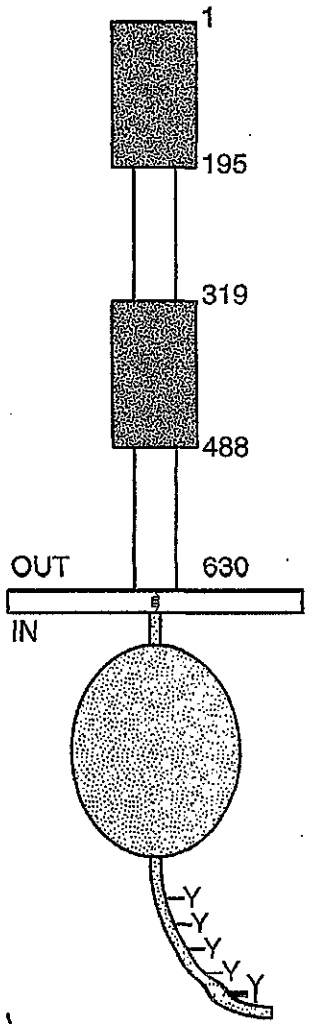



Domain I (L1)

TQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNLELTYLPTNASLSFLQDIQEVQGYV
LIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNGDPLNNTTPVTGASPGGLRELQLRSLT
EILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLALTLIDTNRSRACHPCSPMCKGSRCWGES
SEDCQSLTR (SEQ ID NO. 19)

Domain II (CR1)

TVCAGGCARCKGPLPTDCCHEQCAAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTF
ESMPNPEGRYTFGASCVTACPYNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARV
(SEQ ID NO. 20)

Domain III (L2)

CYGLGMEHLREVRAVTSANIQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLE
EITGYLYISAWPDSLPDLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLAL
IHHNTHLCFVHTVPWDQLFRNPHQALLHTANRPEDECVGEGLA (SEQ ID NO. 21)

Domain IV (CR2)

CHQLCARGHCWGPGPTQCVNCSQFLRGQECVEECRVLQGLPREYVNARHCLPCHPECQPQNGS
VTCFGPEADQCVACAHYKDPPFCVARCPSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVD
LDDKGCPAEQRASPLT (SEQ ID NO. 22)

Transmembrane

Juxtamembrane

Tyrosine Kinase

Regulatory Region

FIG. 1

**Variable Light**

```
                10          20          30          40
2C4     DTVMTQSHKIMSTSVGDRVSITC [KASQDVSIGVA] WYQQRP
         **    ****  *       *                    *
574     DIQMTQSPSSLSASVGDRVTITC [KASQDVSIGVA] WYQQKP
                                  *   ** ***
hum κI  DIQMTQSPSSLSASVGDRVTITC [RASQSISNYLA] WYQQKP

                50          60          70          80
2C4     GQSPKLLIY [SASYRYT] GVPDRFTGSGSGTDFTFTISSVQA
          **                  *  *          *    * *
574     GKAPKLLIY [SASYRYT] GVPSRFSGSGSGTDFTLTISSLQP
                   * *****
hum κI  GKAPKLLIY [AASSLES] GVPSRFSGSGSGTDFTLTISSLQP

                90          100
2C4     EDLAVYYC [QQYYIYPYT] FGGGTKLEIK (SEQ ID NO:1)
           * *                 *   *
574     EDFATYYC [QQYYIYPYT] FGQGTKVEIK (SEQ ID NO:3)
                     *** *
hum κI  EDFATYYC [QQYNSLPWT] FGQGTKVEIK (SEQ ID NO:5)
```

**FIG. 2A**

**Variable Heavy**

```
                10          20          30          40
2C4     EVQLQQSGPELVKPGTSVKISCKAS [GFTFTDYTMD] WVKQS
            **  **  *  * ***  *                   * *
574     EVQLVESGGGLVQPGGSLRLSCAAS [GFTFTDYTMD] WVRQA
                                     ** * *
hum III EVQLVESGGGLVQPGGSLRLSCAAS [GFTFSSYAMS] WVRQA

                50  a       60          70          80
2C4     HGKSLEWIG [DVNPNSGGSIYNQRFKG] KASLTVDRSSRIVYM
        *  *   **                     *** *    **** *
574     PGKGLEWVA [DVNPNSGGSIYNQRFKG] RFTLSVDRSKNTLYL
                   ****** *** ****      * * *
hum III PGKGLEWVA [VISGDGGSTYYADSVKG] RFTISRDNSKNTLYL

          abc       90          100ab       110
2C4     ELRSLTFEDTAVYYCAR [NLGPSFYFDY] WGQGTTLTVSS (SEQ ID NO:2)
        ***  **                                 **
574     QMNSLRAEDTAVYYCAR [NLGPSFYFDY] WGQGTLVTVSS (SEQ ID NO:4)
                           ********
hum III QMNSLRAEDTAVYYCAR [GRVGYSLYDY] WGQGTLVTVSS (SEQ ID NO:6)
```

**FIG. 2B**

**Amino Acid Sequence for Pertuzumab Light Chain**

```
1         10         20         30         40         50         60
|         |          |          |          |          |          |
DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPS

          70         80         90         100        110        120
          |          |          |          |          |          |
RFSGSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIKRTVAAPSVFIFPP

          130        140        150        160        170        180
          |          |          |          |          |          |
SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT

          190        200        210
          |          |          |
LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

**FIG. 3A**

**Amino Acid Sequence for Pertuzumab Heavy Chain**

```
1         10         20         30         40         50         60
|         |          |          |          |          |          |
EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGGSIY

          70         80         90         100        110        120
          |          |          |          |          |          |
NQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVTVSSA

          130        140        150        160        170        180
          |          |          |          |          |          |
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG

          190        200        210        220        230        240
          |          |          |          |          |          |
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP

          250        260        270        280        290        300
          |          |          |          |          |          *|
SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS

          310        320        330        340        350        360
          |          |          |          |          |          |
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEM

          370        380        390        400        410        420
          |          |          |          |          |          |
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ

          430        440        448
          |          |          |
QGNVFSCSVMHEALHNHYTQKSLSLSPG
```

**FIG. 3B**

```
1                               15                              30                              45
M G W S C I I L F L V A T A T G V H S D I Q M T Q S P S S L S A S V G D R V T I T C K A S

46                              60                              75                              90
Q D V S I G V A W Y Q Q K P G K A P K L L I Y S A S Y R Y T G V P S R F S G S G S G T D F

91                              105                             120                             135
T L T I S S L Q P E D F A T Y Y C Q Q Y Y I Y P Y T F G Q G T K V E I K R T V A A P S V F

136                             150                             165                             180
I F P P S D E Q L K S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E

181                             195                             210                             225
S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T

226         233
K S F N R G E C   (SEQ ID NO. 17)
```

FIG. 4A

```
1                               15                              30                              45
M G W S C I I L F L V A T A T G V H S E V Q L V E S G G G L V Q P G G S L R L S C A A S G

46                              60                              75                              90
F T F T D Y T M D W V R Q A P G K G L E W V A D V N P N S G G S I Y N Q R F K G R F T L S

91                              105                             120                             135
V D R S K N T L Y L Q M N S L R A E D T A V Y Y C A R N L G P S F Y F D Y W G Q G T L V T

136                             150                             165                             180
V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P V T V S W N

181                             195                             210                             225
S G A L T S G V H T F P A V L Q S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H

226                             240                             255                             270
K P S N T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D

271                             285                             300                             315
T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D G V E V H N A K T K P R E E

316                             330                             345                             360
Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A

361                             375                             390                             405
K G Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N

406                             420                             435                             450
G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H

