

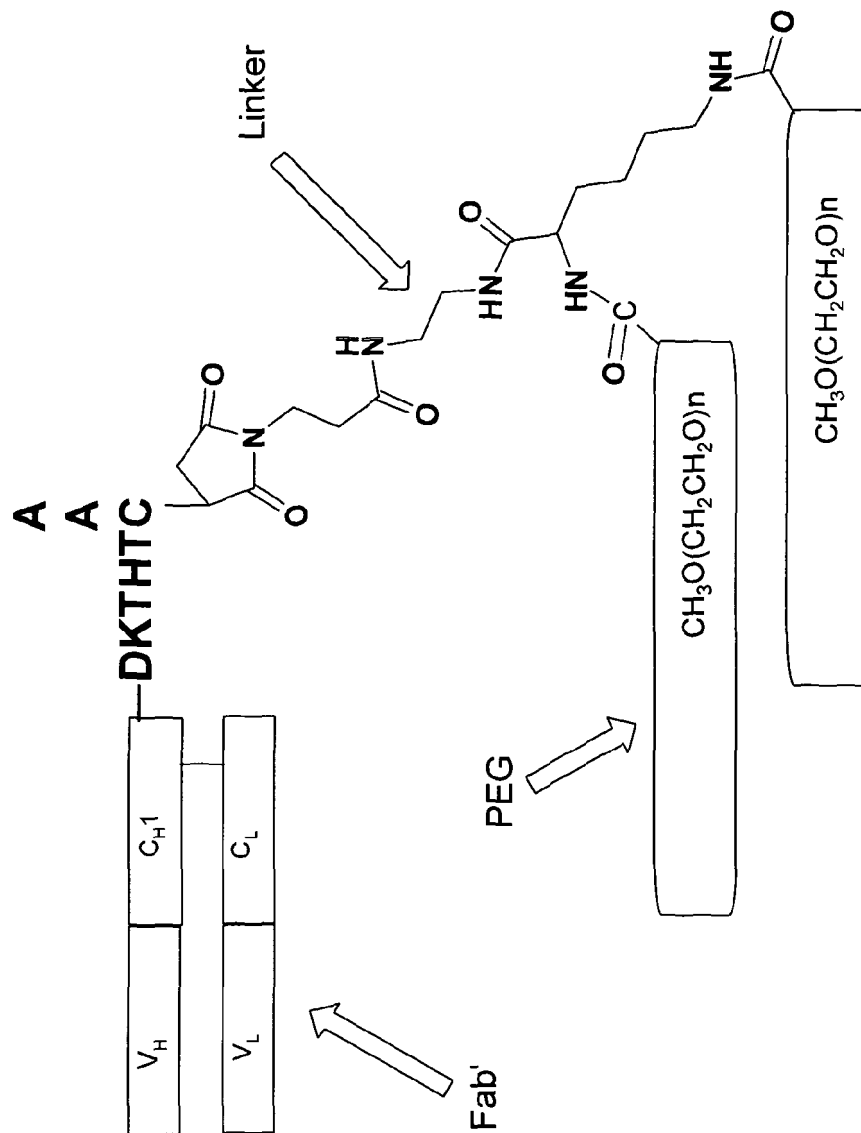


Figure 1 Schematic diagram of a PEGylated Fab' format.

Figure 2 Schematic diagram of a PEGylated Fab' format with deamidation in the Fab' fragment

