EXHIBIT F

Erythropoeitin

Management Report

F. Lin, Product Development Team Leader

May 21,1984

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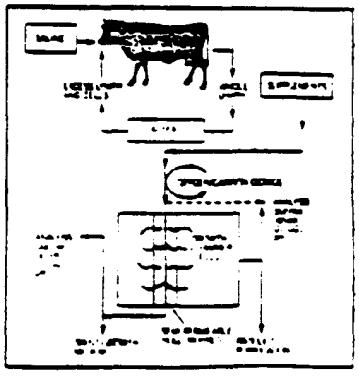

Product Development Team
Quarterly Report

PROGRESS LAST QUARTER

PRODUCT: EPO TEAM LEADER: F. K. Lin DATE: 5/21/84

		Responsibility	Deadline	Date Completed
1.	Mammalian Cell Expression			
1.1	Complete sequence of gene	S.S.	3/30	3/20
1.2	Construct DHFR expression Vector & transform CHO cells	J.B./R.S.	4/15	5/01
1.3	Express monkey EPO at 1ug/ml	J.B./R.S.	5/15	5/10
2.	E.coli Expression			
2.1	Complete synthesis of E.coli gene	A.B./E.L. M.P./S.S.	3/20	3/15
2.2	Sequence synthetic E.coli gene segments	S.S.	3/30	3/15
2.3	Assemble gene segments together and sequence	S.S.	4/15	4/19
2.4	Express EPO in E.coli at ≥1% of cell protein	F.K./S.S.	5/01	4/24
3.	Yeast Expression			
3.1	Complete synthesis of yeast gene	A.B./E.L./ M.P./S.S.	4/01	3/20
3.2	Sequence synthetic yeast gene	S.S.	4/15	5/01
3.3	Assemble gene in expression vector	S.E.	5/07	5/07

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Product Development Team
Quarterly Report:

PROGRESS LAST QUARTER (cont'd)

ACHIEVEMENTS LAST QUARTER:

1. Synthetic EPO gene for E.coli and yeast were completed as planned.

2. Synthetic E.coli EPO gene was tested in 6 different expression systems and expressed at ~5% of the total cell protein.

3. Yeast EPO were cloned into α-factor expression vector.

4. Monkey EPO in CHO, selected, amplified to 300nM MTX.

5. Human EPO expressed in stable transformers in CHO has started.

6. Determine the effect of deglycosylation of EPO on its in vivo and in vitro biological activity. Deglycosylated EPO has full in vitro activity but no in vivo activity.

7. Optimize RIA for EPO to assay clinical samples.

8. Started purification of human urinary EPO.

9. Amino acid sequence of urinary EPO has been completely sequenced except few residues and one disulfide bridge has been determined.

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Product Development Team
Quarterly Report

PLANS FOR NEXT QUARTER

PRODUCT: EPO TEAM LEADER: F. K. Lin DATE: 5/21/84

Activity/Responsible Person	1984 May 15	1984 June 15	1984 July 15 --Aug.15
Initial purification of E.coli EPO (FKL, CHL, JK, TS)	X		
Renaturation and testing for in vitro, in vivo activity (FKL, CHL, JK, TS, JE, CB)	X	X	X
Express yeast EPO at 1-5mg/l	X	X	
Initial purification of yEPO (TS)		X	X
Initial purification of mammalian EPO (TS)		X	X
Select stable CHO transformants (RS)	X		
Establish frozens (RS)		X	
Start Gene amplification (RS, JB)		X	
Establish mammalian culture Process development (JB, DV)		X	
Assays on rEPO samples (JE, JL, CB)	X	X	X
Establish in vivo assay in house (AC)	X	X	X

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Product Development Team
Quarterly Report (cont'd)

PLANS FOR NEXT QUARTER

KEY ISSUES	RISK ASSESSMENT
1. Activity of E.coli-derived EPO	High risk as judged from EndoF experiments. May require special delivery for E.coli EPO to work.
2. Potential differences in carbonydrate compositions in EPO produced by different cell types may be a problem for FDA	Generation of antibody. Study using CHO-mk EPO (and/or COS-mk EPO) on monkey must be run as soon as possible
3. EPO production in animals (e.g., Bioresponse)	No risk in trying the experiment. Long range risk is acceptability of this material by FDA.
4. Establish cell culture fermentation process development group	Processes are potentially difficult and time-consuming. If delay effort could ultimately affect clinical start date.
5. Establish in vivo assay in house	Potential bottleneck on timeline. Needed as a final quality control test item.
6. Characterization of rEPO by peptide mapping and sequencing	Verification of natural sequence. Relatively low risk.
7. Carbonydrate structure analysis	See (2) above

