CLAIMS

1. A peptide or peptide derivative comprising:

(i) WDLYFEIVW (SEQ ID NO: ~~1~~322); or

(ii) a variant amino acid sequence comprising one, two, three or four L-amino acid substitutions in WDLYFEIVW (SEQ ID NO: ~~1~~322), said variant amino acid sequence comprising $X_1X_2X_3YX_4EX_5X_6X_7$, wherein X_1 is W, L or P, X_2 is D or S, X_3 is L or F, X_4 is F, Phg, L, Ebw, Pff, Thi, 1Ni, Hfe, Ece or Cha, X_5 is I or F, X_6 is S, V or G and X_7 is W or L (SEQ ID NO:323)~~, wherein said one, two, three, or four substitutions are substitutions located at positions X_1, X_2, X_3, X_4, X_5, X_6, and/or X_7~~; or

(iii) the retro-inverso variant of the peptide or peptide derivative of either one of parts (i) and (ii), wherein said peptide or peptide derivative has procoagulant activity.

~~2. The peptide or peptide derivative of Claim 1 wherein the variant amino acid sequence comprises an amino acid sequence comprising $X_1X_2X_3YX_4EX_5X_6X_7$ wherein X_1 is W, L or P, X_2 is D or S, X_3 is L or F, X_4 is F, Phg, L, Ebw, Pff, Thi, 1Ni, Hfe, Ece or Cha, X_5 is I or F, X_6 is S, V or G and X_7 is W or L (SEQ ID NO: 1).~~

~~3~~2. The peptide or peptide derivative of Claim 1 wherein the variant amino acid sequence comprises an amino acid sequence comprising $X_1X_2X_3YX_4EX_5X_6X_7$ wherein X_1 is W or L, X_2 is D or S, X_3 is L or F, X_4 is F, Phg or L, X_5 is I or F, X_6 is S, V or G and X_7 is W or L (SEQ ID NO: ~~1~~324).

~~4~~3. The peptide or peptide derivative of Claim 1 comprising:

(1) RMEFDVWDLYFEIVW (SEQ ID NO: ~~2~~325); or

(2) RMKFDVWDLYFEIVW (SEQ ID NO: ~~2~~326); or

(2) a variant amino acid sequence comprising between one and six amino acid substitutions in RMEFDVWDLYFEIVW (SEQ ID NO: ~~2~~325) or RMKFDVWDLYFEIVW (SEQ ID NO: ~~2~~326).

~~5~~4. The peptide or peptide derivative of Claim ~~4~~3 wherein the variant amino acid sequence comprises an amino acid sequence comprising ~~More~~ $X_8X_9X_{10}FDVX_1X_2X_3YX_4EX_5X_6X_7$ wherein X_8 is R or P, X_9 is M, Nva, Moo, N, Nle, Meo, Q, Eag, X_{10} is E, K or D, X_1 is W, L or P, X_2 is D or S, X_3 is L or F, X_4 is F, Phg, L, Ebw, Pff, Thi, 1Ni, Hfe, Ece, Cha, X_5 is I or F, X_6 is S, V or G and X_7 is W or L (SEQ ID NO: ~~2~~327).

~~65~~. The peptide or peptide derivative of Claim ~~5~~ 4 wherein the variant amino acid sequence comprises an amino acid sequence comprising $X_8X_9X_{10}FDVX_1X_2X_3YX_4EX_5X_6X_7$ wherein X_8 is R or P, X_9 is M or Nva, X_{10} is E, K or D, X_1 is W or L, X_2 is D or S, X_3 is L or F, X_4 is F, Phg or L, X_5 is I or F, X_6 is S, V or G and X_7 is W or L (SEQ ID NO: ~~2~~328).

~~76~~. The peptide derivative of Claim 1 which is acetylated at the N-terminus, amidated at the C-terminus and/or PEGylated at either terminus.

~~87~~. The peptide or peptide derivative of Claim 1 which is cyclic.