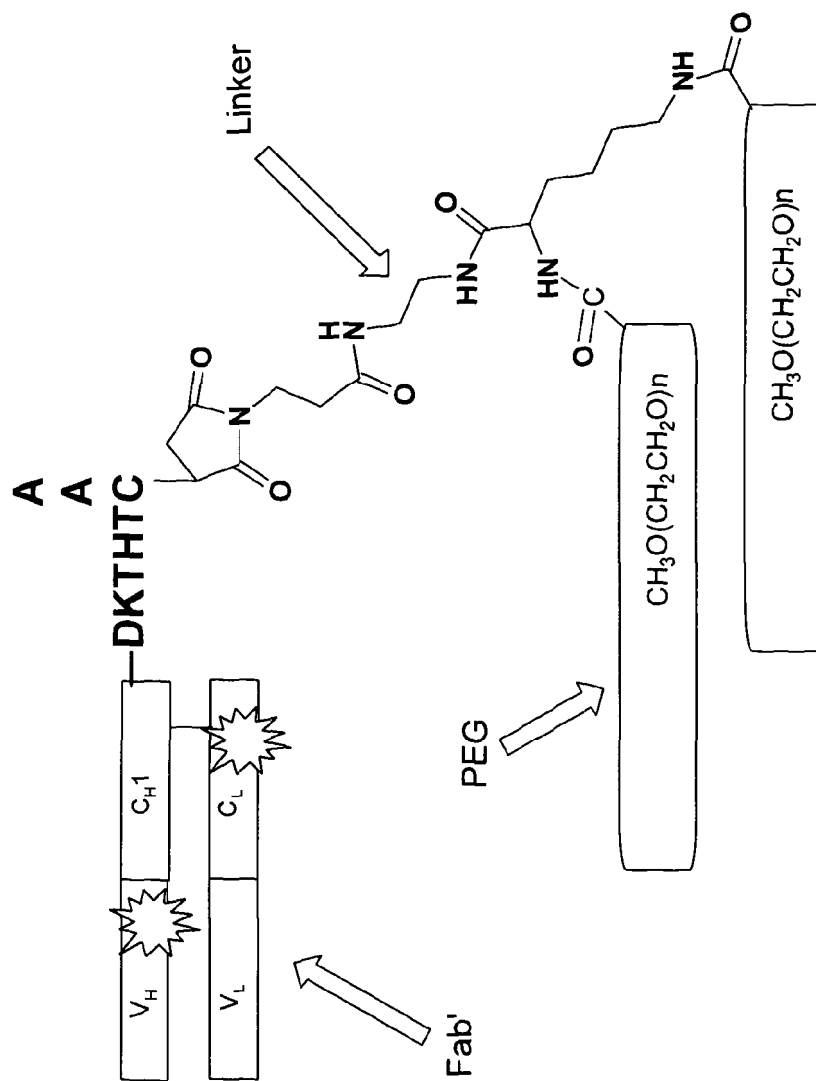


Figure 3 Schematic diagram of a PEGylated Fab' format with deamidation in the Fab' fragment and hydrolysis of the linker to generate acidic species

