VII. DATA ANALYSIS

Individual cost estimates submitted for each protocol and statistical analyses and graphic representations of the data for Tier 1 Screens are found in Appendix A and for Tier 2 Tests in Appendix B. These data are summarized in Table 2 for Tier 1 Screens and in Table 3 for Tier 2 Tests. Total costs for the Tier 1 and Tier 2 batteries were calculated using the means of the individual estimates for the assays and tests, respectively. Means rather than median or midpoint values were used because the graphical representation of the data points generally revealed an uneven distribution of the estimates across the range.

A. Analytical Cost Calculations

Analytical cost ranges were requested rather than single estimates to allow the consideration of analytical costs for chemicals that are easily analyzed versus those that are difficult or resource intensive. For this reason, low and high values were used instead of mean values to calculate total costs of the batteries.

Although respondents submitted analytical cost estimate ranges for each Tier 1 Screening assay, Table 2 lists a single cost range assuming one analytical determination for the battery as a whole. This approach assumes that the battery is run simultaneously by the same laboratory and that one analytical verification can suffice for all Tier 1 Screens. Analytical estimates for *in vitro* assays were not considered in listing the low end of the range in Table 2. The Project Director considered it highly unlikely that an analytical procedure sufficient for an *in vitro* assay would suffice for the dose verifications needed for *in vivo* assays.

Table 3 lists the lowest and highest analytical costs estimated for each test, as well as the midpoint between these values. Analytical Costs for Tier 2 Testing were incorporated into the Totals for the Tier 2 Testing Battery by adding to the mean estimate for each test the low analytical estimate or the high analytical estimate for that test.

There is significant uncertainty in the estimation of analytical costs due to different assumptions made by different respondents and to other factors discussed previously. Numerous factors could increase the likely costs of proper analytical determinations for these assays and tests. On the other hand, it would seem that there are few factors that would decrease analytical costs below those listed in this survey. Therefore, the Project Director considers the higher analytical cost estimates to be the more accurate estimates, while acknowledging that these values may underestimate the actual costs.

B. Tier 1 Screening With Required and Optional Endpoints

Some respondents included both EDSTAC's "required" as well as "optional" endpoints in making estimates for the *in vivo* mammalian tier 1 screens. Other respondents included only the required endpoints and analyses. Several respondents provided an estimate of the cost difference between assessing only the required endpoints versus both required and optional endpoints. It was thus possible to formulate two sets of cost estimates for EDSTAC's recommended (T1S 6, 7, 8) and alternative (T1S 11, 12, 13) Tier 1 *in vivo* mammalian screening assays according to the inclusion or exclusion of EDSTAC's optional endpoints (hormone and neurotransmitter levels; histopathology).

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Based on respondents' comments regarding their estimates for these assays and upon a best professional judgement, the Project Director segregated estimates into two subsets for the mammalian *in vivo* Tier 1 assays. Estimates that generally represent only the EDSTAC's "required" endpoints were categorized in "-" subsets for the assays (i.e. 6-, 7-, 8-, 11-, 12-, and 13-). Estimates that generally represent both the required and the optional endpoints were categorized as "+" subsets for the same assays (i.e. 6+, 7+, 8+, 11+, 12+, and 13+). Table 2 Summary of Estimates lists the means and median values for the *in vivo* mammalian Tier 1 assays according to these subset designations. Appendices A and B also list the estimates accordingly. Table 2 Total Costs provides totals for the T1S battery assuming either the required or the required plus optional endpoints in the recommended mammalian *in vivo* assays.

It should be noted that the delineation of "-" and "+" subsets are not entirely distinct. There was variation among respondents as to the endpoints included within the subsets as well. As such, one cannot be certain that these subsets accurately represent differences in cost between the assays with or without optional endpoints or between the "recommended" and "alternative" Tier 1 *in vivo* screens. Nonetheless, APT believes that the division of these data into subsets does provide a relative indication of the increase in expense that might be expected if the optional endpoints are assessed in the *in vivo* mammalian Tier 1 assays.

C. Estimates Not Used

Given the preliminary nature of cost estimates developed for this survey, APT used all of the estimates submitted with only two exceptions. Estimates were not included in the data set for a protocol if two criteria were met: 1) the estimate was outside the range of other estimates by a factor of 4 or more (either 4 times greater than the next highest estimate or less than 25% the next lowest estimate) and 2) the Project Director was able to determine that the estimate was likely to have been due to a misunderstanding of the protocol. Only two such estimates (one estimate for protocol 18 and one for protocol 19) met both criteria and were not used.

VIII. ESTIMATES FROM CONTRACT VERSUS INDUSTRY LABORATORIES

This survey was designed to obtain information from a broad representation of laboratories that may ultimately conduct endocrine screening and testing for regulatory submissions. To ensure a broad representation, laboratories associated with the chemical and pesticide manufacturing industries as well as contract testing laboratories were invited to participate. It is significant to note that the estimates submitted for this survey were interspersed across a range with no delineation possible as to the business sector affiliation of the laboratory. High and low estimates were submitted by both industry and contract laboratories. In general, estimates from individual laboratories were high, low, or in the middle of the range depending upon the particular assay.