451                             465
E A L H N H Y T Q K S L S L S P G   (SEQ ID NO. 18)
```

**FIG. 4B**

**Ligand-activated EGFR Heterodimerizes with HER2 2C4 Binds at the Heterodimeric Binding Site**

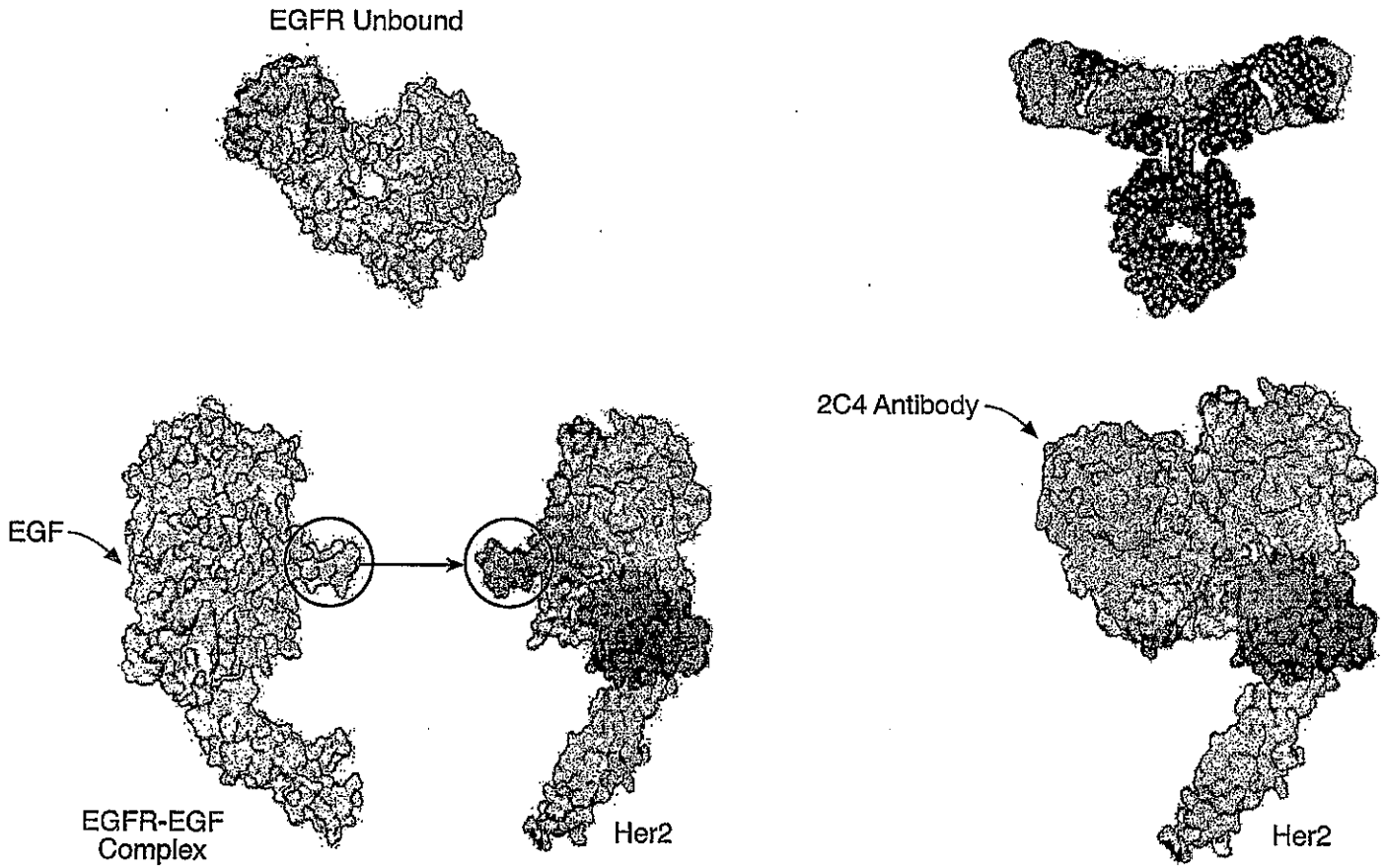



*FIG. 5*

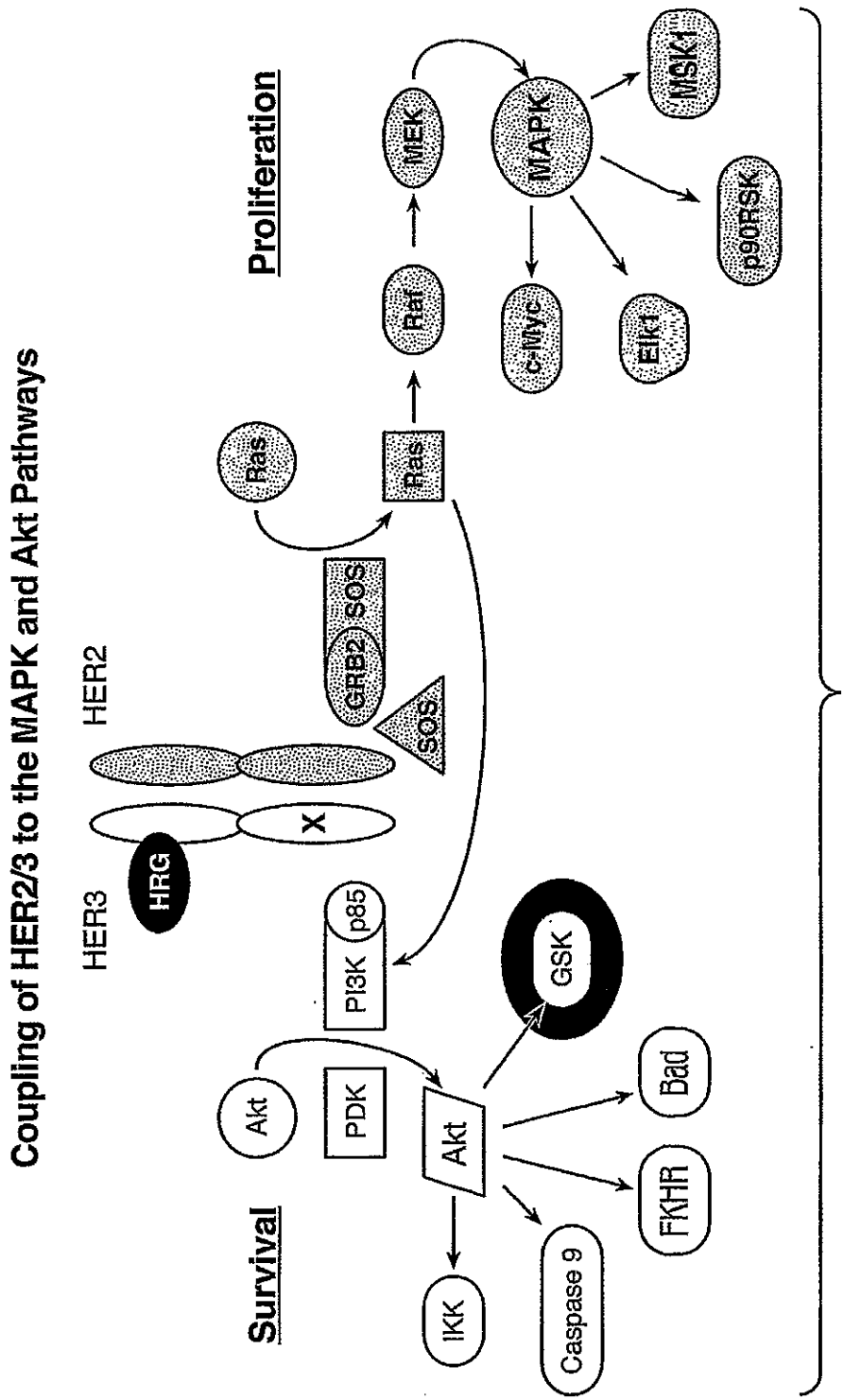
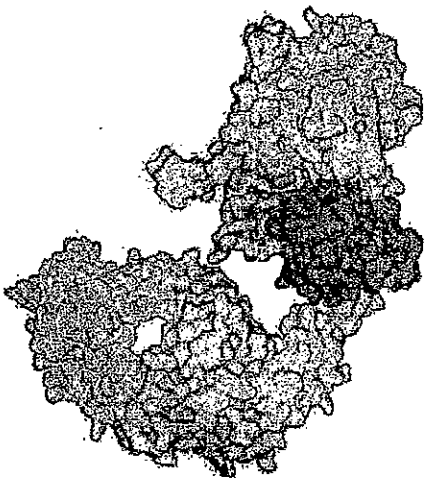

Coupling of HER2/3 to the MAPK and Akt Pathways
HER3
HER2
HRG
X
Ras
GRB2
SOS
SOS
Ras
Raf
MEK
MAPK
MSK1
p90RSK
Elk1
c-Myc
Proliferation
PI3K
p85
Akt
PDK
Akt
GSK
Bad
FKHR
IKK
Caspase 9
Survival

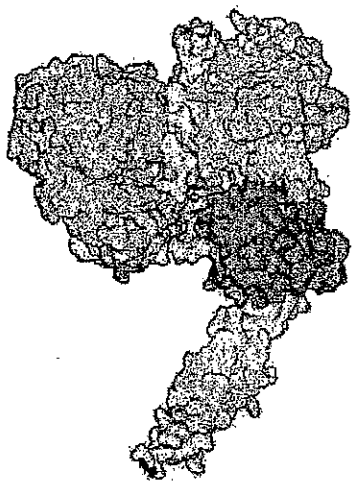
FIG. 6

**Trastuzumab**
**Herceptin**



- Binds in IV near JM.
- Protects against receptor shedding
- Moderately affects receptor down-modulation
- Slight effect on HER2's role as a coreceptor

**Pertuzumab**
**Omnitarg**



- Binds in II at dimerization interface
- Does not prevent receptor shedding
- Moderately affects receptor down-modulation
- Major effect on HER2's role as a coreceptor

*FIG. 7*

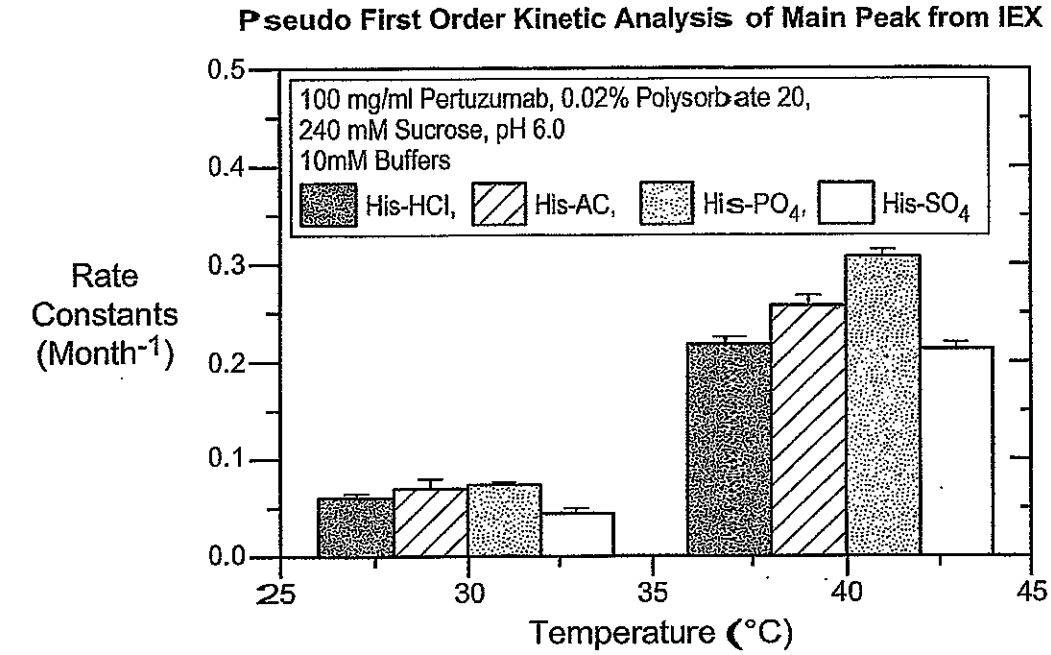

Pseudo First Order Kinetic Analysis of Main Peak from IEX
100 mg/ml Pertuzumab, 0.02% Polysorbate 20,
240 mM Sucrose, pH 6.0
10mM Buffers
His-HCl, His-AC, His-PO4, His-SO4
Rate Constants (Month-1)
0.5
0.4
0.3
0.2
0.1
0.0
25
30
35
40
