599	S	808
0803	78	602	S	814
0604	71	623	S	807
0705	71	.	D	695
0901	71	.	D	722
1001	71	651	D	787
1004	71	651	S	813
0602	71	661	S	807
0605	71	661	S	807
1005	71	665	S	813
0903	71	672	S	808
0805	78	679	S	814
0704	71	693	S	808
0701	71	707	S	808
0702	71	707	S	808
0904	71	707	S	808
0601	71	.	S	807
0603	71	.	S	807
0801	78	.	S	814
0802	78	.	S	814
0703	71	.	S	808
0902	71	.	S	808
1002	71	.	S	813
1003	71	.	S	813

D M 37.5

ID	AFP	T	D	AAD
1903	70	.	D	99
1705	71	.	D	212
2005	71	.	D	395
1904	70	.	D	588
1802	78	.	D	619
1805	78	581	D	775
1704	71	591	D	757
1701	71	591	S	806
1703	71	591	S	806
1702	71	623	S	806
2001	71	630	S	808
1902	70	.	D	732
1901	70	665	D	795
1801	78	679	S	807
2002	71	.	D	754
1601	71	700	S	808
1603	71	700	S	808
1803	78	.	S	807
1804	78	.	S	807
1905	70	.	S	805
1602	71	.	S	808
1604	71	.	S	808
1605	71	.	S	808
2003	71	.	S	808
2004	71	.	S	808

D M 18.75

ID	AFP	T	D	AAD
2702	71	.	D	656
3005	71	588	S	827
2705	71	595	D	731
2701	71	595	D	766
2703	71	595	D	775
3002	71	612	S	827
2601	71	623	D	799
2802	71	631	D	799
2605	71	661	S	806
2801	71	667	S	814
2704	71	688	S	802
2602	71	700	S	806
2903	70	700	S	807
2901	70	.	D	792
3001	71	722	S	827
2603	71	.	S	806
2604	71	.	S	806
2902	70	.	S	807
2904	70	.	S	807
2905	70	.	S	807
2803	71	.	S	814
2804	71	.	S	814
2805	71	.	S	814
3003	71	.	S	827
3004	71	.	S	827

E F 75

ID	AFP	T	D	AAD
0501	66	.	S	490
0103	70	.	D	555
0205	70	.	D	563
0203	70	.	D	587
1305	60	.	D	589
1005	62	.	D	622
0201	70	.	D	655
1405	60	.	D	652
1402	60	.	D	656
1304	60	.	D	669
0504	66	.	D	675
0102	70	.	D	679
1403	60	.	D	678
0602	66	.	D	718
0904	62	.	D	727
0104	70	.	D	756
1002	62	.	D	756

0105	70	.	D	770
1003	62	.	D	763
0502	66	.	S	802
0503	66	.	S	802
0505	66	.	S	802
0601	66	.	S	802
0603	66	.	S	802
0604	66	.	S	802
0605	66	.	S	802
0101	70	.	S	806
0202	70	.	S	806
0204	70	.	S	806
1301	60	.	S	797
1302	60	.	S	797
1303	60	.	S	797
0901	62	.	S	800
0902	62	.	S	800
0903	62	.	S	800
0905	62	.	S	800
1001	62	.	S	800
1004	62	.	S	800
1401	60	.	S	799
1404	60	.	S	799

F F 15

ID	AFP	T	D	AAD
0201	69	.	D	262
1305	59	.	D	494
0601	65	.	D	557
0102	69	.	D	574
0103	69	.	D	615
1304	59	.	D	640
0203	69	.	D	654
1401	59	.	D	650
0604	65	.	D	688
1302	59	.	D	683
1403	59	.	D	698
1301	59	.	D	699
0204	69	.	D	727
0603	65	.	D	748
0504	65	.	D	775
0602	65	.	D	782
1405	59	.	D	780
0205	69	.	D	801
0501	65	.	S	801
0502	65	.	S	801
0503	65	.	S	801
0505	65	.	S	801

0605	65	.	D	801
0101	69	.	S	805
0104	69	.	S	805
0105	69	.	S	805
0202	69	.	S	805
0901	58	.	S	797
0902	58	.	S	797
0903	58	.	S	797
0904	58	.	S	797
0905	58	.	S	797
1001	58	.	S	797
1002	58	.	S	797
1003	58	.	S	797
1004	58	.	S	797
1005	58	.	S	797
1303	59	.	S	798
1402	59	.	S	798
1404	59	.	S	798