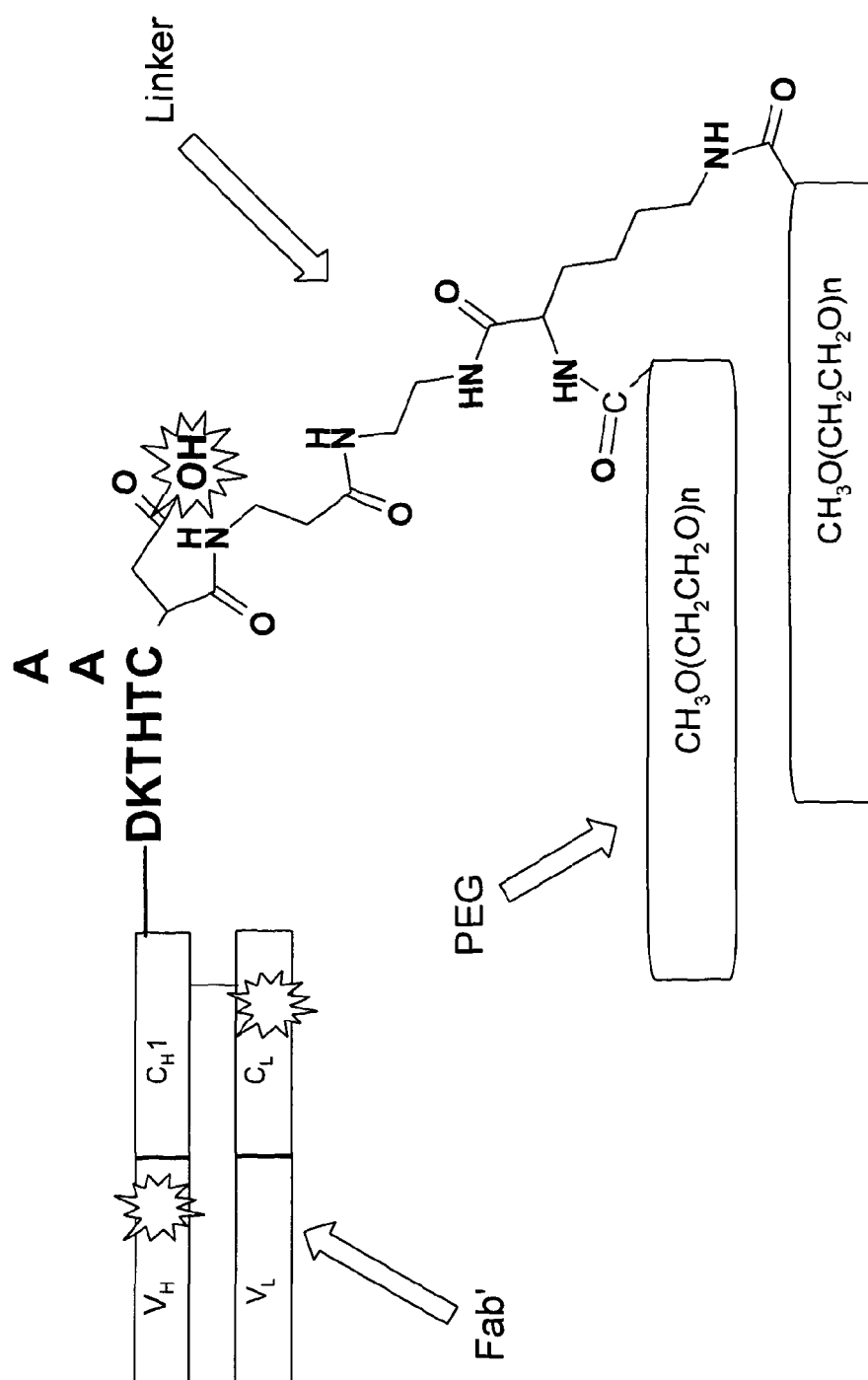


Figure 4 Schematic representation of the hydrolysis of Fab' and PEG maleimide followed by ring opening of the PEG linker succinimide ring