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Product Development Team
Quarterly Report

LONG RANGE PRODUCT PLAN
TIMELINE SUMMARY

PROJECTED PRODUCT MILESTONES

ITEM	TARGET DATES CURRENT	ORIGINAL PLAN
1) Select CHO cell line for human EPO	6/1	4/15 - 5/15
2) Initial purification of material from: yeast	6/01 - 7/30	6/01 - 7/15
from: CHO	5/15 - 7/30	5/15 - 7/01

REASONS FOR REVISED ESTIMATES

1) transfection failure

2) previous estimates were not realistic

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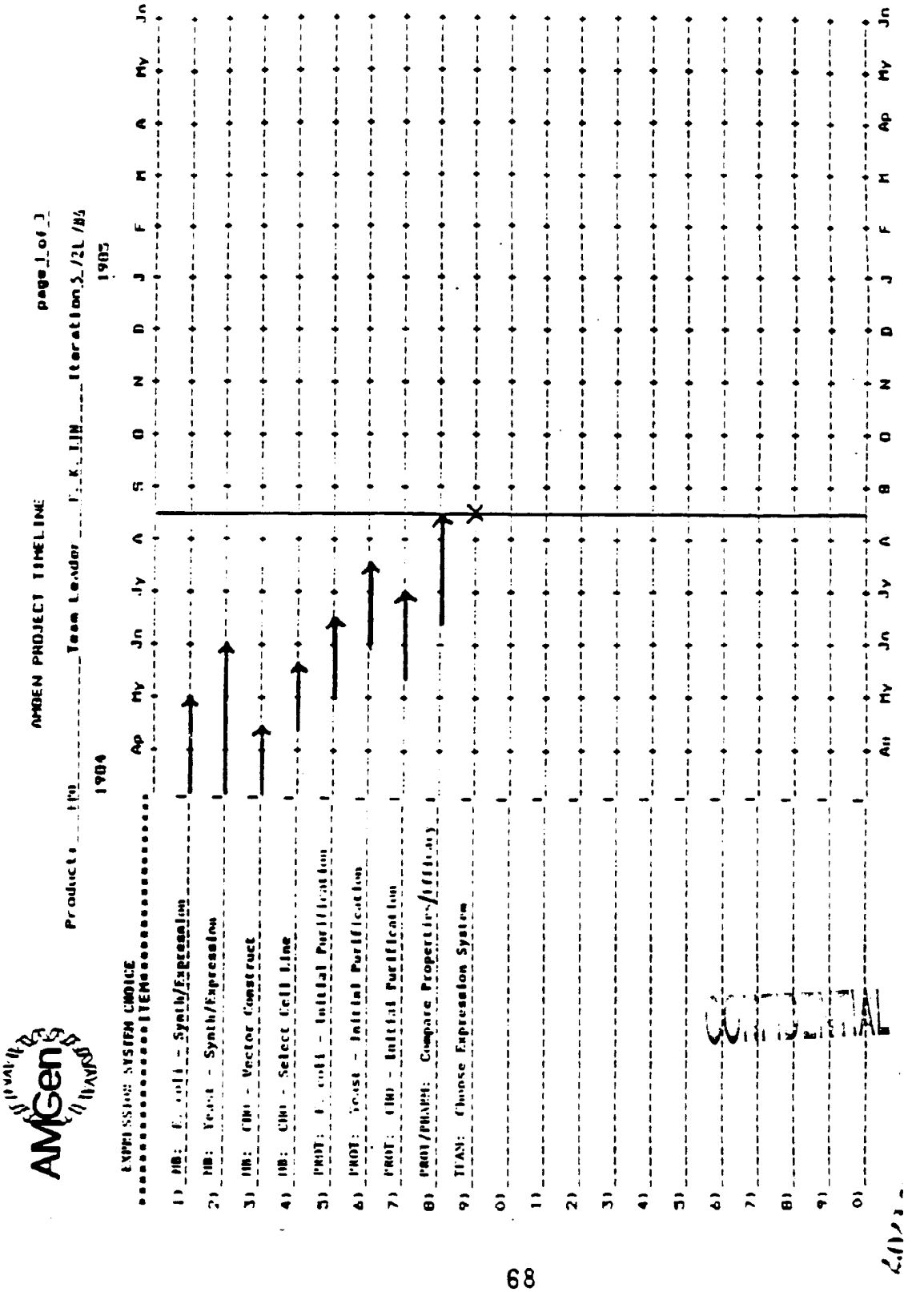
AMGEN PROJECT TIMELINE
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1984
1985
EXPRESSION SYSTEM CHOICE
ITEM
1) HB: E. coli - Synth/Expression
2) HB: Yeast - Synth/Expression
3) HB: CHO - Vector Construct
4) HB: CHO - Select Cell Line
5) PROT: E. coli - Initial Purification
6) PROT: Yeast - Initial Purification
7) PROT: CHO - Initial Purification
8) PROT/PHARM: Compare Properties/Efficacy
9) TRAN: Choose Expression System

