Appendix I-B

A Timetable for the Commercial Production of Compounds Using Genetically Engineered Micro-Organisms in Biotechnology

Objectives

- The estimation of the proportions of various groups of commercial products and processes for which recombinant DNA (rDNA) technology could be applicable.
- The construction of timetables to indicate plausible sequenccs of commercial developments that would result from the application of rDNA technology.

Approaches

The following five industries were evaluated:

1. pharmaceutical,
2. agricultural,
3. food,
4. chemical, and
5. energy .

The manufacturing processes that would result from the application of rDNA technology would be based on fermentation technology, Therefore, a set of parameters was developed to serve as a guide to assess the economics of applying fermentation technology to the manufacture of products currently manufactured by other means.

The chemical industry generates a large number of products that could be attributed to (and is in this study) the other four industries cited, this particular industry was focused on more closely than the others. The following factors were considered in constructing the timetables showing the applicability of rDNA technoloGY:

- the current state of the art of genetic engineering;
- the current economic limitations of fermentat ion technology;
- the length of time to progress from a laboratory process to the pilot plant to large-scale production;
- the plant construction time; and
- the Government regulatory agency approval required (of the products and manufacturing processes, not of the rDNA technology per se).

Sources of information

While much of the information compiled for this report was obtained from published sources, a considerable amount came from prior proprietary studies performed by Genex Corp. In the latter case, information is used that is not proprietary, although the sources must remain confidential. In this connection Genex has had numerous discussions with the technical and corporate management of more than 100 large companies (generally multibillion dollar companies), concerning research interests, product lines, and market trends. Production costs are extrapolated for four fermentation plants of various sizes and capabilities. (See table I-B-1.)

A group of Genex scientists, consisting of a biochemical engineer, two organic chemists, a biochemist, and four molecular geneticists rated the feasibility of devising micro-organisms to produce various chemicals in accordance with the fermentation conditions specified in table I-B-1. For those chemicls that appeared to be capable of being produced microbiologically, dates were assigned for the times when the necessary technology would be achieved in the laboratory. By combining both technical and economic factors, it then became possible to project a timetable for commercial production. (See table I-B-2.)

It should be emphasized that an extremely conservative approach was taken in considering fermentation economics over the next 10 years. only the relatively poor economics of conventional batch fermentation was considered. immobilized cell processes were projected to be 15 years away, and even then, the incremental cost savings projected (see table I-B-1) are lower than the incremental cost savings currently obtained with immobilized cell processes. The assumptions made here, however, did include reasonably high product yields and highly effi-

Table I-B= I.-Unit Cost Assumptions for the Production of Chemicals by Fermentation After Various Intervals of Time

Earliest date (year)	Size of plant (lb)	Type of fermentation	Product yield (%)	Annual c[a] excluding precursor ($ millions)	Unit cost excluding precursor ($/lb)	Precursor	Complete unit cost (W/lb)
5	50	Ordinary batch	12	23.5	0.47	Petrochemical	0.66
10		Ordinary batch	40	24.5	0.25	Petrochemical	0.44
	200	Immobilized cells	40	25.5	0.13	Petrochemical	0.32[d]
20	200	Immobilized cells	40	25.5	0.13	Carbohydrate	0.24[d]

Annual c>sts r >r c rdinary t atch f rmentation v ere e stimated f om r 'oprietary c ata. \ alues c btained f >r t 1e i immobilized ell examples a are omputed a t 3 31.2 ercent below the comparable alues f for ordinary batch fermentation.

Average c>st c f p etrochemical equals $ $0.17/lb. t 9) p percent conversion efficiency, cost contribution of petrochemical quals $0.19/lb c Of prOdUCt.

Average c>st c f c carbohydrate ssumed a at 0.04/lb c of molasses c or 0.02/lb c of cellulose-containing ellets f from biomass esidue. F For 0 p perCent free ugar content c Of molasses, cost of sugar equals 0.08/lb. A At 70 *percent* conversion efficiency from the sugar, cost contribution of molasses equals S0.1 I/lb of product. For 50 percent cellulose content in the biomass pellets, coat of cellulose quals $ $0.04/lb. For 50 percent conversion efficiency to free sugar, followed by 70 percent conversion ffi-ency fi from the sugar, coat contribution of the ellets a also equals $0.1 lb o of product.

These u unit costs maybe further reduced to S0.26 and $0.17/lb., respectively, for products whose annual U.S. production currently exceeds 1 billion lb. ssumptions ii include reduction in precursor cost by 20 percent (presumably because manufacturer controls SUPPlY of precursor); reduction in unit cost of immobilized cell process by 13 percent (d) and 42 percent (e), respectively; maximum of 60 percent product yield (e); and a nearly 100 percent oconversion e efficiency from the petrochemical precursor.

SOURCE: Genex Corp.