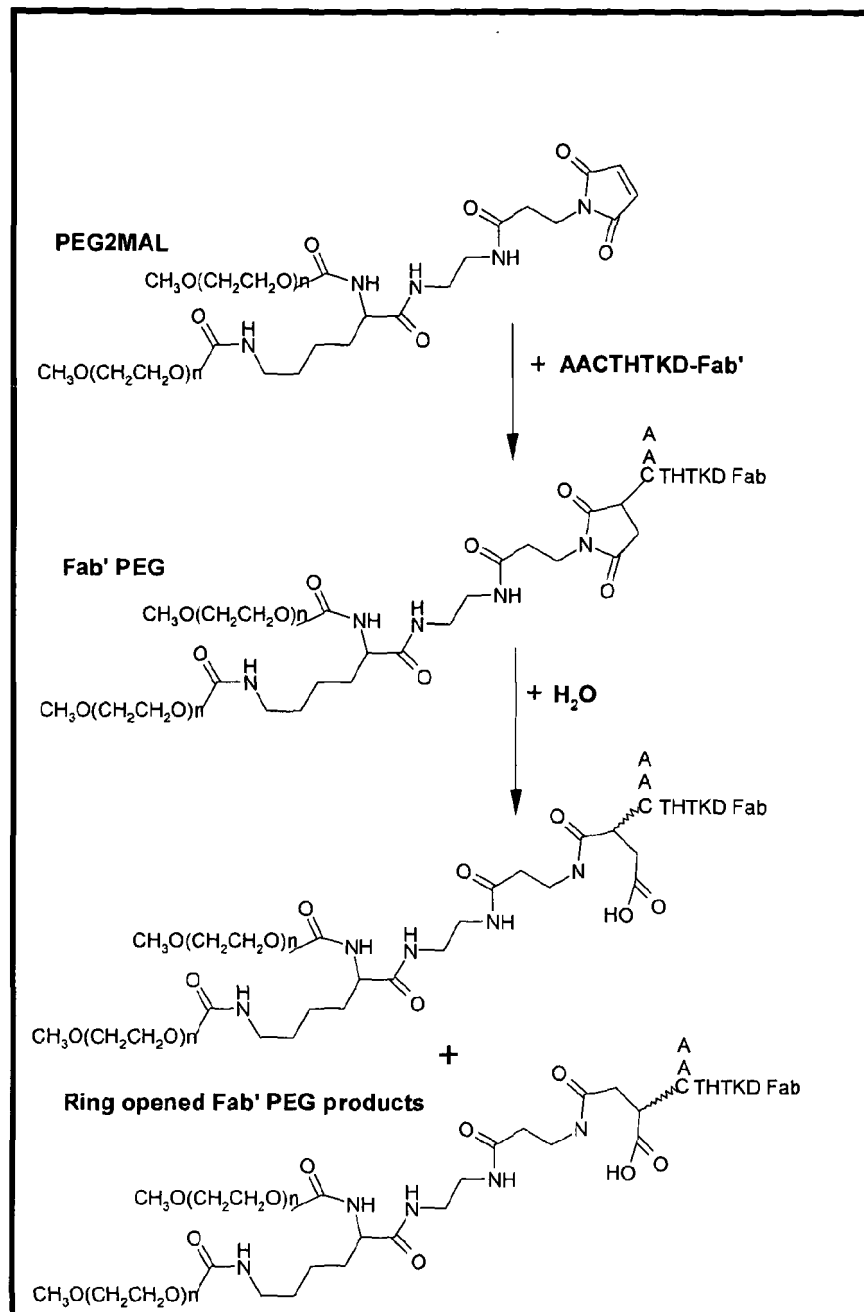
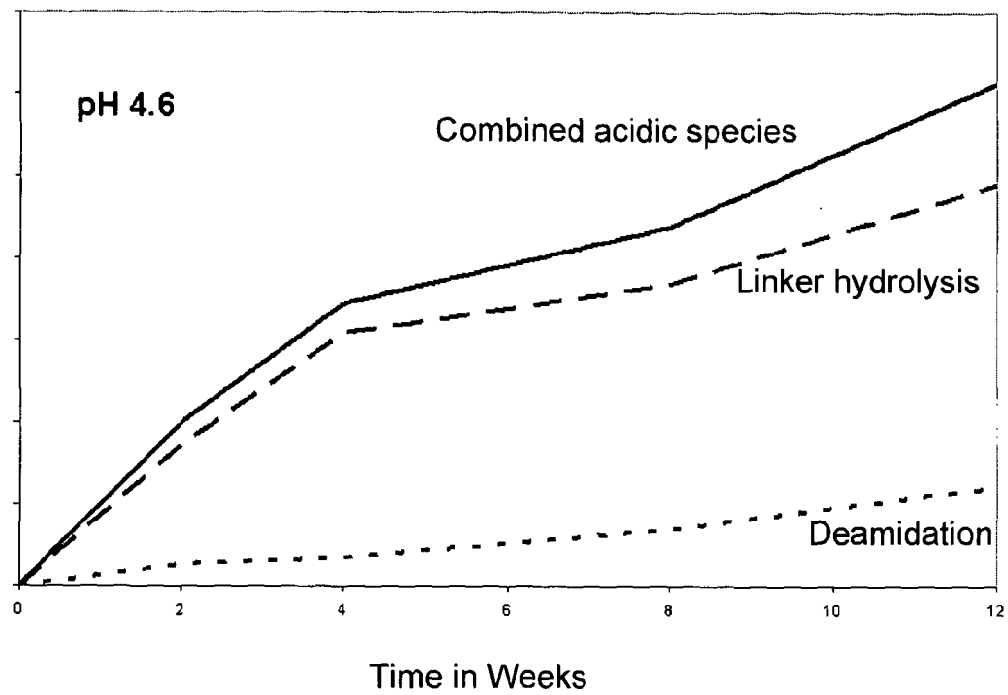