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AMGen
AMGEN PROJECT TIMELINE
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Product: EPO
Team Leader: F. Ka Lim
Iteration 5/21/84
1984
1985
Ap My Jn Jy A S O N D J F M A My Jn
1) PROD: Process Development
Yeast
Cell
2) PROD/QC: Formulation
3) RA: FDA Meeting
X
4) FERM: Initial Cell Process
5) FERM: Cell Seed/Controls
6) FERM: Density Optimization
7) QC: Draft Test Procedures
8) PROD: Manufacture GLP Lot
9) QC: Fill/Test GLP Lot
10) RA: Tox Protocols/Lab Control
11) QC: GLP Lot Stability
12) RA: Toxicity Testing
13) QC: GMP Documentation
14) PROD: GMP Manufacture Quality Lot
15) QC: Final Product Stability Tests
16) RA: Clinical Investigators Identified
17) RA: Clinical Protocols Finalized
18) RA/QC: Prepare & File IND/Master Files
19) RA: Phase I Clinical
20)

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Product Development Team
Quarterly Report

HUMAN RESOURCES

PRODUCT: EPO TEAM LEADER: F. K. Lin DATE: 5/21/84

PERSONNEL CURRENTLY ASSIGNED (indicate PDT members as well as all other personnel contributing greater than 10% of total FTE)

NAME	TITLE	DEPARTMENT	% FTE LAST QUARTER	% FTE NEXT QUARTER
F. K. Lin	RS	CDNA	100	100
J. Klemencic	RS	CDNA	60	100
C. H. Lin	RA	CDNA	10	100
S. Elliott	RS	Yeast	90	90
	RA	Yeast	0	90
J. Egrie	RS	Immunology	100	100
J. Lane	RA	Immunology	100	100
C. Bradley	RA	Quality Assurance	50	100
A. Conen	RS	Pharmacology	0	50
J. Browne	RS	Mammalian Vector	50	50
R. Smalling	RA	Mammalian Vector	90	90
G. Trail	RA	Mammalian Vector	10	10
P. Lai	RS	Protein Chem.	10	10
R. Everett	RA	Protein Chem.	10	10
S. Badrawi	RA	B.V.G.	90	0
A. Banks	RS	A.D.I.	20	0
K. Chen	RA	B.V.G.	40	15
E. Lau	RS	A.D.I.	20	0

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Product Development Team
Quarterly Report

HUMAN RESOURCES

PRODUCT: EPO TEAM LEADER: F. K. LIN DATE: 5/21/84

PERSONNEL CURRENTLY ASSIGNED (indicate PDT members as well as all other personnel contributing greater than 10% of total FTE)

NAME	TITLE	DEPARTMENT	% FTE LAST QUARTER	% FTE NEXT QUARTER
M. Peters	RS	A.D.I.	20	0
S. Suggs	RS	B. V. G.	90	0
J. Fenno	Director	Regulatory Affairs	10	10
		TOTALS (Last Qtr)	970	1025 (Next Qtr)

B.V.G. = Bacterial Vectors Group

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Product Development Team
Quarterly Report

HUMAN RESOURCES (cont'd)

BREAKDOWN BY DEPARTMENT

DEPARTMENT	# FTE
Mammalian Vectors	150
Immunology	200
Yeast	90
Bacterial Vectors	220
Gene Synthesis	60
cDNA	170
Protein Chemistry	20

Total 960

REQUESTED CHANGES

Existing Staff:

1+ staff involved (some less than full time)

Recommendations for hire:

One RA for J. Browne (mammalian cell expression)
One RA for T. Strickland (protein purification)
Two RS for large scale mammalian culture
Two RA for large scale mammalian culture
One RA with 50% FTE in fermentation

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