45
Temperature (°C)

FIG. 8

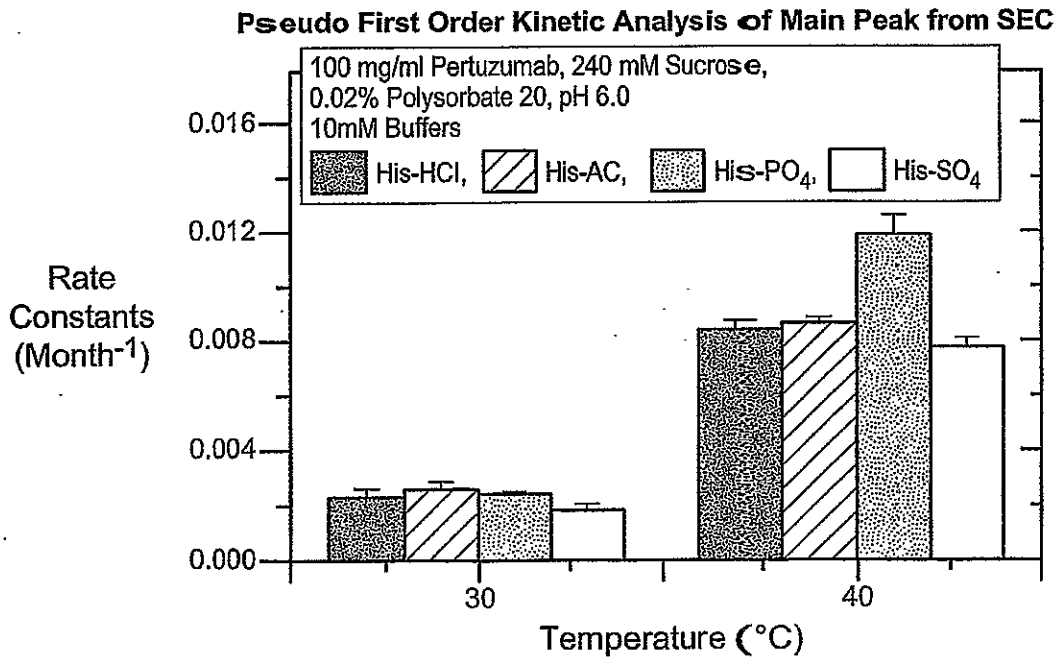

Pseudo First Order Kinetic Analysis of Main Peak from SEC
100 mg/ml Pertuzumab, 240 mM Sucrose,
0.02% Polysorbate 20, pH 6.0
10mM Buffers
His-HCl, His-AC, His-PO4, His-SO4
Rate Constants (Month-1)
0.016
0.012
0.008
0.004
0.000
30
40
Temperature (°C)

FIG. 9

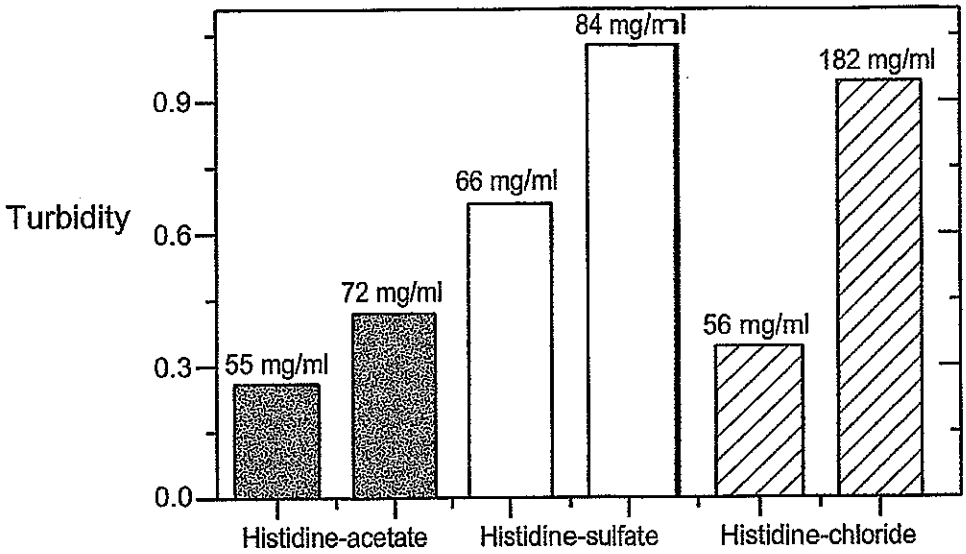

Turbidity
0.0
0.3
0.6
0.9
55 mg/ml
72 mg/ml
66 mg/ml
84 mg/ml
56 mg/ml
182 mg/ml
Histidine-acetate
Histidine-sulfate
Histidine-chloride

FIG. 10

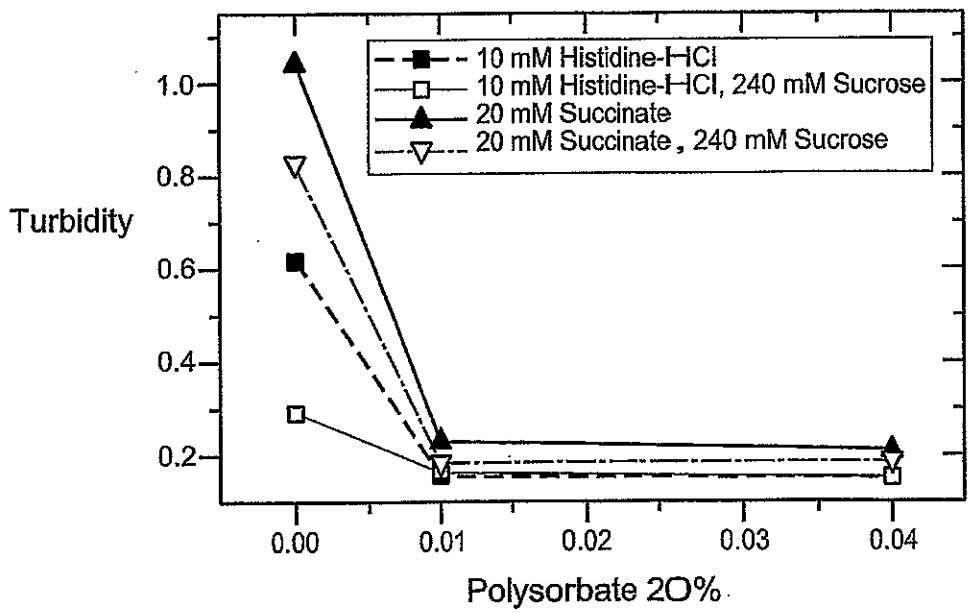

Turbidity
0.2
0.4
0.6
0.8
1.0
10 mM Histidine-HCl
10 mM Histidine-HCl, 240 mM Sucrose
20 mM Succinate
20 mM Succinate, 240 mM Sucrose
0.00
0.01
0.02
0.03
0.04
Polysorbate 20%

FIG. 11

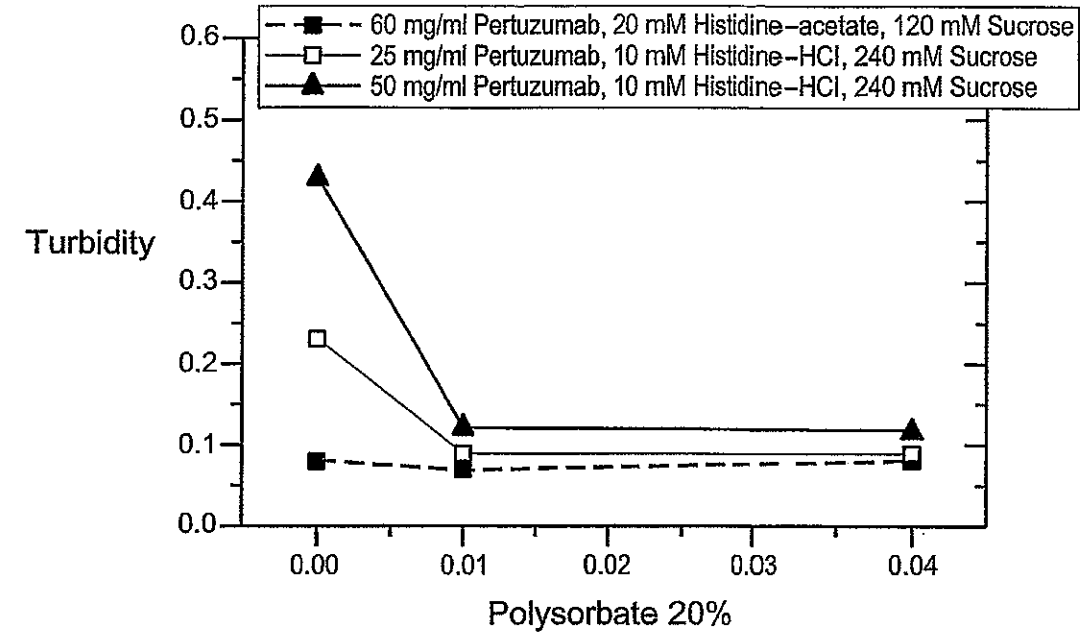

60 mg/ml Pertuzumab, 20 mM Histidine-acetate, 120 mM Sucrose
25 mg/ml Pertuzumab, 10 mM Histidine-HCl, 240 mM Sucrose
50 mg/ml Pertuzumab, 10 mM Histidine-HCl, 240 mM Sucrose
Turbidity
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.00
0.01
0.02
0.03
0.04
Polysorbate 20%

FIG. 12

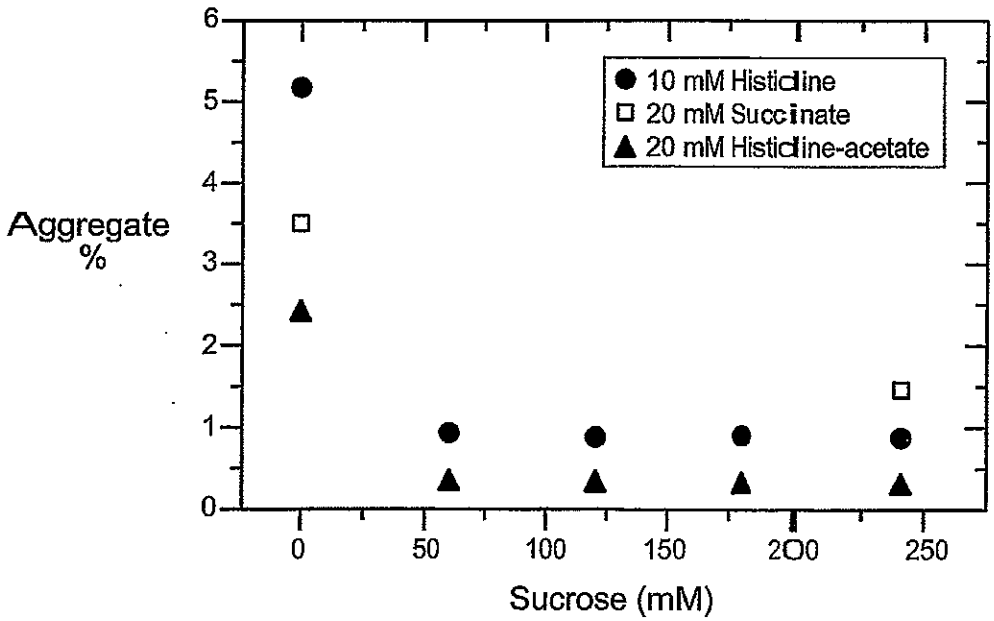

10 mM Histidine
20 mM Succinate
20 mM Histidine-acetate
Aggregate %
6
5
4
3
2
1
0
0
50
100
150
200
250
Sucrose (mM)

FIG. 13

Light Chain