Table I- B-2.-Basis for Estimating the Timetable for Manufacture of Chemicals by Means of Microbial Processes

Earliest date for commercial production is:	If all the technology[b] is achieved by:	And if bulk selling prices[c] (in 1979 dollars) equal or exceed:	Assuming unit costs[d] (in 1979 dollars) equal or exceed:
5 years	2 years	$1.32/lb	$0.66/lb
10	7	0.88	0.44
	12	0.64 (0.43)	0.32(0.26)
20	17	0.48 (0.28)	0.24 (0.17)

t is a sumed tlat d development of the appropriate manufacturing cilities gins at at leaat 5 yeare ior tc to the onset of production.

Technology re refers to both genetic and biochemical engineering. Technology ould b be achieved on demonstrating that the chemical could be biologically produced In the laboratory at commercially desirable yields and reaction fi-encies.

is assumed tl at al b bulk lling p prices are arked u up 0 pe rcent fr>m the corresponding unit costs, except for chemicals whose annual U.S. production currently exceeds 1 lion lt lb. In those ses tr the bulk lling p prices (numbers in parentheses) are assumed to be marked up only 67 rcent.

Init c sts were o obtained from table I-B-I. See footnote of table I-1 f for explanation of mbers in in parentheses.

SOURCE: nex C Corp.

cient transformations of precursor to product, but nothing exceptional with respect to current fermentation technology. Indeed, high product yields and highly efficient reactions would be expected with genetically engineered micro-organisms.

Two points should be stressed that place these projections on the low side. First, they exclude certain groups of products, the end products of which could not be microbially processed, although their basic constituents could be produced microbiologically (e.g., monomers of microbial origin could form chemically synthesized polymers). Second, the projections exclude naturally occurring products of microbial origin, which could be effective or superior substitutes for chemically synthesized products that could not he manufactured microbiologically. As examples, dyes of microbial origin, such as prodigiosin, might advantageously replace those synthesized chemically, because their toxicity is lower than their chemical counterparts. In the case of plastics, a new generation of plastics of microbial origin, e.g., pullulans, would not have to be made from petrochemical feedstocks and would be biodegradable.

Explanation of tables

Tables l-B-3 through l-B-32 present the compounds from two points of view. Tables l-B-3 to l-B-lo group the compounds by industry subgrouped by product category. Tables l-B-l 1 to I-B-32 group the compounds by product category irrespective of industry.

The tables based on industry present end use data for each compound; e.g., in the pharmaceutical industry aspirin is listed as an aromatic used as an analgesic, whereas in the chemical industry aniline is listed as an aromatic used as a cyclic intermediate. Thus, the similarities and differences between compounds of similar origin, i.e., product category, are revealed.

The tables based solely on product category are divided into two types; one type pertaining to market data (tables 1-B-lo, 11, and the subsequent odd numbered ones through table l-B-33), and the other pertaining to technical data (the even numbered tables from I-B-12 through l-B-32.)

The market data were obtained both from published sources and from prior proprietary studies

Table I-B-3.—Pharmaceuticals: Small Molecules

Product category	End use
Amino acids	
Phenylalanine	Intravenous solutions
Tryptophan	Intravenous solutions
Arginine	Therapeutic: liver disease and hyperammonemia
Cysteine	Therapeutic: bronchitis and nasal catarrh
Vitamins	
Vitamin E	Intravenous solutions, prophylactic
Vitamin B_{12}	Intravenous solutions
Aromatics	
Aspirin	Analgesic
p-acetaminophenol	Analgesic
Steroid *hormones*	
Corticoids	
Cortisone	Therapeutic: anti-inflammatory agent
Prednisone	Therapeutic: ant i-inflammatory agent
Prednisolone	Therapeutic: anti-inflammatory agent
Aldosterone	Therapeutic: control of electrolyte imbalance
Androgens	
Testosterone	Therapeutic: infertility, hypogonadism, and hypopituitarism
Estrogens	
Estradiol	Prophylactic, therapeutic: vaginitis
Antibiotics	
Penicillins	Control of infectious diseases
Tetracycline	Control of infectious diseases
Cephalosporins	Control of infectious diseases
Short *peptides*	
Glycirie-Histidine-Lysine	Manufacturing processes: tissue culture

SOURCE: Genex Cor

Table I-B-4.—Pharmaceuticals: Large Molecules

Product category	End use
Peptide hormones	
Insulin	Control of diabetes
Endorphins	Analgesics, narcotics, prophylactics
Enkephalins	Analgesics, narcotics, prophylactics
ACTH[a]	Diagnostic: adrenal instability
Glucagon	Therapeutic: diabetes-induced hypoglycemia
Vasopressin	Therapeutic: antidiuretic
Human growth hormone	Therapeutic: dwarfism
Enzymes	
Glucose oxidase	Diagnostic: measurement of blood sugar
Urokinase	Therapeutic: antithrombotic
Asparaginase	Therapeutic: antineoplastic
Tyrosine hydroxylase	Therapeutic: Parkinson's disease
Viral antigens	
Hepatitis viruses	Vaccine
Influenza viruses	Vaccine
Herpes viruses	Vaccine
Varicella virus	Vaccine
Rubella virus	Vaccine
Reoviruses	Vaccine: common cold
Epstein-Barr virus	Vaccine: infectious mononucleosis, nasopharyngeal carcinoma, Burkitt lymphoma
Miscellaneous proteins	
Interferon	Control of infectious diseases
Human serum albumin	Therapeutic: shock and burns
Monoclinal antibodies	Diagnostics: hepatitis, cancer, etc; therapeutics
Gene preparations	
Sickle-cell anemia	Control of hereditary disorder
Hemophilias,	Control of hereditary disorder
Thallasemias	Control of hereditary disorder

[a]Adrenocorticotrop hormone.