Figure 5

Analysis of combined acidic species, linker hydrolysis generated acidic species and acidic species generated through deamidation

% Acidic Species Generated



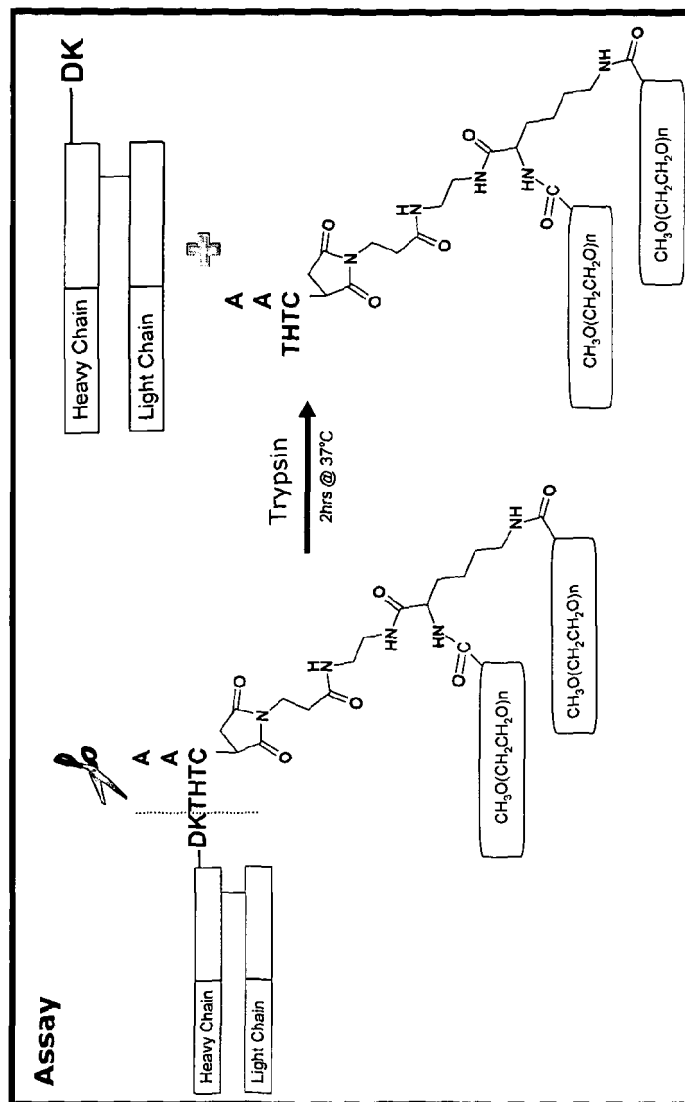


Figure 6

Figure 7 Efficiency of Tryptic Digest Conditions followed by HTRP HPLC

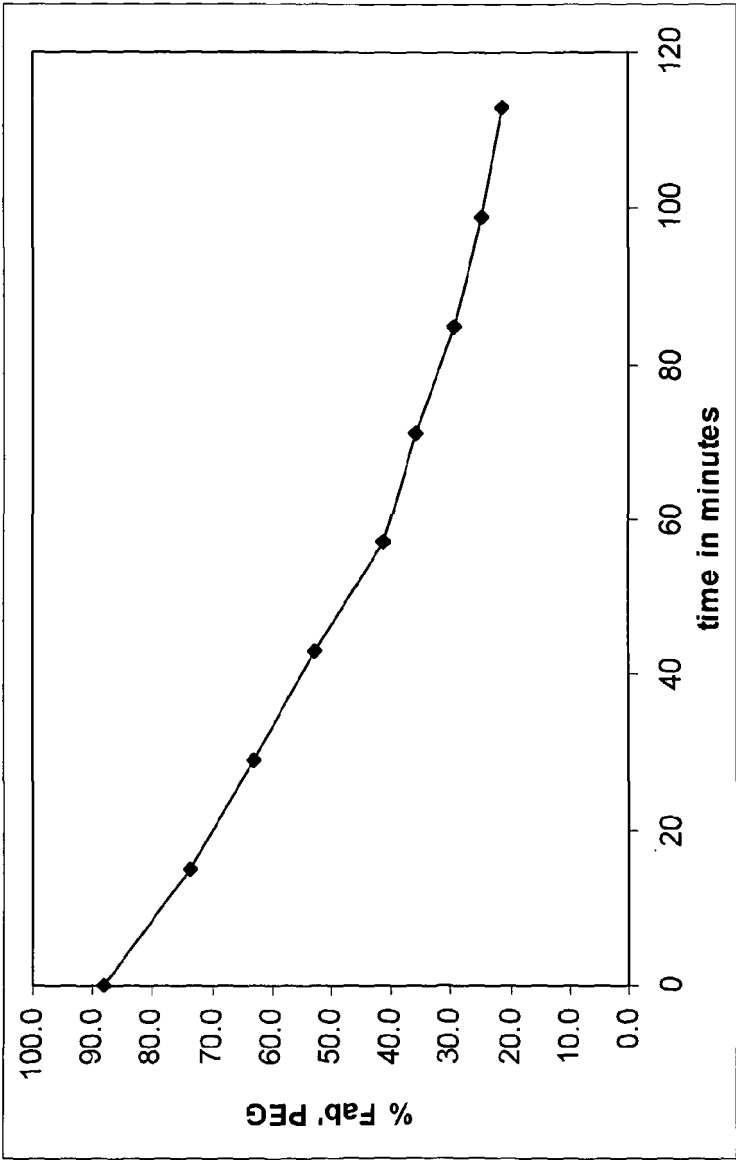


Figure 8 Fab' PEG CEX HPLC digest profile

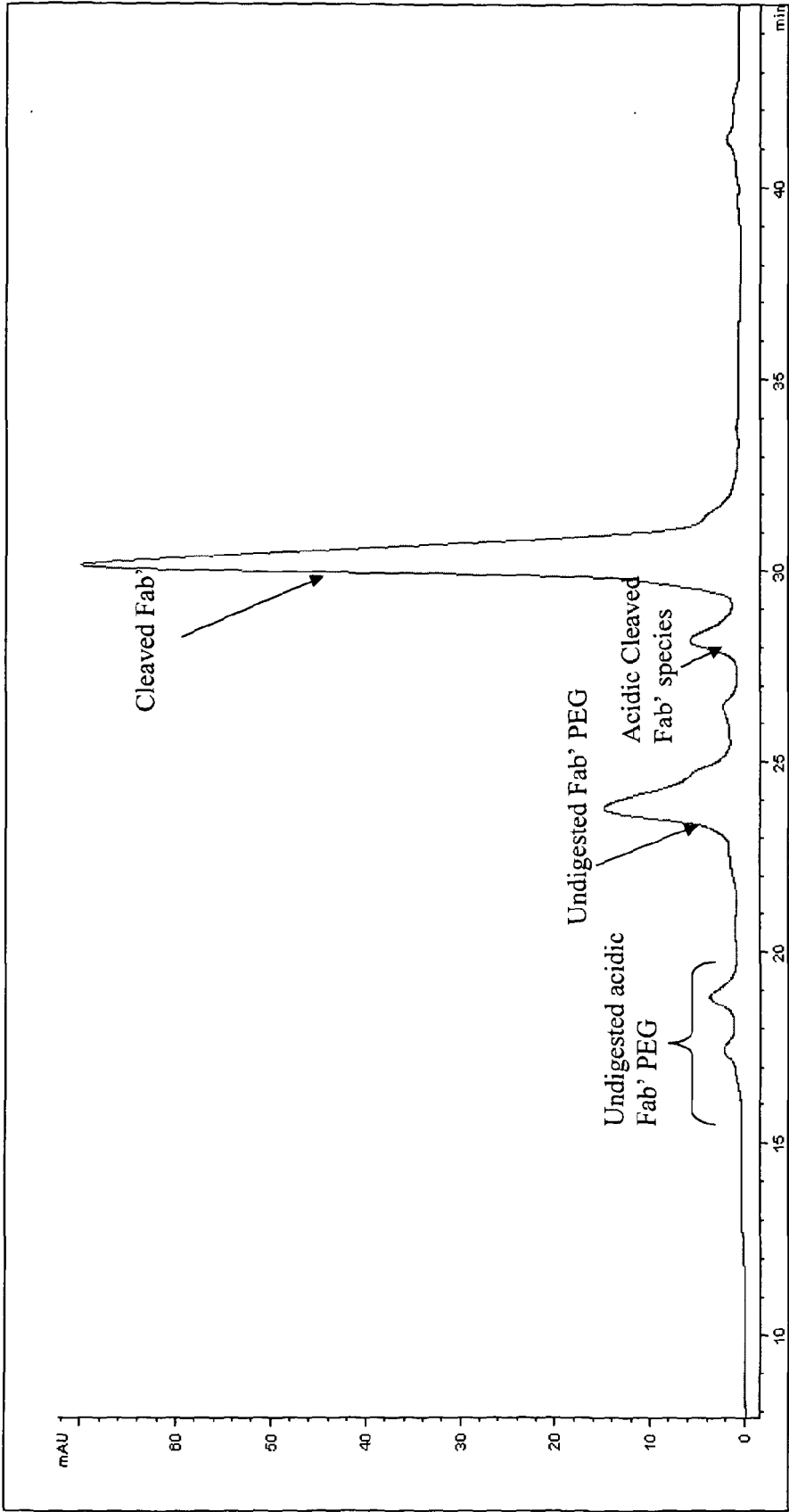


Figure 9 cIEF profile of tryptic digest of Fab' PEG

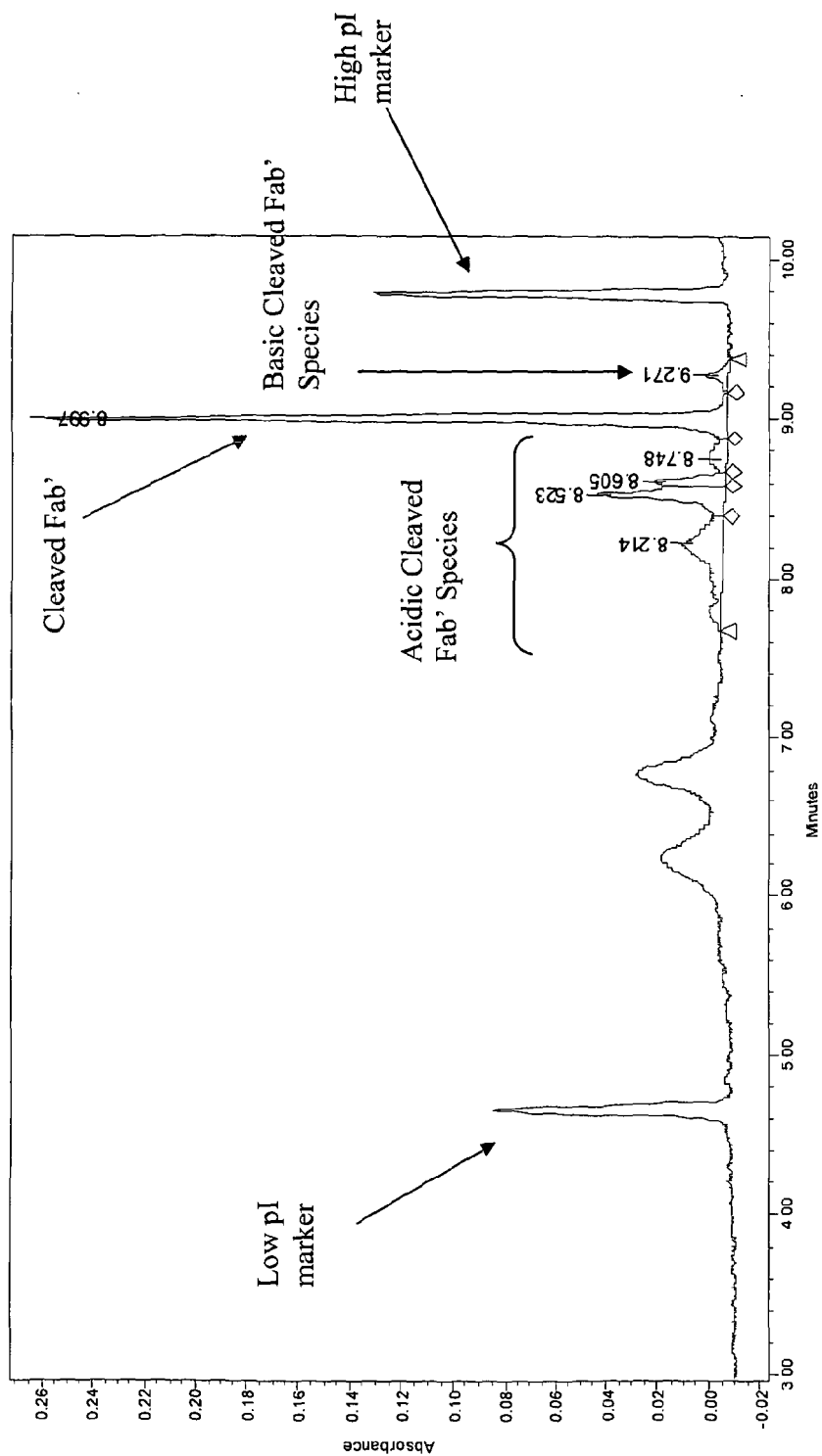


Figure 10

SEQ ID NO: 1 shows the amino acid sequence of CDRH1 of CDP870.

Asp Tyr Gly Met Asn

SEQ ID NO: 2 shows the amino acid sequence of CDRH2 of CDP870