```
1                               15                              30                              45
D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q D V N T A V A W Y Q Q K P G K A P K

46                              60                              75                              90
L L I Y S A S F L Y S G V P S R F S G S R S G T D F T L T I S S L Q P E D F A T Y Y C Q Q

91                              105                             120                             135
H Y T T P P T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L

136                             150                             165                             180
L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T L T

181                             195                             210     214
L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G E C
```

FIG. 14A

Heavy Chain

```
1                               15                              30                              45
E V Q L V E S G G G L V Q P G G S L R L S C A A S G F N I K D T Y I H W V R Q A P G K G L

46                              60                              75                              90
E W V A R I Y P T N G Y T R Y A D S V K G R F T I S A D T S K N T A Y L Q M N S L R A E D

91                              105                             120                             135
T A V Y Y C S R W G G D G F Y A M D Y W G Q G T L V T V S S A S T K G P S V F P L A P S S

136                             150                             165                             180
K S T S G G T A A L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

181                             195                             210                             225
G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K

226                             240                             255                             270
T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V S

271                             285                             300                             315
H E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D

316                             330                             345                             360
W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E

361                             375                             390                             405
M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G

406                             420                             435                             449
S F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G
```

FIG. 14B

```
1                               15                              30                              45
V H S D I Q M T Q S P S S L S A S V G D R V T I T C K A S Q D V S I G V A W Y Q Q K P G K

46                              60                              75                              90
A P K L L I Y S A S Y R Y T G V P S R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y

91                              105                             120                             135
C Q Q Y Y I Y P Y T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V

136                             150                             165                             180
V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S

181                             195                             210             217
T L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G E C   (SEQ ID NO. 23)
```



***FIG. 15A***

```
1                               15                              30                              45
E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T E T D Y T M D W V R Q A P G K G L

46                              60                              75                              90
E W V A D V N P N S G G S I Y N Q R F K G R F T L S V D R S K N T L Y L Q M N S L R A E D

91                              105                             120                             135
T A V Y Y C A R N L G P S F Y F D Y W G Q G T L V T V S S A S T K G P S V F P L A P S S K

136                             150                             165                             180
S T S G G T A A L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G

181                             195                             210                             225
L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T

226                             240                             255                             270
H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I S R T P E V T C V V V D V S H

271                             285                             300                             315
E D P E V K F N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W

316                             330                             345                             360
L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P S R E E M

361                             375                             390                             405
T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S

406                             420                             435                             449
F F L Y S K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
```

(SEQ ID NO. 24)

FIG. 15B

**FIG. 16A**

**Oligosaccharide Structures Commonly Observed in IgG Antibodies**

| Structures | Abbreviation | Mass |
|---|---|---|
| Manα(1–>6)<br>Manα(1–>3) > Manα(1–>6)<br>Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- | Man5 | 1235 |
| GlcNAcβ(1–>2){ Manα(1–>6)<br>Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G-1 | 1260 |
| GlcNAcβ(1–>2)Manα(1–>6)<br>GlcNAcβ(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- | G0-F | 1317 |
| Manα(1–>6)<br>Manα(1–>3) > Manα(1–>6)<br>Manα(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- | Man6 | 1398 |

**Oligosaccharide Structures Commonly Observed in IgG Antibodies**

| Structures | Abbreviation | Mass |
|---|---|---|
| Galβ(1–>4)GlcNAcβ(1–>2){Manα(1–>6), Manα(1–>3)} > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G1-1 | 1423 |
| GlcNAcβ(1–>2)Manα(1–>6), GlcNAcβ(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G0 | 1463 |
| Galβ(1–>4)GlcNAcβ(1–>2)Manα(1–>6), GlcNAcβ(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G1 (1-6) | 1626 |
| GlcNAcβ(1–>2)Manα(1–>6), Galβ(1–>4)GlcNAcβ(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G1 (1-3) | 1626 |
| Galβ(1–>4)GlcNAcβ(1–>2)Manα(1–>6), Galβ(1–>4)GlcNAcβ(1–>2)Manα(1–>3) > Manβ(1–>4)GlcNAcβ(1–>4)GlcNAc- (Fucα(1–>6) on GlcNAc) | G2 | 1788 |

**Masses shown in this figure correspond to the $(M+Na)^+$ values.**

***FIG. 16B***

**Anti-IgE Antibodies: Light Chain ($V_L$ and $C_L$ Domains)**

```
                  10         20         30         40         50         60         70         80
E25       DIQLTQSPSS LSASVGDRVT ITC[RASQSVD YDGDSYMN]WY QQKPGKAPKL LIY[AASYLES] GVPSRFSGSG SGTDFTLTIS
E26       DIQLTQSPSS LSASVGDRVT ITC[RASKPVD GEGDSYLN]WY QQKPGKAPKL LIY[AASYLES] GVPSRFSGSG SGTDFTLTIS
HAE1      DIQLTQSPSS LSASVGDRVT ITC[RASKPVD GEGDSYLN]WY QQKPGKAPKL LIY[AASYLES] GVPSRFSGSG SGTDFTLTIS
Hu-901    DILLTQSPGT LSLSPGERAT LSC RASQSIG TNIH----- WY QQKPGQAPRL LIK YASESIS  GIPSRFSGSG SGTDFTLTIS

                90         100        110     C_L starts
E25       SLQPEDFATY YC[QQSHEDPY T]FGQGTKVEI KRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
E26       SLQPEDFATY YC[QQSHEDPY T]FGQGTKVEI KRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
HAE1      SLQPEDFATY YC[QQSHEDPY T]FGQGTKVEI KRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
Hu-901    RLEPEDFAMY YC QQSDSWPT T FGQGTKVEI KRT VAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD

E25         SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SEQ ID NO.: 37
E26         SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SEQ ID NO.: 38
HAE1        SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SEQ ID NO.: 39
Hu-901      SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SEQ ID NO.: 40
```

***FIG. 17A***

## Anti-IgE Antibodies: Heavy Chain ($V_H$ and $C_H$ Domains)

```
                10        20        30        40        50 a      60        70        80        90
E25     EVQLVESGGG LVQPGGSLRL SCAVSGYSIT S[GYSWNW]IRQ APGKGLEWVA [SITYDGSTNY NPSVKG]RITI SRDDSKNTFY LQMNSLRAED
E26     EVQLVESGGG LVQPGGSLRL SCAVSGYSIT S[GYSWNW]IRQ APGKGLEWVA [SITYDGSTNY NPSVKG]RITI SRDDSKNTFY LQMNSLRAED
HAE1    EVQLVESGGG LVQPGGSLRL SCAVSGYSIT S[GYSWNW]IRQ APGKGLEWVA [SIKYSGETKY NPSVKG]RITI SRDDSKNTFY LQMNSLRAED
Hu-901  QVQLVQSGAE VKKPGASVKV SCKASGYTFT- S MYWLEW VRQ APGHGLEWVG EISPGTFTTNY NEKFKA RATF TADTSTNTAY MELSSLRSED

                100       110ab       120 C_H starts
E25     TAVYYCAR[GS HYFGHWHFAV]  WGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS
E26     TAVYYCAR[GS HYFGHWHFAV]  WGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS
HAE1    TAVYYCAR[GS HYFGHWHFAV]  WGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS
Hu-901  TAVYYCAR FS HFSGSNYDYFDY WGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS

E25       VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
E26       VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
HAE1      VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
Hu-901    VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE

E25       VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
E26       VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
HAE1      VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
Hu-901    VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE

E25       SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ ID NO.: 41
E26       SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ ID NO.: 42
HAE1      SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ ID NO.: 43
Hu-901    SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK SEQ ID NO.: 44
```



FIG. 17B

**Sequence Alignment of Variable Light Domains**

```
                 |----------FR1----------|      CDR1      |----
                          10        20          30          40
2H7              QIVLSQSPAILSASPGEKVTMTC [RASSSVS-YMH] WYQQKP
                 * ***   **     * **
hu2H7.v16        DIQMTQSPSSLSASVGDRVTITC [RASSSVS-YMH] WYQQKP
                                         * * * **
hum kI           DIQMTQSPSSLSASVGDRVTITC [RASQSISNYLA] WYQQKP

                 --FR2--|   CDR2   |----------FR3----------
                        50          60        70        80
2H7              GSSPKPWIY [APSNLAS] GVPARFSGSGSGTSYSLTISRVEA
                  **   *              *         ***    ****
hu2H7.v16        GKAPKPLIY [APSNLAS] GVPSRFSGSGSGTDFTLTISSLQP
                       *     * * *
hum kI           GKAPKLLIY [AASSLES] GVPSRFSGSGSGTDFTLTISSLQP

                 ---------|   CDR3   |--FR4--|
                        90          100
2H7              EDAATYYC [QQWSFNPPT] FGAGTKLELKR
                   *                   *   * *
hu2H7.v16        EDFATYYC [QQWSFNPPT] FGQGTKVEIKR
                          * *** *
hum kI           EDFATYYC [QQYNSLPWT] FGQGTKVEIKR
```

**FIG. 18A**

**Sequence Alignment of Variable Heavy Domains**

```
                 |----------FR1----------|      CDR1      |----
                          10        20          30          40
2H7              QAYLQQSGAELVRPGASVKMSCKAS [GYTFTSYNMH] WVKQT
                 *** **  **  *  * ***  *                   * *
hu2H7.v16        EVQLVESGGGLVQPGGSLRLSCAAS [GYTFTSYNMH] WVRQA
                                           * *   * *
hum III          EVQLVESGGGLVQPGGSLRLSCAAS [GFTFSSYAMS] WVRQA

