

SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG and
 Roche Diagnostics GmbH

 <120> Improved DNA Polymerases and Related Methods

 <130> 24304 WO

 <140> Not yet assigned
 <141> Not yet assigned

 <150> US 60/949,732
 <151> 2007-07-13

 <160> 33

 <170> FastSEQ for Windows Version 4.0

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 thermostable DNA polymerase, polymerase domain
 motif

 <221> MOD_RES
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 <223> Xaa = His, Glu or Gln

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 <223> Xaa = Leu or Ile

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 <223> Xaa = Leu or Val
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 thermostable DNA polymerase, polymerase domain
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<221> MOD_RES
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<223> Xaa = Asn or His

<221> MOD_RES
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<223> Xaa = Leu, Ile or Pro

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caldophilus (Tca)

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 Z05 (Z05)

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aquaticus (Taq)

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flavus (Tfl)

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polymerase of thermophilic bacterium *Thermus*
filiformis (Tfi)

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sps17 (Sps17)

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20 25

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 <220>
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 polymerase of thermophilic bacterium Deinococcus
 radiodurans (Dra)

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 Glu Thr Val Leu Tyr Asp Lys Leu Glu Leu
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 <220>
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 polymerase of thermophilic bacterium Hot Spring
 family B/clone 7 (HspB)

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 Gly Ala Ile Leu Phe Glu Lys Leu Gly Leu
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 <220>
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 polymerase of thermophilic bacterium Bacillus
 stearothermophilus (Bst)

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 Gly Thr Val Leu Phe Asp Lys Leu Gln Leu
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 <220>
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 polymerase of thermophilic bacterium Bacillus
 caldotenax (Bca)

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Gly Val Ile Leu Phe Glu Lys Leu Gln Leu
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polymerase of thermophilic bacterium Escherichia
coli (Eco)

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Gln Thr Ile Leu Phe Glu Lys Gln Gly Ile
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<220>
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polymerase of thermophilic bacterium Thermotoga
maritime (Tma)

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Ser Arg Ile Leu Phe Glu Lys Leu Gly Ile
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<220>
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polymerase of thermophilic bacterium Thermotoga
neapolitana (Tne)

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Ser Asn Ile Leu Phe Glu Lys Leu Gly Ile
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 polymerase of thermophilic bacterium Thermosipho
 africanus (Taf)

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 Ala Tyr Ile Leu Phe Glu Lys Leu Asn Ile
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 <220>
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 polymerase of thermophilic bacterium Hot Spring
 family A (HspA)

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 Gly Ser Leu Leu Phe Glu Lys Leu Lys Leu
 20 25

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 polymerase of Bacteriophage T7 (T7)