F M 75

ID	AFP	T	D	AAD
1105	63	.	D	246
0401	69	.	D	335
0701	68	.	D	491
0801	68	.	D	491
1505	59	.	D	563
0305	69	.	D	588
1203	63	.	D	609
0805	68	.	D	614
1201	63	.	D	626
1101	63	.	D	637
1202	63	.	D	637
1604	59	.	D	634
0703	68	.	D	646
1104	63	.	D	676
0404	69	.	D	730
1603	59	.	D	725
1601	59	.	D	739
0303	69	.	D	762
1204	63	.	D	765
1502	59	.	D	766
1205	63	.	D	781
0402	69	.	D	804
0702	68	.	S	804
0704	68	.	S	804
0705	68	.	S	804
0802	68	.	S	804
0803	68	.	S	804

0804	68	.	S	804
0301	69	.	S	805
0302	69	.	S	805
0304	69	.	S	805
0403	69	.	S	805
0405	69	.	S	805
1501	59	.	S	796
1503	59	.	S	796
1504	59	.	S	796
1102	63	.	S	801
1103	63	.	S	801
1602	59	.	S	798
1605	59	.	S	798

E M 15

ID	AFP	T	D	AAD
1101	62	.	D	503
1505	67	.	D	634
1501	67	.	D	644
1601	67	.	D	681
0702	66	.	D	691
0803	66	.	D	704
0804	66	.	D	706
1104	62	.	D	723
0703	66	.	D	731
0301	69	.	D	734
1603	67	.	D	735
0405	69	.	D	741
0705	66	.	D	748
1105	62	.	D	757
0701	66	.	D	766
1201	62	.	D	776
1504	67	.	D	800
1502	67	.	S	802
1503	67	.	S	802
1602	67	.	S	802
1604	67	.	S	802
1605	67	.	S	802
0704	66	.	S	802
0801	66	.	S	802
0802	66	.	S	802
0805	66	.	S	802
0302	69	.	S	805
0303	69	.	S	805
0304	69	.	S	805
0305	69	.	S	805
0401	69	.	S	805
0402	69	.	S	805

0403	69	.	S	805	1302	71	.	D	780	0103	69	.	S	807
0404	69	.	S	805	2202	71	.	D	780	0104	69	.	S	807
1102	62	.	S	801	1502	71	.	D	781	0105	69	.	S	807
1103	62	.	S	801	1101	69	.	D	780	1301	71	.	S	809
1202	62	.	S	804	0101	69	.	D	783	1305	71	.	S	809
1203	62	.	S	804	0101	80	.	D	794	0304	71	.	D	809
1204	62	.	S	804	0502	71	.	D	794	0102	80	.	S	818
1205	62	.	S	804	0503	71	.	D	799	0104	80	.	S	818
					2502	71	.	D	800	0105	80	.	S	818
ACETONE F				0	2305	71	.	D	801	1101	80	.	S	818
ID	AFP	T	D	AAD	0401	70	.	S	805	1103	80	.	S	818
					0402	70	.	S	805	1104	80	.	S	818
1304	71	.	D	239	0403	70	.	D	805	1105	80	.	S	818
1201	71	.	D	331	0405	70	.	S	805	2502	71	.	S	814
0204	71	.	D	373	0202	71	.	S	806	2503	71	.	S	814
2403	71	.	D	444	0203	71	.	S	806	2504	71	.	S	814
0302	71	.	D	467	0205	71	.	S	806	0502	71	.	S	816
0404	70	.	D	549	1301	71	.	S	807	0301	71	.	S	817
1304	71	.	D	641	1302	71	.	S	807	0303	71	.	S	817
1102	80	.	D	651	1303	71	.	S	807	0304	71	.	S	817
0501	71	.	D	652	1305	71	.	S	807	0305	71	.	S	817
2203	70	.	D	655	1401	71	.	S	807	2401	71	.	S	820
2303	71	.	D	661	1402	71	.	S	807	2402	71	.	S	820
1105	69	.	D	671	1403	71	.	S	807	2403	71	.	S	820
2404	71	.	D	684	1404	71	.	S	807	2501	71	.	S	821
0203	69	.	D	692	1405	71	.	S	807	2503	71	.	S	821
0201	71	.	D	696	1501	71	.	S	807	2504	71	.	S	821
2304	71	.	D	697	1503	71	.	S	807	2505	71	.	S	821
0504	71	.	D	698	1504	71	.	S	807	2201	71	.	S	823
1503	71	.	D	705	1505	71	.	S	807	2203	71	.	S	823
1403	71	.	D	710	2102	71	.	D	807	2205	71	.	S	823
0103	80	.	D	724	0201	69	.	S	806	2104	71	.	D	827
0402	70	.	D	716	0202	69	.	S	806	2105	71	.	D	827
2404	71	.	D	717	0204	69	.	S	806	2302	71	.	S	827
0501	71	.	D	726	0205	69	.	S	806	0503	71	.	S	828
2505	71	.	D	726	1102	69	.	S	806	0505	71	.	S	828
1104	69	.	D	729	1103	69	.	S	806	2401	71	.	D	828
2501	71	.	D	733	1201	69	.	S	806	2402	71	.	S	828
2305	71	.	D	750	1203	69	.	S	806	2405	71	.	S	828
0504	71	.	D	752	1204	69	.	S	806	2103	71	.	D	829
2405	71	.	D	757	1205	69	.	S	806	2301	71	.	S	835
1202	69	.	D	757	1401	71	.	S	808	2302	71	.	S	835
1204	71	.	D	764	1402	71	.	S	808	2303	71	.	S	835
1405	71	.	D	766	1404	71	.	S	808	2201	70	.	S	835
2204	71	.	D	766	2101	71	.	D	808	2202	70	.	S	835
2304	71	.	D	766	1202	71	.	S	808	2204	70	.	S	835
2301	71	.	D	771	1203	71	.	S	808	2205	70	.	S	835
1303	71	.	D	774	1205	71	.	S	808	2102	71	.	S	837
0505	71	.	D	778	0102	69	.	S	807	2103	71	.	S	837