                 --FR2--|      CDR2      |----FR3----
                        50  a       60        70        80
2H7              PRQGLEWIG [AIYPGNGDTSYNQKFKG] KATLTVDKSSSTAYM
                  **   *                      ** **    ** * *
hu2H7.v16        PGKGLEWVG [AIYPGNGDTSYNQKFKG] RFTISVDKSKNTLYL
                         *   * **** * * ****       * *
hum III          PGKGLEWVA [VISGDGGSTYYADSVKG] RFTISRDNSKNTLYL

                 ----------------|      CDR3      |--FR4--|
                   abc       90          100abcde        110
2H7              QLSSLTSEDSAVYFCAR [VVYYSNSYWYFDV] WGTGTTVTVSS
                  **  **  *   *                      *
hu2H7.v16        QMNSLRAEDTAVYYCAR [VVYYSNSYWYFDV] WGQGTLVTVSS
                                   ******* *** *
hum III          QMNSLRAEDTAVYYCAR [GRVGYSLY---DY] WGQGTLVTVSS
```

**FIG. 18B**

## Anti-VEGF Antibody Variable Domain Sequences

anti-VEGF variable light sequence:

DIQMTQTTSSLSASLGDRVIISCSASQDISNYLNWYQQKPDGTVKVLIYFTSSLHSGVPSRFSGS
GSGTDYSLTISNLEPEDIATYYCQQYSTVPWTFGGGTKLEIK
(SEQ ID NO: 31)

anti-VEGF variable heavy sequence of:

EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQAPGKGLKWMGWINTYTGEPTYAADFK
RRFTFSLETSASTAYLQISNLKNDDTATYFCAKYPHYYGSSHWYFDVWGAGTTVTVSS
(SEQ ID NO: 32)

anti-VEGF antibody variable light sequence:

DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIYFTSSLHSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQYSTVPWTFGQGTKVEIK
(SEQ ID NO: 33)

anti-VEGF antibody variable heavy sequence:

EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQAPGKGLEWVGWINTYTGEPTYAADFK
RRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGTLVTVSS
(SEQ ID NO: 34)

anti-VEGF antibody variable light sequence:

DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIYFTSSLHSGVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQQYSTVPWTFGQGTKVEIK
(SEQ ID NO: 35)

anti-VEGF antibody variable heavy sequence:

EVQLVESGGGLVQPGGSLRLSCAASGYDFTHYGMNWVRQAPGKGLEWVGWINTYTGEPTYAADFK
RRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAKYPYYYGTSHWYFDVWGQGTLVTVSS
(SEQ ID NO: 36)

**FIG. 19**

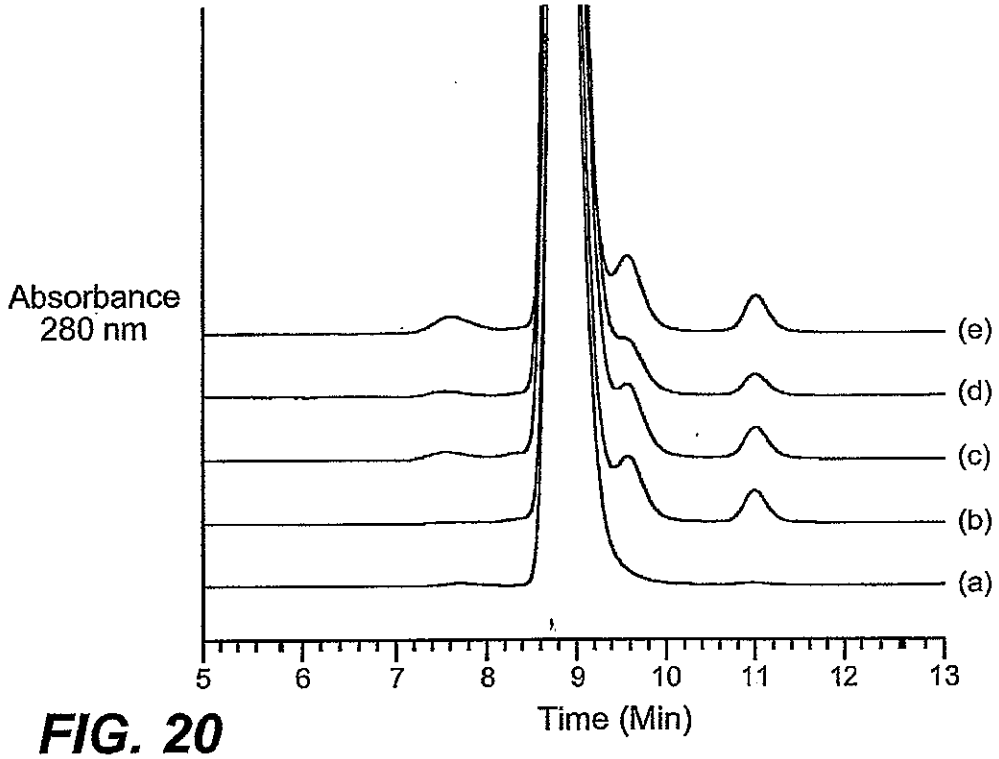

Absorbance
280 nm
(e)
(d)
(c)
(b)
(a)
5
6
7
8
9
10
11
12
13
Time (Min)

FIG. 20

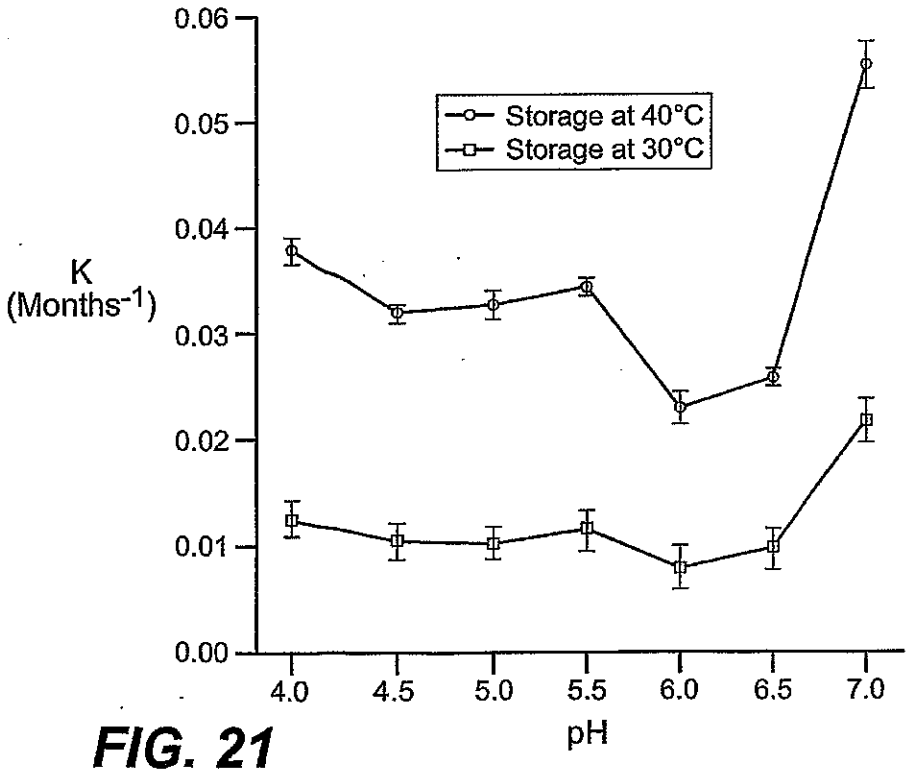

0.06
0.05
0.04
0.03
0.02
0.01
0.00
K
(Months-1)
Storage at 40°C
Storage at 30°C
4.0
4.5
5.0
5.5
6.0
6.5
7.0
pH

FIG. 21

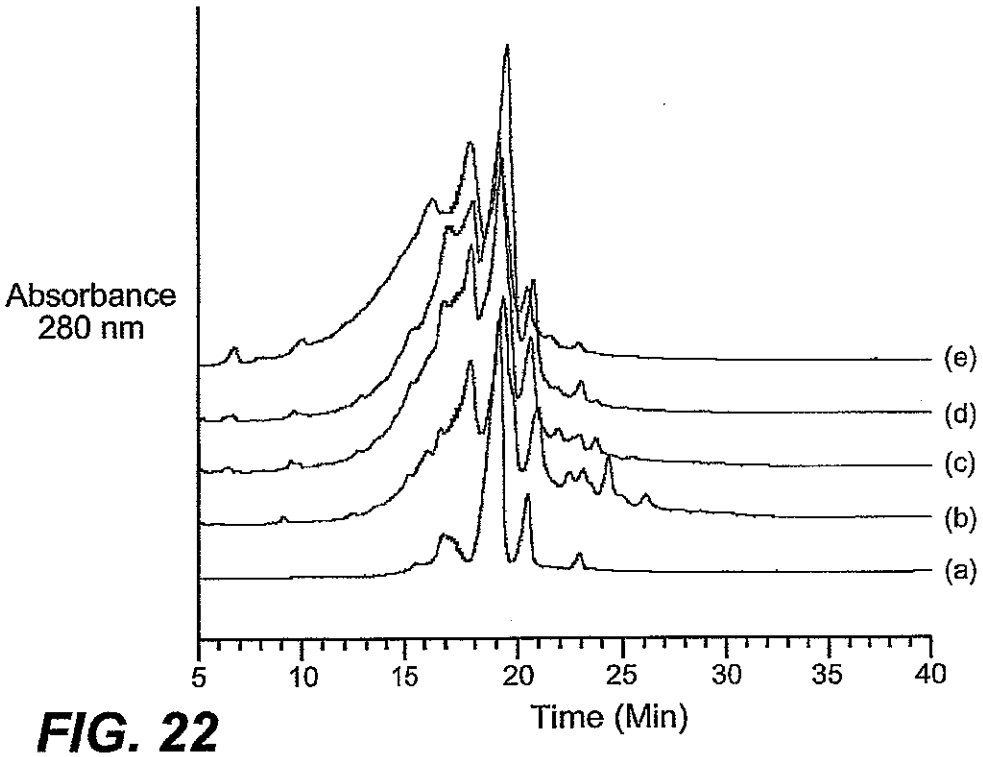

Absorbance
280 nm
(e)
(d)
(c)
(b)
(a)
5
10
15
20
25
30
35
40
Time (Min)

FIG. 22

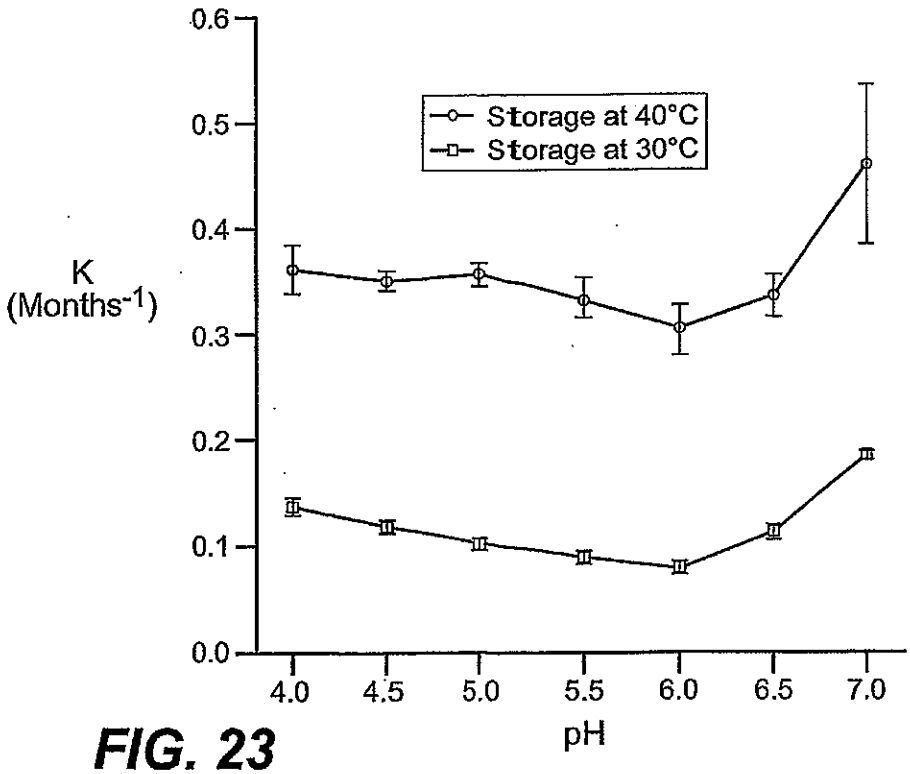

K
(Months-1)
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Storage at 40°C
Storage at 30°C
4.0
4.5
5.0
5.5
6.0
6.5
7.0
pH

FIG. 23