~~98~~. The peptide or peptide derivative of Claim 1 comprising or consisting of:
Ac-RMKFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~329), Ac-PMKFDVWDLYFEIVW-NH_2 (SEQ ID NO: 330), Ac-RMDFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~331), Ac-RMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: 332), Ac-WDLYFEIVW-NH_2 (SEQ ID NO: 333~~2~~), Ac-WDLYFEIVWE (SEQ ID NO: ~~1~~334), Ac-WDLYFEIVW-ttds-E (SEQ ID NO: ~~3~~335), ttds-RMEFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~2~~336), ERMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: 4337), ER(Nva)EFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~5~~338), ttds-RMEFDVWDLY(Phg)EIVW-ttds-NH_2 (SEQ ID NO: 339), Ac-WSLYFEIVWE (SEQ ID NO: ~~6~~340), Ac-WDLYFEISW-ttds-E (SEQ ID NO: ~~1~~341), PEG5000-RMKFDVWDLYFEIVW-NH_2 (SEQ ID NO: 342), PEG5000-WSLYFEIVWE (SEQ ID NO: 343~~6~~), PEG5000-ERMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: 344), Ac-VWDLYFEIVW-NH_2 (SEQ ID NO: ~~7~~345), Ac-FDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~8~~346), EWDLYFEIVW-NH_2 (SEQ ID NO: ~~9~~347), E-ttds-WDLYFEIVW-NH_2 (SEQ ID NO: 348~~1~~), Ac-WDLYFEIVW-ttds-E-NH_2 (SEQ ID NO: 349~~1~~), Ac-RMEFDVWDLYFEIVW (SEQ ID NO: 350~~2~~), RMEFDVWDLYFEIVW (SEQ ID NO: ~~2~~325), Ac-K-ttds-RMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~351), Ac-RMEFDVWDLYFEIVWK (SEQ ID NO: ~~10~~352), Ac-RMEFDVWDLYFEIVWK-NH_2 (SEQ ID NO: ~~10~~353), Ac-RMEFDVWDLYFEIVW-ttds-K-NH_2 (SEQ ID NO: ~~2~~354), Ac-WDLYFEISWE (SEQ ID NO: ~~11~~355), Ac-WDLYLEIVWE (SEQ ID NO: ~~12~~356), Ac-WDLYFEIVLE (SEQ ID NO: ~~13~~357), WDLYFEIVW (SEQ ID NO: ~~1~~322), RMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~358), Ac-RMEFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: 359~~2~~), Ac-KRMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: 360~~14~~), K-ttds-RMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~361), Ac-RMEFDVWDLYFEIVW-ttds-K (SEQ ID NO: 362), Ac-LDLYFEIVW-ttds-E (SEQ ID NO: ~~1~~363), Ac-WDLYFEIVL-ttds-E (SEQ ID NO: 364~~1~~), E-RMEFDVLDLYFEIVW-NH_2 (SEQ ID NO: ~~15~~365), E-RMEFDVWDLYFEIVL-NH_2 (SEQ ID NO: ~~16~~366), Ac-WDFYFEIVWE (SEQ ID NO: ~~17~~367), Ac-WDLYFEFVWE (SEQ ID NO: ~~18~~368), Ac-LDLYFEIVWE (SEQ ID NO: ~~19~~369), Ac-WDLYFEIGWE (SEQ ID NO: ~~20~~370), Ac-