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 Lys Leu Gln Glu Ala Gly Trp Val
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Lys	Ser	Leu	Leu	Lys	Ala	Leu	Lys	Glu	Asp	Gly	Tyr	Lys	Ala	Val	Phe	
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Val	Val	Phe	Asp	Ala	Lys	Ala	Pro	Ser	Phe	Arg	His	Glu	Ala	Tyr	Glu	
65					70					75					80	
Ala	Tyr	Lys	Ala	Gly	Arg	Ala	Pro	Thr	Pro	Glu	Asp	Phe	Pro	Arg	Gln	
				85					90					95		
Leu	Ala	Leu	Ile	Lys	Glu	Leu	Val	Asp	Leu	Leu	Gly	Phe	Thr	Arg	Leu	
			100					105						110		
Glu	Val	Pro	Gly	Phe	Glu	Ala	Asp	Asp	Val	Leu	Ala	Thr	Leu	Ala	Lys	
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Lys	Ala	Glu	Arg	Glu	Gly	Tyr	Glu	Val	Arg	Ile	Leu	Thr	Ala	Asp	Arg	
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Asp	Leu	Tyr	Gln	Leu	Val	Ser	Asp	Arg	Val	Ala	Val	Leu	His	Pro	Glu	
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Gly	His	Leu	Ile	Thr	Pro	Glu	Trp	Leu	Trp	Glu	Lys	Tyr	Gly	Leu	Lys	
				165					170					175		
Pro	Glu	Gln	Trp	Val	Asp	Phe	Arg	Ala	Leu	Val	Gly	Asp	Pro	Ser	Asp	
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Asn	Leu	Pro	Gly	Val	Lys	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Leu	Lys	Leu	
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Leu	Lys	Glu	Trp	Gly	Ser	Leu	Glu	Asn	Ile	Leu	Lys	Asn	Leu	Asp	Arg	
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Val	Lys	Pro	Glu	Ser	Val	Arg	Glu	Arg	Ile	Lys	Ala	His	Leu	Glu	Asp	
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Leu	Lys	Leu	Ser	Leu	Glu	Leu	Ser	Arg	Val	Arg	Ser	Asp	Leu	Pro	Leu	
				245					250					255		
Glu	Val	Asp	Phe	Ala	Arg	Arg	Arg	Glu	Pro	Asp	Arg	Glu	Gly	Leu	Arg	
			260					265					270			
Ala	Phe	Leu	Glu	Arg	Leu	Glu	Phe	Gly	Ser	Leu	Leu	His	Glu	Phe	Gly	
	275						280					285				
Leu	Leu	Glu	Glu	Ser	Glu	Pro	Val	Gly	Tyr	Arg	Ile	Val	Lys	Asp	Leu	
	290					295					300					
Val	Glu	Phe	Glu	Lys	Leu	Ile	Glu	Lys	Leu	Arg	Glu	Ser	Pro	Ser	Phe	
305					310					315					320	
Ala	Ile	Asp	Leu	Glu	Thr	Ser	Ser	Leu	Asp	Pro	Phe	Asp	Cys	Asp	Ile	
				325					330					335		
Val	Gly	Ile	Ser	Val	Ser	Phe	Lys	Pro	Lys	Glu	Ala	Tyr	Tyr	Ile	Pro	
			340					345					350			
Leu	His	His	Arg	Asn	Ala	Gln	Asn	Leu	Asp	Glu	Lys	Glu	Val	Leu	Lys	
	355						360					365				
Lys	Leu	Lys	Glu	Ile	Leu	Glu	Asp	Pro	Gly	Ala	Lys	Ile	Val	Gly	Gln	
	370					375					380					
Asn	Leu	Lys	Phe	Asp	Tyr	Lys	Val	Leu	Met	Val	Lys	Gly	Val	Glu	Pro	
385					390					395					400	
Val	Pro	Pro	Tyr	Phe	Asp	Thr	Met	Ile	Ala	Ala	Tyr	Leu	Leu	Glu	Pro	
				405					410					415		
Asn	Glu	Lys	Lys	Phe	Asn	Leu	Asp	Asp	Leu	Ala	Leu	Lys	Phe	Leu	Gly	
			420					425					430			
Tyr	Lys	Met	Thr	Ser	Tyr	Gln	Glu	Leu	Met	Ser	Phe	Ser	Phe	Pro	Leu	
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Phe	Gly	Phe	Ser	Phe	Ala	Asp	Val	Pro	Val	Glu	Lys	Ala	Ala	Asn	Tyr	
	450					455					460					
Ser	Cys	Glu	Asp	Ala	Asp	Ile	Thr	Tyr	Arg	Leu	Tyr	Lys	Thr	Leu	Ser	
465					470					475					480	
Leu	Lys	Leu	His	Glu	Ala	Asp	Leu	Glu	Asn	Val	Phe	Tyr	Lys	Ile	Glu	
				485					490					495		