SOURCE: Gene Corp.

performe I b Gene In the latter case, data are use that are no proprietary although the sources must remai confidentia Market values were estimated b multiplyin the market volum (total amount of product sold in 1979) by the bulk cost (unit bul selling price in 1 980). Excep fo aromatics an aliphatic a market dat represent worldwide estimates. Mark data fo aromatics and aliphatic are restricte to the 1 Unite States. Data that could not be found wer marked not available (N/A). Compound wh high market valu were identified, and those that coul be produce biologically were selecte fo this report.

Hig market values wor relativ to the industr 1111(1 end list i tin each compound. For exampl wh respe to chemicals, normal on cyclic i-termediate with production volumes (which diffe fro market volumes) exceeding 5 million lb were selected, b in the case of flavor and perfume material compounds with production values generally exceeding million lb were selected. In the case of many pharmaceuticals, clinical importance was weighed heavily in their selection process.

The technical data were also obtained both from published and proprietary sources. Wit respect to the timetable fo commercial production, the stated lengh oft tim is the t i me required to develo existin technolog (including both genetic and biochemica engineering) to the point w'here it ma he applied to appropriat man ufact urin faci li t itie fo the larg scale produ ion o the desired compounds. These tim intervas shoul be sufficient fo undertaking

Table I-B-5.—Food Products

Product category	End use
Amino acids	
Glutamate	Food enrichment agent, flavoring agent
Cysteine	Food enrichment agent, manufacturing processes
Aspartame	Flavoring agent
Vitamins	
Vitamin C	Food additive, food enrichment agent
Vitamin D	Food enrichment agent
Aromatics	
Benzoic acid	Food preservative
Aliphatics	
Propionic acid	Food preservative
Short peptides	
Aspartame	Artificial sweetener
Enzymes	
Rennin	Manufacturing processes
Amyloglucosidase	Manufacturing processes
a-amylase	Food enrichment agent, manufacturing processes
Glucose isomerase	Manufacturing processes: sweetener
Nucleotides	
5'-IMP[a]	Flavoring agent
5'-GMP[b]	Flavoring agent

[a]5'-inosinic acid.
[b]5'-guanylic acid.

SOURCE: Genex Corp.

Table I-B-6.—Agricultural Products

Product category	End use
Amino acids	
Lysine	Feed additive
Methionine	Feed additive
Threonine	Feed additive
Tryptophan	Feed additive
Vitamins	
Nicotinic acid	Feed additive
Riboflavin (B_2)	Feed additive
Vitamin C	Feed additive
Aliphatics	
Sorbic acid	Feed preservative
Antibiotics	
Penicillins	Feed additive, prophylactic
Erythromycins	Feed additive, prophylactic
Peptide hormones	
Bovine growth hormone	Growth promoter
Porcine growth hormone	Growth promoter
Ovine growth hormone	Growth promoter
Viral antigens	
Foot-and-mouth disease virus	Vaccine
Rous sarcoma virus	Vaccine
Avian leukemiavirus	Vaccine
Avian myeloblastosis virus	Vaccine
Enzymes	
Papain	Feed additive
Glucose oxidase	Feed preservative
Pesticides	
Microbial	Insecticide
Aromatic	Insecticide
Inorganic	
Ammonia	Fertilizer

SOURCE: Genex Corp.

all the R&D starting from the current knowledge base necessary to demonstrate that the desired compounds can be biologically produced first in the laboratory and then in the pilot plant at commercially desirable yields and reaction efficiencies. The timetable does not consider delays caused by construction of new facilities nor delays required to obtain Government regulatory approval of new products.

It should be noted that in the technical data charts, when glucose is listed as an alternate precursor by fermentation, other carbohydrates, e.g., cellulose and cornstarch, could be used. Moreover, if glucose were the precursor of choice, the actual feedstock would probably be a commodity like molasses as opposed to pure glucose.

Summary

Over 100 compounds representing 17 different product categories that span the five industries under evaluation are represented in table I-B-10. The current market value of all these products exceeds $27 billion. One particular compound, methane, accounts for over $12 billion. The even-numbered tables from 1-B-12 to I-B-32 project that within 20 years all these products could be manufactured using genetically engineered microbial strains on a more economical basis than using today's conventional technologies. In many cases, the time required to apply genetically engineered strains in commercial fermentations could be reduced to as little as 5 years.

The impact of genetic engineering on selected markets is shown in table I-B-33. only five product categories are considered here, and in one, amino acids, only a few of the compounds comprising it are evaluated. The products represented in the five categories currently have a total market value exceeding $800 million. However, within 20 years this market value could rise to over $5 billion (in 1980 dollars) due largely to the application of genetic engineering. In a number of cases, the desired products would most likely not be available in significant quantities if not for the application of genetic engineering technology.