Trp Ile Asn Thr Tyr Ile Gly Glu Pro Ile Tyr Ala Asp Ser Val Lys Gly

SEQ ID NO: 3 shows the amino acid sequence of CDRH3 of CDP870.

Gly Tyr Arg Ser Tyr Ala Met Asp Tyr

SEQ ID NO: 4 shows the amino acid sequence of CDRL1 of CDP870.

Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala

SEQ ID NO: 5 shows the amino acid sequence of CDRL2 of CDP870.

Ser Ala Ser Phe Leu Tyr Ser

SEQ ID NO: 6 shows the amino acid sequence of CDRL3 of CDP870.

Gln Gln Tyr Asn Ile Tyr Pro Leu Thr

SEQ ID NO: 7 shows the amino acid sequence of the light chain variable region CDP870

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala
Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn
Ile Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

SEQ ID NO:8 shows the amino acid sequence of the heavy chain variable region CDP870.

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
Ala Ser Gly Tyr Val Phe Thr Asp Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
Trp Met Gly Trp Ile Asn Thr Tyr Ile Gly Glu Pro Ile Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
Val Tyr Tyr Cys Ala Arg Gly Tyr Arg Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
Val Ser Ser

Figure 11

SEQ ID NO: 9 shows the amino acid sequence of a grafted anti-TNF α Fab CDP870 light chain.

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Ala
Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn
Ile Tyr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val
Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
Ser Phe Asn Arg Gly Glu Cys

SEQ ID NO: 10 shows the amino acid sequence of a grafted anti-TNF α Fab CDP870 heavy chain.

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
Ala Ser Gly Tyr Val Phe Thr Asp Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
Trp Met Gly Trp Ile Asn Thr Tyr Ile Gly Glu Pro Ile Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr
Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
Val Tyr Tyr Cys Ala Arg Gly Tyr Arg Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Ala Ala