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			500					505					510				
Val	Asp	Thr	Glu	Phe	Leu	Lys	Lys	Leu	Ser	Glu	Glu	Tyr	Gly	Lys	Lys		
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Leu	Glu	Glu	Leu	Ala	Glu	Glu	Ile	Tyr	Arg	Ile	Ala	Gly	Glu	Pro	Phe		
	530					535					540						
Asn	Ile	Asn	Ser	Pro	Lys	Gln	Val	Ser	Arg	Ile	Leu	Phe	Glu	Lys	Leu		
545					550					555					560		
Gly	Ile	Lys	Pro	Arg	Gly	Lys	Thr	Thr	Lys	Thr	Gly	Asp	Tyr	Ser	Thr		
			565						570						575		
Arg	Ile	Glu	Val	Leu	Glu	Glu	Leu	Ala	Gly	Glu	His	Glu	Ile	Ile	Pro		
			580					585							590		
Leu	Ile	Leu	Glu	Tyr	Arg	Lys	Ile	Gln	Lys	Leu	Lys	Ser	Thr	Tyr	Ile		
	595						600								605		
Asp	Ala	Leu	Pro	Lys	Met	Val	Asn	Pro	Lys	Thr	Gly	Arg	Ile	His	Ala		
	610					615					620						
Ser	Phe	Asn	Gln	Thr	Gly	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp		
625					630					635					640		
Pro	Asn	Leu	Gln	Asn	Leu	Pro	Thr	Lys	Ser	Glu	Glu	Gly	Lys	Glu	Ile		
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Arg	Lys	Ala	Ile	Val	Pro	Gln	Asp	Pro	Asn	Trp	Trp	Ile	Val	Ser	Ala		
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Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Ile	Leu	Ala	His	Leu	Ser	Gly	Asp		
		675					680					685					
Glu	Asn	Leu	Leu	Arg	Ala	Phe	Glu	Glu	Gly	Ile	Asp	Val	His	Thr	Leu		
	690					695					700						
Thr	Ala	Ser	Arg	Ile	Phe	Asn	Val	Lys	Pro	Glu	Glu	Val	Thr	Glu	Glu		
705					710						715					720	
Met	Arg	Arg	Ala	Gly	Lys	Met	Val	Asn	Phe	Ser	Ile	Ile	Tyr	Gly	Val		
				725					730						735		
Thr	Pro	Tyr	Gly	Leu	Ser	Val	Arg	Leu	Gly	Val	Pro	Val	Lys	Glu	Ala		
			740					745							750		
Glu	Lys	Met	Ile	Val	Asn	Tyr	Phe	Val	Leu	Tyr	Pro	Lys	Val	Arg	Asp		
		755					760								765		
Tyr	Ile	Gln	Arg	Val	Val	Ser	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg		
	770					775						780					
Thr	Leu	Phe	Gly	Arg	Lys	Arg	Asp	Ile	Pro	Gln	Leu	Met	Ala	Arg	Asp		
785					790						795				800		
Arg	Asn	Thr	Gln	Ala	Glu	Gly	Glu	Arg	Ile	Ala	Ile	Asn	Thr	Pro	Ile		
				805					810						815		
Gln	Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Leu	Ala	Met	Ile	Glu	Ile	Asp		
			820					825						830			
Arg	Glu	Leu	Lys	Glu	Arg	Lys	Met	Arg	Ser	Lys	Met	Ile	Ile	Gln	Val		
		835					840								845		
His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Leu		
	850					855									860		
Val	Glu	Leu	Val	Lys	Asp	Arg	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val		
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Pro	Leu	Glu	Val	Asp	Val	Thr	Ile	Gly	Lys	Thr	Trp	Ser					
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<220>
 <223> chimeric thermostable DNA polymerase CS6