```
  1 TTTCCTCACTGACTATAAAAGAATAGAGAAGGAAGGGCTTCAGTGACCGGCTGCCTGGCTGACTTACAGCAGTCAGACTCTGACAGGATC

  1 ATGGCTATGATGGAGGTCCAGGGGGGACCCAGCCTGGGACAGACCTGCGTGCTGATCGTGATCTTCACAGTGCTCCTGCAGTCTCTCTGT
  1 MetAlaMetMetGluValGlnGlyGlyProSerLeuGlyGlnThrCysValLeuIleValIlePheThrValLeuLeuGlnSerLeuCys

181 GTGGCTGTAACTTACGTGTACTTTACCAACGAGCTGAAGCAGATGCAGGACAAGTACTCCAAAAGTGGCATTGCTTGTTTCTTAAAAGAA
 31 ValAlaValThrTyrValTyrPheThrAsnGluLeuLysGlnMetGlnAspLysTyrSerLysSerGlyIleAlaCysPheLeuLysGlu

271 GATGACAGTTATTGGGACCCCAATGACGAAGAGAGTATGAACAGCCCCTGCTGGCAAGTCAAGTGGCAACTCCGTCAGCTCGTTAGAAAG
 61 AspAspSerTyrTrpAspProAsnAspGluGluSerMetAsnSerProCysTrpGlnValLysTrpGlnLeuArgGlnLeuValArgLys

361 ATGATTTTGAGAACCTCTGAGGAAACCATTTCTACAGTTCAAGAAAAGCAACAAAATATTTCTCCCCTAGTGAGAGAAAGAGGTCCNCAG
 91 MetIleLeuArgThrSerGluGluThrIleSerThrValGlnGluLysGlnGlnAsnIleSerProLeuValArgGluArgGlyProGln
                                                  *

451 AGAGTAGCAGCTCACATAACTGGGACCAGAGGAAGAAGCAACACATTGTCTTCTCCAAACTCCAAGAATGAAAAGGCTCTGGGCCGCAAA
121 ArgValAlaAlaHisIleThrGlyThrArgGlyArgSerAsnThrLeuSerSerProAsnSerLysAsnGluLysAlaLeuGlyArgLys

541 ATAAACTCCTGGGAATCATCAAGGAGTGGGCATTCATTCCTGAGCAACTTGCACTTGAGGAATGGTGAACTGGTCATCCATGAAAAAGGG
151 IleAsnSerTrpGluSerSerArgSerGlyHisSerPheLeuSerAsnLeuHisLeuArgAsnGlyGluLeuValIleHisGluLysGly

631 TTTTACTACATCTATTCCCAAACATACTTTCGATTTCAGGAGGAAATAAAAGAAAACACAAAGAACGACAAACAAATGGTCCAATATATT
181 PheTyrTyrIleTyrSerGlnThrTyrPheArgPheGlnGluGluIleLysGluAsnThrLysAsnAspLysGlnMetValGlnTyrIle

721 TACAAATACACAAGTTATCCTGACCCTATATTGTTGATGAAAAGTGCTAGAAATAGTTGTTGGTCTAAAGATGCAGAATATGGACTCTAT
211 TyrLysTyrThrSerTyrProAspProIleLeuLeuMetLysSerAlaArgAsnSerCysTrpSerLysAspAlaGluTyrGlyLeuTyr

811 TCCATCTATCAAGGGGGAATATTTGAGCTTAAGGAAAATGACAGAATTTTTGTTTCTGTAACAAATGAGCACTTGATAGACATGGACCAT
241 SerIleTyrGlnGlyGlyIlePheGluLeuLysGluAsnAspArgIlePheValSerValThrAsnGluHisLeuIleAspMetAspHis

901 GAAGCCAGTTTTTTCGGGGCCTTTTTAGTTGGCTAACTGACCTGGAAAGAAAAAGCAATAACCTCAAAGTGACTATTCAGTTTTCAGGAT
271 GluAlaSerPhePheGlyAlaPheLeuValGlyStp

991 GATACACTATGAAGATGTTTCAAAAAATCTGACCAAAACAAACAAACAGAAA
```

FIG. 24

```
  1 CCCACGCGTC CGCATAAATC AGCACGCGGC CGGAGAACCC CGCAATCTCT GCGCCCACAA AATACACCGA CGATGCCCGA TCTACTTTAA GGGCTGAAAC
    GGGTGCGCAG GCGTATTTAG TCGTGCGCCG GCCTCTTGGG GCGTTAGAGA CGCGGGTGTT TTATGTGGCT GCTACGGGCT AGATGAAATT CCCGACTTTG

101 CCACGGGCCT GAGAGACTAT AAGAGCGTTC CCTACCGCCA TGGAACAACG GGGACAGAAC GCCCCGGCCG CTTCGGGGGC CCGGAAAAGG CACGGCCCAG
    GGTGCCCGGA CTCTCTGATA TTCTCGCAAG GGATGGCGGT ACCTTGTTGC CCCTGTCTTG CGGGGCCGGC GAAGCCCCCG GGCCTTTTCC GTGCCGGGTC
  1                                   M etGluGlnAr gGlyGlnAsn AlaProAlaA laSerGlyAl aArgLysArg HisGlyProGly

201 GACCCAGGGA GGCGCGGGGA GCCAGGCCTG GGCTCCGGGT CCCCAAGACC CTTGTGCTCG TTGTCGCCGC GGTCCTGCTG TTGGTCTCAG CTGAGTCTGC
    CTGGGTCCCT CCGCGCCCCT CGGTCCGGAC CCGAGGCCCA GGGGTTCTGG GAACACGAGC AACAGCGGCG CCAGGACGAC AACCAGAGTC GACTCAGACG
 22   ProArgGl uAlaArgGly AlaArgProG lyLeuArgVa lProLysThr LeuValLeuV alValAlaAl aValLeuLeu LeuValSerA laGluSerAla

301 TCTGATCACC CAACAAGACC TAGCTCCCCA GCAGAGAGCG GCCCCACAAC AAAAGAGGTC CAGCCCCTCA GAGGGATTGT GTCCACCTGG ACACCATATC
    AGACTAGTGG GTTGTTCTGG ATCGAGGGGT CGTCTCTCGC CGGGGTGTTG TTTTCTCCAG GTCGGGGAGT CTCCCTAACA CAGGTGGACC TGTGGTATAG
 55  LeuIleThr GlnGlnAspL euAlaProGl nGlnArgAla AlaProGlnG lnLysArgSe rSerProSer GluGlyLeuC ysProProGl yHisHisIle

401 TCAGAAGACG GTAGAGATTG CATCTCCTGC AAATATGGAC AGGACTATAG CACTCACTGG AATGACCTCC TTTTCTGCTT GCGCTGCACC AGGTGTGATT
    AGTCTTCTGC CATCTCTAAC GTAGAGGACG TTTATACCTG TCCTGATATC GTGAGTGACC TTACTGGAGG AAAAGACGAA CGCGACGTGG TCCACACTAA
 88 SerGluAspG lyArgAspCy sIleSerCys LysTyrGlyG lnAspTyrSe rThrHisTrp AsnAspLeuL euPheCysLe uArgCysThr ArgCysAspSer

501 CAGGTGAAGT GGAGCTAAGT CCCTGCACCA CGACCAGAAA CACAGTGTGT CAGTGCGAAG AAGGCACCTT CCGGGAAGAA GATTCTCCTG AGATGTGCCG
    GTCCACTTCA CCTCGATTCA GGGACGTGGT GCTGGTCTTT GTGTCACACA GTCACGCTTC TTCCGTGGAA GGCCCTTCTT CTAAGAGGAC TCTACACGGC
122   GlyGluVa lGluLeuSer ProCysThrT hrThrArgAs nThrValCys GlnCysGluG luGlyThrPh eArgGluGlu AspSerProG luMetCysArg