Table I- B-7.—Chemicals: Aliphatics

Compound	End use
Acetic acid[a]	Miscellaneous acyclic
Acrylic acid[a]	Miscellaneous acyclic
Adipic acid[a]	Misceilaneous acyclic
Bis (2-ethylhexyl) adipate	Plasticizer
Citronella	Flavor/perfume material
Citronellol	Flavor/perfume material
Ethanol[a]	Miscellaneous acylic
Ethanolamine	Miscellaneous acyclic
Ethylene glycol[a]	Miscellaneous acyclic
Ethylene oxide[a]	Miscellaneous acyclic
Geraniol	Flavor/perfume material
Glycerol[a]	Miscellaneous acyclic
Isobutylene	Miscellaneous acyciic, flavor/perfume material
Itaconic acid	Plastics/resin
Linalool	Flavor/perfume material
Linalyl acetate	Flavor/perfume material
Methane	Primary petroleum product
Nerol	Flavor/perfume material
Pentaerythritol	Miscellaneous acyclic
Propylene giycol[a]	Miscellaneous acyiic
Sorbitol	Miscellaneous acyclic
a-terpineol	Flavor/perfume material
a-terpinylacetate	Flavor/perfume material

[a]Indicates compounds also identified by the Massachusetts Institute of Technology. The following additional chemicals were identified by MIT as amenable to biotechnological production methods: acetaldehyde, acetoin, acetone, acetylene, acrylic acid, butadiene, butanol, butyl acetate, butyraldehyde, dihydroxyacetone, ethyl acetate, ethyl acrylate, ethylene, formaldehyde, isoprene, isopropanol, methanol, methyl ethyl ketone, methyl acrylate, propylene, propylene oxide, styrene, vinyl acetate.

SOURCE: Genex Corp. and the Massachusetts Institute of Technology.

Table I-B-8.—Chemicals: Aromatics and Miscellaneous

Product category	End use
Aromatics	
Aniline	Cyclic intermediate
Benzoic acid	Cyclic intermediate
Cresols	Cyclic intermediate
Phenol	Cyclic intermediate
Phthalic anhydride	Cyclic intermediate
Cinnamaldehyde	Flavor/perfume material
Diisodecyl phthalate	Plasticizer
Dioctyle phthalate	Plasticizer
Inorganic	
Ammonia	Manufacturing processes
Hydrogen	Manufacturing processes
Enzymes	
Pepsin	Manufacturing processes
Bacillus protease	Manufacturing processes
Mineral leaching	
Transition metals (cobalt, nickel, manganese, iron)	Inorganic intermediates; catalysts
Biodegradation	Removal of organic phosphates, aryl sulfonates, and haloaromatics

SOURCE: Genex Corp.

Table I- B-9.—Energy Products

Product category	End use
Enzymes	
Ethanol dehydrogenase	Manufacturing processes
Hydrogenate	Manufacturing processes
Biodegradation	Petroleum byproducts removal
Aliphatics	
Methane	Fuel
Ethanol	Fuel
Inorganic	
Hydrogen	Fuel
Mineral leaching	
Uranium	Fuel

SOURCE: Genx Corp.

Table I- B- 10.—Total Market Values for the Various Product Categories

Product category	Number of compounds	Current value ($ millions)
Amino acids	9	$ 1,703.0
Vitamins	6	667.7
Enzymes	11	217.7
Steroid hormones	6	376.8
Peptide hormones	9	263.7
Viral antigens	9	N/A
Short peptides	2	4.4
Nucleotides	2	72.0
Miscellaneous proteins	2a	300.0
Antibiotics	4[b]	4,240.0
Gene preparations	3	N/A
Pesticides	2[b]	100.0
Aliphatics:		
Methane		12,572.0
Other	24[c]	2,737.5
Aromatics	10[c]	1,250.9
Inorganic	2	2,681.0
Mineral leaching	5	N/A
Biodegradation	N/A	N/A
Totals	107	$27,186.7[d]

[a]Only two of a number of compounds are considered here.
[b]These numbers refer to major classes of compounds; not actual numbers of compounds.
[c]These numbers refer only to those compounds representing the largest market volume in classes specified in the text.
[d]Current value excluding methane = $14,614,700,000

SOURCE: Genex Corp.

Table I-B-11.-Amino Acids: Market Information

	Current market data		
Compound	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Arginine	900	12.73	11.46
Aspartate	3,000	2.86	8.6
Cysteine.	600	22.75	13.6
Glutamate.	600,000	1.80	1,080.0
Lysine	129,000	2.10	258.0
Methionine.	210,000	1.40	294.0
Phertylalanine. . . .	300	38.18	11.46
Threonine.	300	58.18	16.2
Tryptophan.	225	43.18	9.71

SOURCE: Compiled by Genex Corp. from data in references 1,2, and 3.