WDLYLEISLE (SEQ ID NO: ~~21~~371), Ac-WDLYXEIVLE (SEQ ID NO: 372), Ac-WSLYXEIVWE (SEQ ID NO: 373), Ac-LDLYFEIVLE (SEQ ID NO: ~~22~~374), Ac-LDLYFEISLE (SEQ ID NO: ~~23~~375), Ac-LDLYXEISWE (SEQ ID NO: 376), Ac-LSLYFEIVWE (SEQ ID NO: ~~24~~377), Ac-LSLYFEIVLE (SEQ ID NO: ~~25~~378), Ac-LSLYFEISLE (SEQ ID NO: ~~26~~379), Ac-WDLYFEIVW-ttds-K (SEQ ID NO: ~~1~~380), Ac-DVWDLYFEIVW-NH_2 (SEQ ID NO: ~~27~~381), Ac-wviefyldwvdfkmr-NH_2 (SEQ ID NO: 382), -Ac-WDLYFEIVW (SEQ ID NO: ~~1~~383), Ac-ttds-WDLYFEIVW-NH_2 (SEQ ID NO: ~~1~~384), -ttds-WDLYFEIVW-NH_2 (SEQ ID NO: ~~1~~385), -Ac-WDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~1~~386), Ac-ttds-WDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~1~~387), ttds-WDLYFEIVW-ttds (SEQ ID NO: ~~1~~388), ttds-WDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~1~~389), Ac-KWDLYFEIVW-NH_2 (SEQ ID NO: ~~28~~390), Ac-K-ttds-WDLYFEIVW-NH_2 (SEQ ID NO: 391), Ac-WDLYFEIVWK (SEQ ID NO: ~~29~~392), Ac-WDLYFEIVWK-NH_2 (SEQ ID NO: ~~29~~393), E-R(Moo)EFDVWDLYFEIVW-NH_2 (SEQ ID NO: 394), E-RNEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~30~~395), ttds-RMEFDVWDLY(Ebw)EIVW-ttds-NH_2 (SEQ ID NO: 396), ttds-RMEFDVWDLY(Pff)EIVW-ttds-NH_2 (SEQ ID NO: 397), Ac-PDLYFEIVWE (SEQ ID NO: 3~~1~~98), Ac-LSLYLEIVLE (SEQ ID NO: 3~~2~~99), Ac-LSLYLEISLE (SEQ ID NO: ~~33~~400), Ac-LSLYXEIVLE (SEQ ID NO: 401), Ac-WDLYFEIVW-ttds-K-NH_2 (SEQ ID NO: ~~1~~402), E-PMKFDVWDLYFEIVW-NH_2 (SEQ ID NO: 403~~34~~), ttds-RMDFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: 404~~2~~), PEG5000-RMKFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~405), WDLYFEIVW-NH_2 (SEQ ID NO: ~~1~~406), KRMEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~14~~407), ttds-PMKFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~2~~408), E-RMDFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~35~~409), (Coh)-ttds-RMEFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: 410), Glucosyl-aminooxyacetyl-ttds-RMEFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: 411), Ac-P(Moo)KFDVWDLYFEIVW-NH_2 (SEQ ID NO: 412), Ac-P(Nle)KFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~413), Ac-PNKFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~414), Ac-R(Moo)DFDVWDLYFEIVW-NH_2 (SEQ ID NO: 415), Ac-R(Nle)DFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~416), Ac-RNDFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~2~~417), ttds-R(Nle)EFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~2~~418), ttds-RNEFDVWDLYFEIVW-ttds-NH_2 (SEQ ID NO: ~~2~~419), E-R(Nle)EFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~321~~420), E-R(Meo)EFDVWDLYFEIVW-NH_2 (SEQ ID NO: 421), E-RQEFDVWDLYFEIVW-NH_2 (SEQ ID NO: ~~36~~422), E-R(Eag)EFDVWDLYFEIVW-NH_2 (SEQ ID NO: 423), ttds-RMEFDVWDLY(Thi)EIVW-ttds-NH_2 (SEQ ID NO: 424), ttds-RMEFDVWDLY(1Ni)EIVW-ttds-NH_2 (SEQ ID NO: 425), —ttds-RMEFDVWDLY(Hfe)EIVW-ttds-NH_2 (SEQ ID NO: 426), ttds-RMEFDVWDLY(Ece)EIVW-ttds-NH_2 (SEQ ID NO: 427), ttds-RMEFDVWDLY(Cha)EIVW-ttds-NH_2 (SEQ ID NO: 428), KWDLYFEIVW-NH_2 (SEQ ID NO: ~~28~~429), or K-ttds-WDLYFEIVW-NH_2 (SEQ ID NO: 430~~1~~), wherein -ttds- is 4,7,10-trioxa-1,13-tridecanediamine, (Nva) is norvaline, (Phg)