0302	71	. D	845	
2101	71	. S	849	
2104	71	. S	849	
2105	71	. S	849	
0301	71	. S	855	
0303	71	. D	855	
0305	71	. S	855	
0401	70	. S	855	
0403	70	. S	855	
0404	70	. S	855	
0405	70	. S	855	
1501	71	. S	863	
1502	71	. S	863	
1504	71	. S	863	
1505	71	. S	863	

ACETONE M 0

ID	AFP	T	D	AAD
0804	78	.	D	303
2704	70	.	D	532
0603	66	.	D	544
1703	71	.	D	551
2704	70	.	D	553
1604	66	.	D	560
2001	71	.	D	565
1901	71	.	D	568
1603	66	.	D	573
0905	70	.	D	581
2702	70	.	D	583
1903	71	.	D	589
0904	70	.	D	639
1703	78	.	D	659
1605	66	.	D	665
0905	70	.	D	672
1005	71	.	D	687
1004	71	.	D	689
0602	66	.	D	686
2905	71	.	D	697
1905	71	.	D	701
1601	66	.	D	705
1903	71	.	D	721
0805	71	.	D	743
3003	71	.	D	743
2602	71	.	D	759
2005	71	.	D	759
1003	71	.	D	760
1001	71	.	D	766
1002	71	.	D	771
0903	70	.	D	777
0805	78	.	D	785
0605	66	.	D	777
0703	71	.	D	782
3002	71	.	D	787
2705	70	.	D	787
1605	66	.	D	788
3004	71	.	D	801
0701	71	.	S	802
0702	71	.	S	802
0704	71	.	S	802
0705	71	.	S	802
2004	71	.	D	802
2805	71	.	D	803
0601	70	.	S	806
0602	70	.	S	806
0603	70	.	S	806
0604	70	.	S	806
0605	70	.	S	806
2904	71	.	D	807
1901	71	.	S	807
1902	71	.	S	807
1904	71	.	S	807
2001	71	.	S	807
2002	71	.	S	807
2003	71	.	S	807
1601	66	.	S	803
1602	66	.	S	803
1603	66	.	S	803
1604	66	.	S	803
1902	71	.	S	808
1904	71	.	S	808
1905	71	.	S	808
2002	71	.	S	808
2003	71	.	S	808
2004	71	.	S	808
2005	71	.	S	808
0601	66	.	S	808
0604	66	.	S	808
1602	66	.	S	808
1701	71	.	S	814
1702	71	.	S	814
1704	71	.	S	814
1705	71	.	S	814
0801	78	.	S	823
0802	78	.	S	823
0803	78	.	S	823
0701	71	.	D	821
1701	78	.	D	832
2901	71	.	S	828
2902	71	.	S	828
2903	71	.	S	828
2905	71	.	S	828
3001	71	.	S	828
3003	71	.	S	828
3005	71	.	S	828
3001	71	.	S	828
3002	71	.	S	828
3004	71	.	S	828
3005	71	.	S	828
0901	70	.	S	829
0902	70	.	S	829
0903	70	.	S	829
0705	71	.	D	830
1001	71	.	D	831
1004	71	.	S	834
2801	71	.	S	835
2802	71	.	S	835
2803	71	.	S	835
2804	71	.	S	835
2805	71	.	S	835
2801	71	.	S	835
2802	71	.	S	835
2803	71	.	S	835
2804	71	.	S	835
2901	71	.	S	835
2902	71	.	S	835
2903	71	.	S	835
2904	71	.	S	835
1002	71	.	S	837
1003	71	.	S	837
1005	71	.	S	837
0801	71	.	S	842
0802	71	.	D	842
0803	71	.	S	842
0804	71	.	S	842
1702	78	.	S	851
1704	78	.	S	851
1705	78	.	S	851
2701	70	.	S	847
2703	70	.	S	847
2705	70	.	S	847
0901	70	.	S	847
0902	70	.	S	847
0904	70	.	S	847
2701	70	.	S	847
2702	70	.	S	847
2703	70	.	S	847