Table I-B-12.—Amino Acids: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Arginine	fermentation	glucose and NH_4^+[a]	renewable		5 yrs.
Aspartate	fermentation	fumaric acid and ammonia	limited		5 yrs.
Cysteine	extraction	protein hydrolysis	renewable		5 yrs.
Glutamate.	fermentation	glucose and NH_4^+	renewable		5 yrs.
Lysine.	fermentation	glucose and NH_4^+	renewable		5 yrs.
Methionine.	chemical	B-methylmercapto proplonaldehyde	nonrenewable	glucose and NH_4^+	10 yrs.
Phenylalanine. . . .	chemical	a-acetamino-cinnamic acid	limited	glucose and NH_4^+	5 yrs. 5 yrs.
Threonine.	fermentation	glucose and NH_4^+	renewable		5 yrs.
Tryptophan.	chemical	a-ketoglutaric phenylhydrazone	nonrenewable	glucose and NH_4^+	5 yrs.

[a]Ammonium ion.

SOURCE: Compiled by Genex Corp. from data in references 2,3,4, and 5

Table I- B-13.-Vitamins: Market Information

	Current market data		
Compound	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Nicotinic acid. . . .	1,400	1.82	2.5
Riboflavin (B_2). . . .	22	15.40	0.34
Vitamin B_{12}		6,991.60	153.8
Vitamin C	90,0%	4.50	405.0
Vitamin D	12	42.50	0.51
Vitamin E	3,641	29.00	105.6

SOURCE: Compiled by Genex Corp. from data in references 1,6,7,8, and 9.

Table I- B-14.—Vitamins: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Nicotinic Acid . . .	chemical	aikyl a-subst.	nonrenewable	glucose and NH_4^{+a}	10 yrs.
Riboflavin (B_2). . . .	fermentation	pyridines glucose	renewable	—	10 yrs.
Vitamin B_{12}	fermentation	carbohydrates	renewable	—	10 yrs.
Vitamin C	semisynthetic	glucose or sorbitol	renewable		10 yrs.
Vitamin D	fermentation	glucose	renewable	glucose	10 yrs.
Vitamin E	extraction	wheat germ oil	limited	glucose	15 yrs.

[a]Ammoniur ion,

SOURCE: Compiled by Gene Corp. from data in references 4,7,8, 10,11, and 12.

Table I-B-1 5.—Enzymes: Market Information

Compound	Current market data: Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
a-amylase. , ...	600	19.33	11.6
Amyloglucosidase	600		
Asparaginase. . . .	(Information not available)		
Bacillus protease.	1,000	8.28	8.2
Ethanol dehydrogenase .	(Information not available)		
Glucose isomerase	100	40000	400
Glucose oxidase .			0.80
Hydrogenate	(Iformation not available)		
Papain.	200	59.00	11.8
Pepsin.	10	360.00	3.8
Rennin.	24	696.00	40.0
Tyrosine hydroxylase	(Information not available)		
Urokinase.		60,000 IU[a]	89.5

[a]I : internation units.

SOURCE: Compiled by Genex Corp. from data in references 9,13,14,15, and 16.

Table I- B-16.-Enzymes: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
a-amylase.	fermentation	molasses	renewable		5 yrs.
Amyloglucosidase	fermentation	molasses	renewable		5 yrs.
Asparaginase. . . .	extraction	tissue culture	renewable	glucose and NH_4^+	5 yrs.
Bacillus protease.	fermentation	molasses	renewable		5 yrs.
Ethanol dehydrogenase		(Information not available)		glucose and NH_4^+	10 yrs.
Glucose isomerase.	fermentation	glucose and NH_4^{+a}	renewable		5 yrs.
Glucose oxidase .	fermentation	molasses	renewable		5 yrs.
Hydrogenate		(Information not available)		glucose and NH_4^+	10 yrs.
Papain.	extraction	papaya	renewable	glucose and NH_4^+	5 yrs.
Pepsin.	fermentation	molasses	renewable		5 yrs.
Rennin.	fermentation	molasses	renewable		5 yrs.
Tyrosine	extraction	tissue culture	renewable	glucose and NH_4^+	5 yrs.
Urokinase.	extraction	tissue culture	renewable	glucose	5 yrs.

Ammonium i ion.

SOURCE: Compiled by enex Corp. from data in references 4,5,13,14,16,17, and 18.

Table I=B=17.-Sterold Hormones: Market information

	Current market data		
Compound	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Corticoids. . . . •. .			305.8
Cortisone	N/A	208.84	N/A
Prednisone.	N/A	467.62	N/A
Prenisolone	N/A	463.06	N/A
Aldosterone	N/A	N/A	N/A
Androgens			10,8
Testosterone	(Information not available)		
Estrogens.			60.2
Estradiol	(Information not available)		

SOURCE: Compiled by Genex Corp. from data In references 1 and 4.

Table I-B-18.—Steroid Hormones: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Corticoids					
Cortisone					
Prednisone.	semisynthetic	diosgenin or stigmasterol	renewable	glucose	10 yrs.
Predisolone					
Aldosterone					
Androgens					
Testosterone	semisynthetic	chemical modification of cholesterol	renewable	glucose	10 yrs.
Estrogens					
Estradiol	semisynthetic	chemical modification of cholesterol	renewable	glucose	10 yrs.

SOURCE: Compiled by Genex Corp. from data in references 4,19,20,21, and 22.