~~109~~. A dual peptide comprising a peptide or peptide derivative as defined in any one of claims Claim ~~1~~ 1 to 8 conjugated to a further peptide or peptide derivative as defined in any preceding claim, wherein the peptide or peptide derivative may be the same as or different from the further peptide or peptide derivative, and wherein the dual peptide has procoagulant activity.

~~11~~10. The peptide or peptide derivative of any one of Claims 1 to 8 which has a molecular weight of between 0.5 and 3.5kD.

~~12~~11. The peptide or peptide derivative of any one of Claims 1 to 8, wherein the procoagulant activity is a thrombin generation time of 25, 50 or 100 μM of peptide, peptide derivative or dual peptide equivalent to that of at least 100 mU/mL Factor Eight Inhibitor Bypassing Activity (FEIBA), preferably at least 300 mU/mL FEIBA, more preferably at least 900 mU/mL FEIBA, most preferably at least 1200 mU/mL FEIBA in the Defined Intrinsic Thrombin Generation Assay.

~~13~~12. The peptide or -peptide derivative of any one of Claims 1 to 8, wherein the procoagulant activity is a thrombin generation time of 25, 50 or 100 μM of peptide, peptide derivative or dual peptide in a Defined Intrinsic Thrombin Generation Assay peaking within 30 minutes, preferably within 15 minutes and most preferably within 10 minutes.

~~14~~13. The peptide or peptide derivative of any one of Claims 1 to 8 which can at least partially compensate for the absence of biologically active FVIII when administered in an animal model of severe human hemophilia A.

~~15~~14. The peptide or peptide derivative of any one of Claims 1 to 8 which has a stability in human plasma at 30 minutes of at least 50%, preferably at least 70%, more preferably at least 80% and most preferably at least 90%.

~~16~~15. The peptide or peptide derivative of any one of Claims 1 to 8 which has an aqueous solubility in phosphate buffered saline pH 7.4 of at least 25 μM, preferably at least 60 μM and most preferably at least 100 μM.

~~17~~16. A pharmaceutical composition comprising the peptide or peptide derivative of any one of Claim 1 to 8 or the dual peptide of claim 9 and one or more pharmaceutically acceptable excipients, carriers and/or diluents.

~~18~~17. The pharmaceutical composition of Claim ~~17~~ 16 suitable for subcutaneous, nasal, buccal, oral or pulmonary administration.

~~19~~18. The pharmaceutical composition of Claim ~~18~~ 17 suitable for intravenous administration.

~~20~~19. The peptide or peptide derivative of any one of Claims 1 to 8 for use in medicine.

~~21~~20. The peptide or peptide derivative of any one of Claims 1 to 8 for treating a patient having a deficiency in FV, FVII, FVIII, FX and/or FXI.

~~22~~21. Use of a peptide or peptide derivative of any one of Claims 1 to 8 in the manufacture of a medicament for the treatment of a deficiency in FV, FVII, FVIII, FX and/or FXI.

~~23~~22. The use of claim ~~22~~21, wherein said medicament is suitable for subcutaneous, nasal, buccal, oral or pulmonary administration.

~~24~~23. The use of claim ~~23~~22, wherein said medicament is suitable for intravenous administration.

~~25~~24. The peptide or peptide derivative of Claim ~~21~~20, wherein the patient has inhibitor antibodies against FV, FVII, FVIII, FX and/or FXI.

~~26~~25. The use of Claim ~~22~~21, wherein the patient has inhibitor antibodies against FV, FVII, FVIII, FX and/or FXI.

~~27~~26. A method of making the peptide or peptide derivative of any one of Claims 1 to 8 by solid phase synthesis.