Christopher J. Borgert

Christopher J. Borgert, Ph.D.
Project Director

June 19, 1998
Date

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APT

LEGEND FOR STUDY TITLES

1.	T1S:	Rat Estrogen Receptor Equilibrium Exchange Assay
2.	T1S:	Rat Androgen Receptor Equilibrium Exchange Assay
3.	T1S:	MVLN Estrogen Specific Transcription Assay
4.	T1S:	CV1 Transcriptional Activation of Androgen Receptor
5.	T1S:	Steroidogenesis Assay in Minced Testes
6.-	T1S:	Uterotrophic Assay in Ovariectomized Rats; Required Endpoints Only
6.+	T1S:	Uterotrophic Assay in Ovariectomized Rats; + Optional Endpoints
7.-	T1S:	The "Hershberger" Assay in Male Rats; Required Endpoints Only
7.+	T1S:	The "Hershberger" Assay in Male Rats; + Optional Endpoints
8.-	T1S:	Pubertal Assay in Female Rat; Required Endpoints Only
8.+	T1S:	Pubertal Assay in Female Rat; + Optional Endpoints
9.	T1S:	Fish Gonadal Recrudescence Assay
10.	T1S:	Frog Metamorphosis Assay
11.-	T1S	In Vivo Biossay in Female Crl:Cd Br Rats; Required Endpoints Only
11.+	T1S:	In Vivo Biossay in Female Crl:Cd Br Rats;+Optional Endpoints
12.-	T2T	In Vivo Biossay in Adult Male Crl:Cd Br Rats; Required Endpoints Only
12.+	T1S:	In Vivo Bioassay in Adult Male Crl:Cd Br Rats; +Optional Endpoints
13.-	T2T	In Vivo Bioassay Immature Male Crl:Cd Br Rats; Required Endpoints Only
13.+	T1S:	In Vivo Bioassay Immature Male Crl:Cd Br Rats;+Optional Endpoints
14.	T2T:	Two-Generation Reproductive Toxicity Study in Rats
15.	T2T:	Alternative Mammalian Reproduction Test
16.	T2T:	One-Generation Mammalian Reproduction Test
17.	T2T:	Avian Reproductive Toxicity Test
18.	T2T:	Fish Life Cycle Toxicity Test
19.	T2T:	Mysid Toxicity Test
20.	T2T:	Amphibian Reproductive / Developmental Toxicity Test

T1S = Tier 1 Screen

T2T = Tier 2 Test

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TABLE I

Participants in APT's Cost Estimate Survey for Endocrine Disrupter Screening and Testing Batteries

1. ABC Laboratories, Inc.
   Columbia, MO
   G. Scott Ward, Ph.D.
2. Argus Research Laboratories, Inc.
   Horsham, PA
   Robert Parker, Ph.D.
3. Bio-Life Associates, Ltd.
   Neillsville, WI,
   Andrew J. Marias
4. Covance Laboratories, Inc.
   Princeton, NJ
   Larry Ballantine
5. Dow Chemical Company
   Midland, MI
   Edward W. Carney, Ph.D.
6. DuPont Agricultural Products, Haskel Laboratory
   Wilmington, DE
   John C. O'Conner, Ph.D./ Jon Cook, Ph.D.
7. Exxon Chemical Company
   East Millstone, NJ
   Renee Bergeron, Ph.D.
8. Research Triangle Institute (RTI)
   Research Triangle Park, NC
   Patrica A. Fail, Ph.D.
9. Ricerca, Inc.
   Painesville, OH
   Mike Watson
10. Rohm and Haas Company
    Spring House, PA
    Clay B. Frederick, Ph.D.
11. Springborn Laboratories, Inc.,
    Wareham, MA
    Laurie A. Staveski / Joe Siglin, Ph.D./ Ron Biever
12. The Stover Group
    Stillwater, OK
    Douglas Fort, Ph.D.
13. T.R. Wilbury Laboratories, Inc.
    Marblehead, MA
    Timothy J. Ward
14. Wildlife International Ltd.
    Easton, Maryland,
    David L. Palmer / Mark Jaber

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TABLE 2: SUMMARY OF ESTIMATES FOR TIER 1 SCREENING ASSAYS

(In Thousands of Dollars)

*TIER 1 SCREEN	LOW	HIGH	MIDPOINT	MEDIAN	MEAN	N
1. T1S	1.1	26.0	13.6	4.1	7.2	6
2. T1S	1.1	26.0	13.6	4.2	7.3	6
3. T1S	1.8	20.0	10.9	4.9	7.1	6
4. T1S	1.9	20.0	11.0	4.6	7.0	6
5. T1S	6.1	30.0	18.1	7.5	11.6	5
6.- T1S	22.5	40.0	31.3	26	29.6	5
6.+ T1S	40.0	119.2	79.6	67.5	70.1	5
7.- T1S	27.5	52.0	39.8	34.4	37.2	5
7.+ T1S	78.0	129.1	103.6	105.5	100.7	5
8.- T1S	26.0	60.0	43.0	34.7	38.9	5
8.+ T1S	58.0	117.9	88.0	81	86.7	5
9. T1S	12.0	68.0	40.0	40.0	37.8	7
10. T1S	3.0	60.0	31.5	17.0	22.2	8
11.- T1S	14.0	34.0	24.0	18.7	21.3	4
11.+ T1S	40.5	85.7	63.1	63.1	63.1	2
12.- T1S	20.0	38.0	29.0	27.5	27.5	5
12.+ T1S	55.9	107.7	81.8	81.8	81.8	2
13.- T1S	20.0	46.0	33.0	31.9	32.5	6
13.+ T1S	69.5	108.9	89.2	78.0	85.5	3
ANALYTICAL COST RANGE:	$5,400.00 - $30,000.00					

*See Legend for Study Titles

N = number of estimates

Individual cost estimates, statistical analyses and graphic representations of the data for Tier 1 Screens are found in Appendix A.

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