Table I- B-19.—Peptide Hormones: Market Information

	Current market data		
Compound	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
ACTH[a].	N/A	N/A	5.6
Bovine growth hormone.	0.0		0.0
Endorphins.	(Information not available)		
Enkephalins	(Information not available)		
Glucagon	(Information not available)		
Human growth hormone.	N/A	N/A	75.0
Insulin.	N/A	N/A	163.1
Ovine growth hormone.	0.0	0.0	0.0
Porcine growth hormone.	0.0		0.0
Vasopressin.	(Information not available)		

[a]Adrenocorticotrop hormone.

SOURCE: Compiled by Genex Corp. from data in reference 4.

Table I- B-20.-Peptide Hormones: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
ACTH[a]	extraction	adrenal cortex	limited	glucose and NH_4^+[b]	5 yrs.
Bovine growth hormone.	extraction	anterior pituitary	limited	glucose and NH_4^+	5 yrs.
Endorphins.	extraction	brain	limited	glucose and NH_4^+	5 yrs.
Enkephalins.	extraction	brain	limited	glucose and NH_4^+	5 yrs.
Glucagon	extraction	pancreas	limited	glucose and NH_4^+	5 yrs.
Human growth hormone.	extraction	anterior pituitary	limited	glucose and NH_4^+	5 yrs.
Insulin.	extraction	pancreas	limited	glucose and NH_4^+	5 yrs.
Ovine growth hormone.	extraction	anterior pituitary	limited	glucose and NH_4^+	10 yrs.
Porcine growth hormone.	extraction	anterior pituitary	limited	glucose and NH_4^+	10 yrs.
Vasopressin.	extraction	posterior pituitary	limited	glucose, and NH_4^+	5 yrs.

[a]Adrenocorticotropic h hormone.
[b]Ammonium ic ion.
SOURCE: Compiled by enex C Corp. from data in references 4,23, and 24.

Table I- B-21.—Vjral Antigens: Market Information

Compound	Current market data: Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Avian leukemia virus.	(Information not available)		
Avian myeloblastosis virus.	(information not available)		
Epstein-Barr virus	0.0	0.0	0.0
Hepatitis virus . . .	0.0	0.0	0.0
Herpes virus.	0.0	0.0	0.0
Hoof and mouth disease virus . .	0.0		
influenza virus . . .	(Information not available)		
Reoviruses	0.0	0.0	0.0
Rous sarcoma virus.	(Information not available)		
Rubella virus.	(Information not available)		
Varicella virus . . .	(information not available)		

SOURCE: Compiled by Genex Corp. from data in reference 4.

Table I-B-22.—Viral Antigens: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Avian leukemia virus		(Information not available)		glucose and NH_4^+ [a]	5 yrs.
Avian myeloblastosis virus		(Information not available)		glucose and NH_4^+	5 yrs.
Epstein-Barr virus	tissue culture	lymphoblasts	renewable	glucose and NH_4^+	5 yrs.
Hepatitis viruses		(Information not available)		glucose and NH_4^+	5 yrs.
Herpes viruses		(Information not available)		glucose and NH_4^+	5 yrs.
Hoof and mouth disease virus		(Information not available)		glucose and NH_4^+	5 yrs.
Influenza viruses		(Information not available)		glucose and NH_4^+	10 yrs.
Reoviruses		(Information not available)		glucose and NH_4^+	15 yrs.
Rous sarcoma virus		(Information not available)		glucose and NH_4^+	5 yrs.
Rubella virus	tissue culture	duck embryonic cells	renewable	glucose and NH_4^+	5 yrs.
Varicella virus		(Information not available)		glucose NH_4^+	5 yrs.

[a]Ammonium ion.

SOURCE: Compiled by [illegible] Corp. from data in references 4 and 25.

Table I-B-23.—Short Peptides, Nucleotides, and Miscellaneous Proteins: Market Information

	Current market data		
Product category	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Short peptides[a]			
Aspartame	40	110.00	4.4
Glycine-histidine-lysine	(Information not available)		
Nucleotides[b]			
5'-IMP [c]	4,000	12.00	48.0
5'-GMP [d]	2,000	12.00	24.0
Miscellaneous proteins[a]			
Interferon	N/A	N/A	50.0
Human serum albumin	250	1,000.00	250.0
Monoclinal antibodies	(Information not available)		

[a]Da[illegible] from references 4 and [illegible]
[b]D[illegible] from references 4 and 27.
[c]5'-inosi[illegible] acid.
[d]5'-guany[illegible] acid.
'Data from reference 4.

SOURCE: Compiled by [illegible] Corp.

Table I- B-24.—Short Peptides, Nucleotides, and Miscellaneous Proteins: Technical information

Product category	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Short peptides[a]					
Aspartame	chemical	phenylalanine & aspartic acid	renewable	glucose and NH_4^+	5 yrs.
Glycine-histidine-lysine.	extraction	human serum	renewable	glucose and NH_4^+	5 yrs.
Nucleotides[c]					
5'-IMP[d].	extraction	yeast	renewable	glucose and NH_4^+	10 yrs.
5'-GMP[e].	extraction	yeast	renewable	glucose and NH_4^+	10 yrs.
MIscellaneous proteins[f]					
Interferon	extraction or tissue culture	leukocytes, lymphoblasts, or fibroblasts	renewable	glucose and NH_4^+	5 yrs.
Human serum albumin	extraction	human serum	renewable	glucose and NH_4^+	5 yrs.
Monoclinal antibodies	somatic cell hybridization	various cells	renewable	glucose and NH_4^+	10 yrs.