601 GAAGTGCCGC ACAGGGTGTC CCAGAGGGAT GGTCAAGGTC GGTGATTGTA CACCCTGGAG TGACATCGAA TGTGTCCACA AAGAATCAGG CATCATCATA
    CTTCACGGCG TGTCCCACAG GGTCTCCCTA CCAGTTCCAG CCACTAACAT GTGGGACCTC ACTGTAGCTT ACACAGGTGT TTCTTAGTCC GTAGTAGTAT
155  LysCysArg ThrGlyCysP roArgGlyMe tValLysVal GlyAspCysT hrProTrpSe rAspIleGlu CysValHisL ysGluSerGl yIleIleIle

701 GGAGTCACAG TTGCAGCCGT AGTCTTGATT GTGGCTGTGT TTGTTTGCAA GTCTTTACTG TGGAAGAAAG TCCTTCCTTA CCTGAAAGGC ATCTGCTCAG
    CCTCAGTGTC AACGTCGGCA TCAGAACTAA CACCGACACA AACAAACGTT CAGAAATGAC ACCTTCTTTC AGGAAGGAAT GGACTTTCCG TAGACGAGTC
188 GlyValThrV alAlaAlaVa lValLeuIle ValAlaValP heValCysLy sSerLeuLeu TrpLysLysV alLeuProTy rLeuLysGly IleCysSerGly

801 GTGGTGGTGG GGACCCTGAG CGTGTGGACA GAAGCTCACA ACGACCTGGG GCTGAGGACA ATGTCCTCAA TGAGATCGTG AGTATCTTGC AGCCCACCCA
    CACCACCACC CCTGGGACTC GCACACCTGT CTTCGAGTGT TGCTGGACCC CGACTCCTGT TACAGGAGTT ACTCTAGCAC TCATAGAACG TCGGGTGGGT
222   GlyGlyGl yAspProGlu ArgValAspA rgSerSerGl nArgProGly AlaGluAspA snValLeuAs nGluIleVal SerIleLeuG lnProThrGln
```

FIG. 25A

```
 901 GGTCCCTGAG CAGGAAATGG AAGTCCAGGA GCCAGCAGAG CCAACAGGTG TCAACATGTT GTCCCCCGGG GAGTCAGAGC ATCTGCTGGA ACCGGCAGAA
     CCAGGGACTC GTCCTTTACC TTCAGGTCCT CGGTCGTCTC GGTTGTCCAC AGTTGTACAA CAGGGGGCCC CTCAGTCTCG TAGACGACCT TGGCCGTCTT
 255  ValProGlu GlnGluMetG luValGlnGl uProAlaGlu ProThrGlyV alAsnMetLe uSerProGly GluSerGluH isLeuLeuGl uProAlaGlu

1001 GCTGAAAGGT CTCAGAGGAG GAGGCTGCTG GTTCCAGCAA ATGAAGGTGA TCCCACTGAG ACTCTGAGAC AGTGCTTCGA TGACTTTGCA GACTTGGTGC
     CGACTTTCCA GAGTCTCCTC CTCCGACGAC CAAGGTCGTT TACTTCCACT AGGGTGACTC TGAGACTCTG TCACGAAGCT ACTGAAACGT CTGAACCACG
 288 AlaGluArgS erGlnArgAr gArgLeuLeu ValProAlaA snGluGlyAs pProThrGlu ThrLeuArgG lnCysPheAs pAspPheAla AspLeuValPro

1101 CCTTTGACTC CTGGGAGCCG CTCATGAGGA AGTTGGGCCT CATGGACAAT GAGATAAAGG TGGCTAAAGC TGAGGCAGCG GGCCACAGGG ACACCTTGTA
     GGAAACTGAG GACCCTCGGC GAGTACTCCT TCAACCCGGA GTACCTGTTA CTCTATTTCC ACCGATTTCG ACTCCGTCGC CCGGTGTCCC TGTGGAACAT
 322    PheAspSe rTrpGluPro, LeuMetArgL ysLeuGlyLe uMetAspAsn GluIleLysV alAlaLysAl aGluAlaAla GlyHisArgA spThrLeuTyr

1201 CACGATGCTG ATAAAGTGGG TCAACAAAAC CGGGCGAGAT GCCTCTGTCC ACACCCTGCT GGATGCCTTG GAGACGCTGG GAGAGAGACT TGCCAAGCAG
     GTGCTACGAC TATTTCACCC AGTTGTTTTG GCCCGCTCTA CGGAGACAGG TGTGGGACGA CCTACGGAAC CTCTGCGACC CTCTCTCTGA ACGGTTCGTC
 355  ThrMetLeu IleLysTrpV alAsnLysTh rGlyArgAsp AlaSerValH isThrLeuLe uAspAlaLeu GluThrLeuG lyGluArgLe uAlaLysGln

1301 AAGATTGAGG ACCACTTGTT GAGCTCTGGA AAGTTCATGT ATCTAGAAGG TAATGCAGAC TCTGCCWTGT CCTAAGTGTG ATTCTCTTCA GGAAGTGAGA
     TTCTAACTCC TGGTGAACAA CTCGAGACCT TTCAAGTACA TAGATCTTCC ATTACGTCTG AGACGGAACA GGATTCACAC TAAGAGAAGT CCTTCACTCT
 388 LysIleGluA spHisLeuLe uSerSerGly LysPheMetT yrLeuGluGl yAsnAlaAsp SerAlaXaaS erOC*

1401 CCTTCCCTGG TTTACCTTTT TTCTGGAAAA AGCCCAACTG GACTCCAGTC AGTAGGAAAG TGCCACAATT GTCACATGAC CGGTACTGGA AGAAACTCTC
     GGAAGGGACC AAATGGAAAA AAGACCTTTT TCGGGTTGAC CTGAGGTCAG TCATCCTTTC ACGGTGTTAA CAGTGTACTG GCCATGACCT TCTTTGAGAG

1501 CCATCCAACA TCACCCAGTG GATGGAACAT CCTGTAACTT TTCACTGCAC TTGGCATTAT TTTTATAAGC TGAATGTGAT AATAAGGACA CTATGGAAAT
     GGTAGGTTGT AGTGGGTCAC CTACCTTGTA GGACATTGAA AAGTGACGTG AACCGTAATA AAAATATTCG ACTTACACTA TTATTCCTGT GATACCTTTA

1601 GTCTGGATCA TTCCGTTTGT GCGTACTTTG AGATTTGGTT TGGGATGTCA TTGTTTTCAC AGCACTTTTT TATCCTAATG TAAATGCTTT ATTTATTTAT
     CAGACCTAGT AAGGCAAACA CGCATGAAAC TCTAAACCAA ACCCTACAGT AACAAAAGTG TCGTGAAAAA ATAGGATTAC ATTTACGAAA TAAATAAATA

1701 TTGGGCTACA TTGTAAGATC CATCTACAAA AAAAAAAAAA AAAAAAAAAG GGCGGCCGCG ACTCTAGAGT CGACCTGCAG AAGCTTGGCC GCCATGGCC
     AACCCGATGT AACATTCTAG GTAGATGTTT TTTTTTTTTT TTTTTTTTTC CCGCCGGCGC TGAGATCTCA GCTGGACGTC TTCGAACCGG CGGTACCGG
```

*FIG. 25B*

```
ATG GAA CAA CGG GGA CAG AAC GCC CCG GCC GCT TCG GGG GCC CGG AAA     48
Met Glu Gln Arg Gly Gln Asn Ala Pro Ala Ala Ser Gly Ala Arg Lys
  1               5                  10                  15

AGG CAC GGC CCA GGA CCC AGG GAG GCG CGG GGA GCC AGG CCT GGG CCC     96
Arg His Gly Pro Gly Pro Arg Glu Ala Arg Gly Ala Arg Pro Gly Pro
            20                  25                  30

CGG GTC CCC AAG ACC CTT GTG CTC GTT GTC GCC GCG GTC CTG CTG TTG    144
Arg Val Pro Lys Thr Leu Val Leu Val Val Ala Ala Val Leu Leu Leu
        35                  40                  45

GTC TCA GCT GAG TCT GCT CTG ATC ACC CAA CAA GAC CTA GCT CCC CAG    192
Val Ser Ala Glu Ser Ala Leu Ile Thr Gln Gln Asp Leu Ala Pro Gln
    50                  55                  60

CAG AGA GCG GCC CCA CAA CAA AAG AGG TCC AGC CCC TCA GAG GGA TTG    240
Gln Arg Ala Ala Pro Gln Gln Lys Arg Ser Ser Pro Ser Glu Gly Leu
65                  70                  75                  80

TGT CCA CCT GGA CAC CAT ATC TCA GAA GAC GGT AGA GAT TGC ATC TCC    288
Cys Pro Pro Gly His His Ile Ser Glu Asp Gly Arg Asp Cys Ile Ser
                85                  90                  95

TGC AAA TAT GGA CAG GAC TAT AGC ACT CAC TGG AAT GAC CTC CTT TTC    336
Cys Lys Tyr Gly Gln Asp Tyr Ser Thr His Trp Asn Asp Leu Leu Phe
            100                 105                 110

TGC TTG CGC TGC ACC AGG TGT GAT TCA GGT GAA GTG GAG CTA AGT CCG    384
Cys Leu Arg Cys Thr Arg Cys Asp Ser Gly Glu Val Glu Leu Ser Pro
        115                 120                 125

TGC ACC ACG ACC AGA AAC ACA GTG TGT CAG TGC GAA GAA GGC ACC TTC    432
Cys Thr Thr Thr Arg Asn Thr Val Cys Gln Cys Glu Glu Gly Thr Phe
    130                 135                 140

CGG GAA GAA GAT TCT CCT GAG ATG TGC CGG AAG TGC CGC ACA GGG TGT    480
Arg Glu Glu Asp Ser Pro Glu Met Cys Arg Lys Cys Arg Thr Gly Cys
145                 150                 155                 160

CCC AGA GGG ATG GTC AAG GTC GGT GAT TGT ACA CCC TGG AGT GAC ATC    528
Pro Arg Gly Met Val Lys Val Gly Asp Cys Thr Pro Trp Ser Asp Ile
                165                 170                 175

GAA TGT GTC CAC AAA GAA TCA GGT ACA AAG CAC AGT GGG GAA GCC CCA    576
Glu Cys Val His Lys Glu Ser Gly Thr Lys His Ser Gly Glu Ala Pro
            180                 185                 190

GCT GTG GAG GAG ACG GTG ACC TCC AGC CCA GGG ACT CCT GCC TCT CCC    624
Ala Val Glu Glu Thr Val Thr Ser Ser Pro Gly Thr Pro Ala Ser Pro
        195                 200                 205