2601	71	.	S	856
2602	71	.	S	856
2603	71	.	S	856
2604	71	.	S	856
2605	71	.	S	856
1801	71	.	S	858
1802	71	.	S	858
1803	71	.	S	858
1804	71	.	S	858
1805	71	.	S	858
0702	71	.	S	862
0703	71	.	S	862
0704	71	.	S	862
2601	71	.	S	863
2603	71	.	S	863
2604	71	.	S	863
2605	71	.	S	863
1801	71	.	S	865
1802	71	.	S	865
1803	71	.	S	865
1804	71	.	S	865
1805	71	.	D	865

ACETONE F 0

ID	AFP	T	D	AAD
1002	62	.	D	539
0505	68	.	S	551
1305	67	.	D	606
0501	68	.	D	621
1003	62	.	D	657
1005	62	.	D	672
1403	67	.	D	707
0503	68	.	D	726
0903	62	.	D	722
0602	68	.	D	735
0901	62	.	D	744
0601	68	.	D	755
0504	68	.	S	768
1301	67	.	D	784
1302	67	.	D	784
0205	63	.	D	786
0201	63	.	D	798
0101	63	.	S	802
0102	63	.	S	802
0103	63	.	S	802
0104	63	.	S	802
0105	63	.	S	802
0202	63	.	S	802
0203	63	.	S	802
0204	63	.	S	802
1304	67	739	S	806
1303	67	.	S	806
1401	67	.	S	806
1402	67	.	S	806
1404	67	.	S	806
1405	67	.	S	806
0902	62	.	S	805
0904	62	.	S	805
0905	62	.	S	805
1001	62	.	S	805
1004	62	.	S	805
0502	68	.	S	811
0603	68	.	S	811
0604	68	.	S	811
0605	68	.	S	811

ACETONE M 0

ID	AFP	T	D	AAD
1101	60	.	D	364
0403	66	.	D	549
0303	66	.	D	592
0402	66	.	D	615
1604	66	.	D	622
0802	70	.	D	666
0302	66	.	D	683
0405	66	.	D	691
1503	66	.	D	706
1201	60	.	D	712
0703	70	.	D	728
0705	70	.	D	742
1204	60	.	D	739
0704	70	.	D	749
0805	70	.	D	767
0401	66	.	D	784
1202	60	.	D	789
1105	60	.	D	795
0301	66	.	S	805
0304	66	.	S	805
0305	66	.	S	805
0404	66	.	S	805
1501	66	.	S	805
1502	66	.	S	805
1504	66	.	S	805
1505	66	.	S	805
1601	66	.	S	805
1602	66	.	S	805
1603	66	.	S	805
1605	66	.	S	805
0701	70	.	S	813
0702	70	.	S	813
0801	70	.	S	813
0803	70	.	S	813
0804	70	.	S	813
1102	60	.	S	804
1103	60	.	S	804
1104	60	.	S	804
1203	60	.	S	804
1205	60	.	S	804

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