[a]Data from reference 4 and 27.
[b]Ammonium ion.
[c]Data from references 4 and [illegible].
[d]5'-inosinic acid.
[e]5'-guanylic acid.
[f]Data from reference 4.

SOURCE: Compiled by [illegible]enex C Corp.

Table I- B-25.-Antibiotics, Gene Preparations, and Pesticides: Market information

Product category	Current market data: Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Antibiotic@			
Penicillins.	49,300	22.11	1,080.0
Tetracycline.	29,300	34.13	1,000.O
Cephalosporins. .	4,210	114.00	460.0
Erythromycins . . .	(Information not available)		
Gene preperations[b]			
Sickle cell anemia	0.0	0.0	0.0
Hemophilias.			0.0
Thallasemias	0.0	0.0	0.0
Pesticides[c]			
Microbial.	N/A	N/A	25.0
Aromatics	N/A	N/A	75.0

[a]Data from references 4,28, and 9.
[b]Data from references 4 and [illegible].
[c]Data from references 4 and [illegible].

SOURCE: Compiled by [illegible]enex C Corp.

Table I- B-26.—Antibiotics, Gene Preparations, and Pesticides: Technical Information

Product category	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Antibiotics					
Penicillins.	fermentation semisynthetic	lactose & nitrogenous oils	limited		10 yrs.
Tetracycline . .	fermentation	lactose & nitrogenous oils	limited	—	10 yrs.
Cephalosporins .	fermentation	lactose & nitrogenous oils	limited		10 yrs.
Erythromycins .	fermentation	lactose & nitrogenous oils	limited		10 yrs.
Gene preprations[b]					
Sickle cell anemia		(No process exists currently)		glucose and NH_4^{+}[d]	15 yrs.
Hemophilias.		(No process exists currently)		glucose and NH_4^{+}	20 yrs.
Thallasemias		(No process exists currently)		glucose and NH_4^{+}	20 yrs.
Pestlcides[c]					
Microbial.	fermentation	molasses & fishmeal	renewable		5 yrs.
Aromatics.	semi synthetic	naphthalene	nonrenewable	—	10 yrs.

[a]Dat from references 4,5,28, 3, an d 3
[b]Dat from reference 4.
[c]Dat from references 4 and d 3
[d]Ammonium ion.

SOURCE: Compiled by Gene Corp.

Table I= B-27. -Aliphatics: Market Information

Compound	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
	Current market data		
Acetic acid	823,274	0.23	189.4
Acrylic acid.	46,503	0.43	20.0
Adipic acid	181,097	0.50	90.5
Bis (2-ethylehexyl) adipate	43,015	0.49	21.1
Citronella	394	3.90	
Citronellol.	1,443	4.50	6.5
Ethanol	1,048,000	0.24	251.5
Ethanolamine. . . .	320,236	0.46	147.3
Ethylene glycol . .	3,137,000	0.31	972.5
Ethylene oxide . . .	525,113		189.0
Geraniol	2,307	3.25	7.5
Glycerol	116,612	0.54	63.0
Isobutylene.	597,712	0.95	567.2
Itaconic acid.	200	0.83	0.2
Linalool.	3,341	2.60	8.7
Linalyl acetate . . .	1,535	3.50	5.4
Methane	878,000,000	0.013	11,573.0
Nerol.	462	4.20	1.9
Pentaerythritol. . .	117,085	0.62	72.6
Propionic acid . . .	62,848	0.21	13.2
Propylene glycol .	525,527	0.73	173.4
Sorbic acid	20,000	2.15	43.0
Sorbitol.	160,267	0.36	57.7
a-terpineol	2,416	1.28	3.0
a-terpinyl acetate.	1,066	1.30	1.4

SOURCE: Compiled by Gen Corp. from data in references 1,4,9, and 33.