<400> 21

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			20					25					30		
Leu	Thr	Thr	Ser	Arg	Gly	Glu	Pro	Val	Gln	Ala	Val	Tyr	Gly	Phe	Ala
		35					40					45			
Lys	Ser	Leu	Leu	Lys	Ala	Leu	Lys	Glu	Asp	Gly	Tyr	Lys	Ala	Val	Phe
	50					55					60				
Val	Val	Phe	Asp	Ala	Lys	Ala	Pro	Ser	Phe	Arg	His	Glu	Ala	Tyr	Glu
65					70					75					80
Ala	Tyr	Lys	Ala	Gly	Arg	Ala	Pro	Thr	Pro	Glu	Asp	Phe	Pro	Arg	Gln
				85					90					95	
Leu	Ala	Leu	Ile	Lys	Glu	Leu	Val	Asp	Leu	Leu	Gly	Phe	Thr	Arg	Leu
			100					105					110		
Glu	Val	Pro	Gly	Phe	Glu	Ala	Asp	Asp	Val	Leu	Ala	Thr	Leu	Ala	Lys
		115					120					125			
Lys	Ala	Glu	Arg	Glu	Gly	Tyr	Glu	Val	Arg	Ile	Leu	Thr	Ala	Asp	Arg
	130					135					140				
Asp	Leu	Tyr	Gln	Leu	Val	Ser	Asp	Arg	Val	Ala	Val	Leu	His	Pro	Glu
145					150					155					160
Gly	His	Leu	Ile	Thr	Pro	Glu	Trp	Leu	Trp	Glu	Lys	Tyr	Gly	Leu	Lys
				165					170					175	
Pro	Glu	Gln	Trp	Val	Asp	Phe	Arg	Ala	Leu	Val	Gly	Asp	Pro	Ser	Asp
			180					185					190		
Asn	Leu	Pro	Gly	Val	Lys	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Leu	Lys	Leu
	195						200					205			
Leu	Lys	Glu	Trp	Gly	Ser	Leu	Glu	Asn	Ile	Leu	Lys	Asn	Leu	Asp	Arg
	210					215					220				
Val	Lys	Pro	Glu	Ser	Val	Arg	Glu	Arg	Ile	Lys	Ala	His	Leu	Glu	Asp
225					230					235					240
Leu	Lys	Leu	Ser	Leu	Glu	Leu	Ser	Arg	Val	Arg	Ser	Asp	Leu	Pro	Leu
				245					250					255	
Glu	Val	Asp	Phe	Ala	Arg	Arg	Arg	Glu	Pro	Asp	Arg	Glu	Gly	Leu	Arg
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Ala	Phe	Leu	Glu	Arg	Leu	Glu	Phe	Gly	Ser	Leu	Leu	His	Glu	Phe	Gly
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Leu	Leu	Glu	Glu	Ser	Glu	Pro	Val	Gly	Tyr	Arg	Ile	Val	Lys	Asp	Leu
	290					295					300				
Val	Glu	Phe	Glu	Lys	Leu	Ile	Glu	Lys	Leu	Arg	Glu	Ser	Pro	Ser	Phe
305					310					315					320
Ala	Ile	Ala	Leu	Ala	Thr	Ser	Ser	Leu	Asp	Pro	Phe	Asp	Cys	Asp	Ile
				325					330					335	
Val	Gly	Ile	Ser	Val	Ser	Phe	Lys	Pro	Lys	Glu	Ala	Tyr	Tyr	Ile	Pro
				340				345					350		
Leu	His	His	Arg	Asn	Ala	Gln	Asn	Leu	Asp	Glu	Lys	Glu	Val	Leu	Lys
		355					360					365			
Lys	Leu	Lys	Glu	Ile	Leu	Glu	Asp	Pro	Gly	Ala	Lys	Ile	Val	Gly	Gln
	370					375					380				
Asn	Leu	Lys	Phe	Asp	Tyr	Lys	Val	Leu	Met	Val	Lys	Gly	Val	Glu	Pro
385					390					395					400
Val	Pro	Pro	Tyr	Phe	Asp	Thr	Met	Ile	Ala	Ala	Tyr	Leu	Leu	Glu	Pro
				405					410					415	
Asn	Glu	Lys	Lys	Phe	Asn	Leu	Asp	Asp	Leu	Ala	Leu	Lys	Phe	Leu	Gly
			420					425					430		
Tyr	Lys	Met	Thr	Ser	Tyr	Gln	Glu	Leu	Met	Ser	Phe	Ser	Phe	Pro	Leu
		435					440					445			
Phe	Gly	Phe	Ser	Phe	Ala	Asp	Val	Pro	Val	Glu	Lys	Ala	Ala	Asn	Tyr
	450					455					460				
Ser	Cys	Glu	Asp	Ala	Asp	Ile	Thr	Tyr	Arg	Leu	Tyr	Lys	Thr	Leu	Ser
465					470					475					480

Leu	Lys	Leu	His	Glu	Ala	Asp	Leu	Glu	Asn	Val	Phe	Tyr	Lys	Ile	Glu		
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			500					505					510				
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Gly	Ile	Lys	Pro	Arg	Gly	Lys	Thr	Thr	Lys	Thr	Gly	Asp	Tyr	Ser	Thr		
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Arg	Ile	Glu	Val	Leu	Glu	Glu	Leu	Ala	Gly	Glu	His	Glu	Ile	Ile	Pro		
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Leu	Ile	Leu	Glu	Tyr	Arg	Lys	Ile	Gln	Lys	Leu	Lys	Ser	Thr	Tyr	Ile		
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Ser	Phe	Asn	Gln	Thr	Gly	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp		
625					630					635					640		
Pro	Asn	Leu	Gln	Asn	Leu	Pro	Thr	Lys	Ser	Glu	Glu	Gly	Lys	Glu	Ile		
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Met	Arg	Arg	Ala	Gly	Lys	Met	Val	Asn	Phe	Ser	Ile	Ile	Tyr	Gly	Val		
			725						730					735			
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Tyr	Ile	Gln	Arg	Val	Val	Ser	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg		
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His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Leu		
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Val	Glu	Leu	Val	Lys	Asp	Arg	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val		
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<210> 22

<211> 2682

<212> DNA

<213> Artificial Sequence

<220>

<223> chimeric thermostable DNA polymerase CS5

<400> 22

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<210> 23

<211> 2682

<212> DNA

<213> Artificial Sequence

<220>

<223> chimeric thermostable DNA polymerase CS6

<400> 23

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<210> 24

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> consensus sequence of region from polymerase
domain of thermostable DNA polymerase, polymerase
domain motif consensus sequence