TGT TCT CTC TCA GGC ATC ATC ATA GGA GTC ACA GTT GCA GCC GTA GTC    672
Cys Ser Leu Ser Gly Ile Ile Ile Gly Val Thr Val Ala Ala Val Val
    210                 215                 220
```

FIG. 26A

```
TTG ATT GTG GCT GTG TTT GTT TGC AAG TCT TTA CTG TGG AAG AAA GTC   720
Leu Ile Val Ala Val Phe Val Cys Lys Ser Leu Leu Trp Lys Lys Val
225                 230                 235                 240

CTT CCT TAC CTG AAA GGC ATC TGC TCA GGT GGT GGT GGG GAC CCT GAG   768
Leu Pro Tyr Leu Lys Gly Ile Cys Ser Gly Gly Gly Gly Asp Pro Glu
                245                 250                 255

CGT GTG GAC AGA AGC TCA CAA CGA CCT GGG GCT GAG GAC AAT GTC CTC   816
Arg Val Asp Arg Ser Ser Gln Arg Pro Gly Ala Glu Asp Asn Val Leu
            260                 265                 270

AAT GAG ATC GTG AGT ATC TTG CAG CCC ACC CAG GTC CCT GAG CAG GAA   864
Asn Glu Ile Val Ser Ile Leu Gln Pro Thr Gln Val Pro Glu Gln Glu
        275                 280                 285

ATG GAA GTC CAG GAG CCA GCA GAG CCA ACA GGT GTC AAC ATG TTG TCC   912
Met Glu Val Gln Glu Pro Ala Glu Pro Thr Gly Val Asn Met Leu Ser
    290                 295                 300

CCC GGG GAG TCA GAG CAT CTG CTG GAA CCG GCA GAA GCT GAA AGG TCT   960
Pro Gly Glu Ser Glu His Leu Leu Glu Pro Ala Glu Ala Glu Arg Ser
305                 310                 315                 320

CAG AGG AGG AGG CTG CTG GTT CCA GCA AAT GAA GGT GAT CCC ACT GAG  1008
Gln Arg Arg Arg Leu Leu Val Pro Ala Asn Glu Gly Asp Pro Thr Glu
                325                 330                 335

ACT CTG AGA CAG TGC TTC GAT GAC TTT GCA GAC TTG GTG CCC TTT GAC  1056
Thr Leu Arg Gln Cys Phe Asp Asp Phe Ala Asp Leu Val Pro Phe Asp
            340                 345                 350

TCC TGG GAG CCG CTC ATG AGG AAG TTG GGC CTC ATG GAC AAT GAG ATA  1104
Ser Trp Glu Pro Leu Met Arg Lys Leu Gly Leu Met Asp Asn Glu Ile
        355                 360                 365

AAG GTG GCT AAA GCT GAG GCA GCG GGC CAC AGG GAC ACC TTG TAC ACG  1152
Lys Val Ala Lys Ala Glu Ala Ala Gly His Arg Asp Thr Leu Tyr Thr
    370                 375                 380

ATG CTG ATA AAG TGG GTC AAC AAA ACC GGG CGA GAT GCC TCT GTC CAC  1200
Met Leu Ile Lys Trp Val Asn Lys Thr Gly Arg Asp Ala Ser Val His
385                 390                 395                 400

ACC CTG CTG GAT GCC TTG GAG ACG CTG GGA GAG AGA CTT GCC AAG CAG  1248
Thr Leu Leu Asp Ala Leu Glu Thr Leu Gly Glu Arg Leu Ala Lys Gln
                405                 410                 415

AAG ATT GAG GAC CAC TTG TTG AGC TCT GGA AAG TTC ATG TAT CTA GAA  1296
Lys Ile Glu Asp His Leu Leu Ser Ser Gly Lys Phe Met Tyr Leu Glu
            420                 425                 430

GGT AAT GCA GAC TCT GCC ATG TCC TAA                             1323
Gly Asn Ala Asp Ser Ala Met Ser *
        435                 440
```

FIG. 26B

EVQLVQSGGGVERPGGSLRLSCAASGFTFDDYAMSWVRQAPGKGLEWVSGINWQGGSTGY
ADSVKGRVTISRDNAKNSLYLQMNSLRAEDTAVYYCAKILGAGRGWYFDYWGKGTTVTVS
SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS
SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

<451 residues; 0 stop; molecular weight: 49167.50

**FIG. 27**

SELTQDPAVSVALGQTVRITCSGDSLRSYYASWYQQKPGQAPVLVIYGANNRPSGIPDRF
SGSSSGNTASLTITGAQAEDEADYYCNSADSSGNHVVFGGGTKLTVLGQPKAAPSVTLFP
PSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS
LTPEQWKSHKSYSCQVTHEGSTVEKTVAPTECS

<213 residues; 0 stop; molecular weight: 22400.70

**FIG. 28**

**Alignment, 16ES and Apomab 7.3 Heavy Chains**

```
16E2          1 EVQLVQSGGGVERPGGSLRLSCAASGFTFDDYGMSW
                                                 *
Apomab7.3     1 EVQLVQSGGGVERPGGSLRLSCAASGFTFDDYAMSW

16E2         37 VRQAPGKGLEWVSGINWNGGSTGYADSVKGRVTISRDNAKNSLYLQMNSL
                                  *
Apomab7.3    37 VRQAPGKGLEWVSGINWQGGSTGYADSVKGRVTISRDNAKNSLYLQMNSL

16E2         87 RAEDTAVYYCAKILGAGRGWYFDLWGKGTTVTVSSASTKGPSVFPLAPSS
                                           *
Apomab7.3    87 RAEDTAVYYCAKILGAGRGWYFDYWGKGTTVTVSSASTKGPSVFPLAPSS

16E2        137 KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL
Apomab7.3   137 KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL

16E2        187 SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP
Apomab7.3   187 SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAP

16E2        237 ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
Apomab7.3   237 ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV

16E2        287 EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
Apomab7.3   287 EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI

16E2        337 EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
Apomab7.3   337 EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE

16E2        387 SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
Apomab7.3   387 SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL

16E2.huIgG1 437 HNHYTQKSLSLSPGK
Apomab7.3   437 HNHYTQKSLSLSPGK
```

***FIG. 29***

**Alignment, 16E2 and Apomab 7.3 Light Chains**

```
16E2          1 SELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKN
                                *                             *
Apomab7.3     1 SELTQDPAVSVALGQTVRITCSGDSLRSYYASWYQQKPGQAPVLVIYGAN

16E2         51 NRPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGG
                                              *
Apomab7.3    51 NRPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSADSSGNHVVFGG

16E2        101 GTKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWK
Apomab7.3   101 GTKLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWK

16E2        151 ADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSHKSYSCQVTHEG
Apomab7.3   151 ADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSHKSYSCQVTHEG

16E2        201 STVEKTVAPTECS
Apomab7.3   201 STVEKTVAPTECS
```

***FIG. 30***

**Apomab Variable Heavy Domain Sequence**

CDR H1
EVQLVQSGGGVERPGGSLRLSCAAS**GFTFDDYAM**WVRQAPGKGLEWV

CDR H2
S**GINWQGGSTGYADSVKG**RVTISRDNAKNSLYLQMNSLRAEDTAVYYCAK

CDR H3
**ILGAGRGWYFDY**WGKGTTVTVSSASTKGP

***FIG. 31A***

**Apomab Variable Light Domain Sequence**

CDR L1
SELTQDPAVSVALGQTVRITC**SGDSLRSYYAS**WYQQKPGQAPVLVIY

CDR L2 CDRL3
**GANNRPS**GIPDRFSGSSSGNTASLTITGAQAEDEADYYC**NSADSSGNHVV**

FGGGTKLTVLG

***FIG. 31B***

**Light Chain Alignment**

```
                1                                32
hu2H7.v16       DIQMTQSPSSLSASVGDRVTITCRASSSVSYMHWYQQKPGKAPKPLIYAP
                ********************************.**********
hu2H7.v511      DIQMTQSPSSLSASVGDRVTITCRASSSVSYLHWYQQKPGKAPKPLIYAP

               52
hu2H7.v16       SNLASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQWSFNPPTFGQG
                ****************************************.*********
hu2H7.v511      SNLASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQWAFNPPTFGQG

              102
hu2H7.v16       TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD
                **************************************************
hu2H7.v511      TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD

              152
hu2H7.v16       NALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL
                **************************************************
hu2H7.v511      NALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL

              202         214
hu2H7.v16       SSPVTKSFNRGEC
                *************
hu2H7.v511      SSPVTKSFNRGEC
```

***FIG. 32***

## Heavy Chain Alignment

```
                1
hu2H7.v16       EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYNMHW
                ************************************
hu2H7.v511      EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYNMHW

               37              52a                                82abc
hu2H7.v16       VRQAPGKGLEWVGAIYPGNGDTSYNQKFKGRFTISVDKSKNTLYLQMNSL
                ****************** ****************************
hu2H7.v511      VRQAPGKGLEWVGAIYPGNGATSYNQKFKGRFTISVDKSKNTLYLQMNSL

               83               100abcde          113
hu2H7.v16       RAEDTAVYYCARVVYYSNSYWYFDVWGQGTLVTVSS
                ****************  *****************
hu2H7.v511      RAEDTAVYYCARVVYYSYRYWYFDVWGQGTLVTVSS

              118
hu2H7.v16       ASTKGPSVFPLAPS
                **************
hu2H7.v511      ASTKGPSVFPLAPS

              132
hu2H7.v16       SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
                **************************************************
hu2H7.v511      SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS

              182
hu2H7.v16       LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA
                **************************************************
hu2H7.v511      LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA

              232
hu2H7.v16       PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
                **************************************************
hu2H7.v511      PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG

              282
hu2H7.v16       VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
                ***************.************************** *****
hu2H7.v511      VEVHNAKTKPREEQYNATYRVVSVLTVLHQDWLNGKEYKCKVSNAALPAP

              332
hu2H7.v16       IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
                *  **************************************************
hu2H7.v511      IAATISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW

              382
hu2H7.v16       ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
                **************************************************
hu2H7.v511      ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA

              432             447
hu2H7.v16       LHNHYTQKSLSLSPGK
                ****************
hu2H7.v511      LHNHYTQKSLSLSPGK
```

**FIG. 33**