Table I- B-28.—Aliphatics: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain[b]
Acetic acid.	chemical	methanol or ethanol	nonrenewable	glucose	10 yrs.
Acrylic acid	chemical	ethylene	nonrenewable	glucose	10 yrs.
Adipic acid.	chemical	phenol	nonrenewable	glucose	10 yrs.
Bis (2-ethylhexyl). . . . adipate	chemical	phenol	nonrenewable	glucose	20 yrs.
Citronella	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Citronellol	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Ethanol.	chemical	ethylene	nonrenewable	glucose	5 yrs.
Ethanolamine	chemical	ethylene	nonrenewable	glucose	10 yrs.
Ethylene glycol	chemical	ethylene	nonrenewable	glucose	5 yrs.
Ethylene oxide.	chemical	ethylene	nonrenewable	glucose	5 yrs.
Geraniol	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Glycerol	chemical	soap manuf.	nonrenewable	glucose	5 yrs.
Isobutylene	chemical	petroleum	nonrenewable	glucose	10 yrs.
Itaconic acid	fermentation	molasses	renewable	...	5 yrs.
Linalool	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Linalyl acetate	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Methane.	chemical	natural gas	nonrenewable	sewage	10 yrs.
Nerol.	chemical	isobutylene	nonrenewable	glucose	20 yrs.
Pentaerythritol	chemical	acetaldehyde & formaldehyde	nonrenewable	glucose	10 yrs.
Propionic acid	chemical	ethanol & carbon monoxide	limited	glucose	10 yrs.
Propylene glycol	chemical	propylene	nonrenewable	glucose	10 yrs.
Sorbic acid.	chemical	crotonaldehyde & malonic acid	nonrenewable	glucose	15 yrs.
Sorbitol.	chemical	glucose	renewable		10 yrs.
a-terpineol	chemical	isobutylene	nonrenewable	glucose	20 yrs.
a-terpinyl acetate . . .	chemical	isobutylene	nonrenewable	glucose	20 yrs.

Vherever gl glucose m mentioned, other carbohydrates maybe ıbstituted, ir including starch and cellulose.
n m any cases tr ese ti nes ar are ısed o on more readily developed fermentations using nonrenewable or limited hydrocarbons as Precursors.

SOURCE: ompiled b by Genex Corp. from data in references 4,33,34, and 35.

Table I= B-29.-Aromatics: Market Information

Compound	Current market data: Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Aniline	187,767	0.42	78.9
Aspirin	32,247	1.41	45.5
Benzoic acid	36,822	0.47	17.3
Cinnamaldehyde. . . .	1,098	2.10	3.4
Cresols.	94,932	0.54	51.2
Diisodecyl phthalate	151,319	0.42	63.6
Dioctyl phthalate. . . .	391,131	0.42	164.3
p-acetaminophenol. .	20,000	2.65	53.0
Phenol	1,431,000	0.36	515.2
Phthalic anhydride . .	646,289	0.40	258.5

SOURCE: Compiled by Genex Corp. from data in references 1 and 9.

Table I- B-30.-Aromatics: Technical Information

Compound	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Aniline	chemical	benzene	nonrenewable	aromatic[a]	10 yrs.
Aspirin	chemical	phenol	nonrenewable	aromatic	5 yrs.
Benzoic acid	chemical	tar oil	nonrenewable	aromatic	10 yrs.
Cinnamaidehyde. . . .	chemical	benzaldehyde acetaldehyde	nonrenewable	aromatic	20 yrs.
Cresols.	chemical	phthalic an hydride	nonrenewable	aromatic	10 yrs.
Diisodecyl . . . . phthalate	chemical	coal tar	nonrenewable	aromatic	20 yrs.
Dioctyl . . . . phthalate	chemical	coal tar	nonrenewable	aromatic	20 yrs.
p-acetaminophenol. .	chemical	nitrobenzene	nonrenewable	aromatic	5 yrs.
Phenol	chemical	coal tar	nonrenewable	aromatic	10 yrs.
Phthalic . . . . anhydride	chemical	coal tar	nonrenewable	aromatic	15 yrs.

[a]Aromat[illegible] refe[illegible] t. benzene or benzene derivative. Eventually it [illegible] anticipated that [illegible] lign[illegible] a renewable resourc[illegible] would [illegible] as a Precursor.

SOURCE: Compiled by Genex Corp. from data in references 4 and 35.

Table I-B-31 .—Inorganics and Mineral Leaching: Market Information

	Current market data		
Product category	Market volume 1,000 lb	Bulk cost $/lb	Market value ($ millions)
Inorganic			
Ammonia	33,400,000	0.06	2,004.0
Hydrogen	451,000	0.15	677.0
Mineral leaching			
Uranium	(Information not available)		
Transition metals. (cobalt, nickel, manganese, iron)	(Information not avaiiable)		

SOURCE: Compiled by Genex Corp. from data in reference 4.

Table I- B-32.-Inorganics and Mineral Leaching: Technical Information

Product category	Typical synthetic process	Typical precursor	Is precursor renewable/non-renewable limited	Alternate precursor by fermentation	Time to implement commercial fermentation by genetically engineered strain
Inorganic					
Ammonia	chemical	water and coke	nonrenewable	nitrogen(air)	15 yrs.
Hydrogen	catalytic reforming	petroleum	nonrenewable	water and air	15 yrs.
Mineral leaching					
Uranium		(Information not available)			
Transition metals. (cobalt, nickel, manganese, iron)		(Information not available)			

SOURCE: Compiled by Genex Corp. from data in references 4 and 35.

Table I- B-33.-Projected Growth of Selected Markets Involving Applications of Genetic Engineering

Product category	Current market $ millions	Projected market in 20 yrs. $ millions
Amino acids[a]	300	[illegible]
Miscellaneous proteins.	300	1,000
Gene preparations	0	
Short peptides	5	2,100
Peptide hormones		
Totals	865	5,100

[a]Only f[illegible] four amino acids are considered here.
SOURCE: [illegible] Corp.

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