<221> MOD_RES

<222> (1)...(26)

<223> Xaa = any amino acid

<400> 24

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          20             25

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<210> 25
 <211> 16
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> region from polymerase domain of mutant
 thermostable DNA polymerase, polymerase domain
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 <221> MOD_RES
 <222> (1)...(1)
 <223> Xaa = Ile or Leu

 <221> MOD_RES
 <222> (2)...(2)
 <223> Xaa = Gln or Leu

 <221> MOD_RES
 <222> (3)...(3)
 <223> Xaa = Gln, His or Glu

 <221> MOD_RES
 <222> (4)...(4)
 <223> Xaa = Tyr, His or Phe

 <221> MOD_RES
 <222> (6)...(6)
 <223> Xaa = Glu, Gln or Lys

 <221> MOD_RES
 <222> (7)...(7)
 <223> Xaa = Ile, Leu or Tyr

 <221> MOD_RES
 <222> (8)...(8)
 <223> Xaa = Gln, Thr, Met, Gly or Leu

 <221> MOD_RES
 <222> (11)...(11)
 <223> Xaa = Lys or Gln

 <221> MOD_RES
 <222> (12)...(12)
 <223> Xaa = Ser or Asn

 <221> MOD_RES
 <222> (15)...(15)
 <223> Xaa = Ile or Val

 <221> MOD_RES
 <222> (16)...(16)
 <223> Xaa = Glu or Asp

 <400> 25
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 1 5 10 15

<210> 26
 <211> 13
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> region from polymerase domain of mutant
 thermostable DNA polymerase, polymerase domain
 motif

 <221> MOD_RES
 <222> (7)...(7)
 <223> Xaa = Ser or Thr

 <221> MOD_RES
 <222> (8)...(8)
 <223> Xaa = Asp, Glu or Asn

 <400> 26
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 1 5 10

 <210> 27
 <211> 15
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> region from polymerase domain of mutant
 thermostable DNA polymerase, polymerase domain
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 <221> MOD_RES
 <222> (1)...(1)
 <223> Xaa = Gly, Asn or Asp

 <221> MOD_RES
 <222> (2)...(2)
 <223> Xaa = Trp or His

 <221> MOD_RES
 <222> (3)...(3)
 <223> Xaa = Trp, Ala, Leu or Val

 <221> MOD_RES
 <222> (4)...(4)
 <223> Xaa = Ile or Leu

 <221> MOD_RES
 <222> (5)...(5)
 <223> Xaa = Val, Phe or Leu

 <221> MOD_RES
 <222> (6)...(6)
 <223> Xaa = Ser, Ala, Val or Gly

 <221> MOD_RES
 <222> (7)...(7)
 <223> Xaa = Ala or Leu

<400> 27
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1 5 10 15

<210> 28
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide template primer for M13mp18 (M13
DNA) extension assay screen

<400> 28
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30

<210> 29
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> region from polymerase domain of unmodified form
of thermostable DNA polymerase, polymerase domain
motif

<221> MOD_RES
<222> (3)...(3)
<223> Xaa = His, Glu or Gln

<221> MOD_RES
<222> (4)...(4)
<223> Xaa = any amino acid

<221> MOD_RES
<222> (6)...(6)
<223> Xaa = Asn or His

<221> MOD_RES
<222> (7)...(7)
<223> Xaa = Leu or Ile

<221> MOD_RES
<222> (8)...(8)
<223> Xaa = any amino acid

<221> MOD_RES
<222> (10)...(10)
<223> Xaa = any amino acid

<221> MOD_RES
<222> (11)...(11)
<223> Xaa = Asp, Lys or Thr

<221> MOD_RES
<222> (13)...(13)
<223> Xaa = Leu or Val

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<221> MOD_RES
<222> (14)...(15)
<223> Xaa = any amino acid

<221> MOD_RES
<222> (16)...(16)
<223> Xaa = Val, Ile or Leu

<221> MOD_RES
<222> (18)...(18)
<223> Xaa = Phe or Tyr

<221> MOD_RES
<222> (19)...(19)
<223> Xaa = Asp or Glu

<221> MOD_RES
<222> (20)...(20)
<223> Xaa = Lys or Glu

<221> MOD_RES
<222> (21)...(21)
<223> Xaa = Leu or Gln

<400> 29
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Leu Xaa Xaa Xaa Xaa
                20

<210> 30
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> conserved DNA polymerase active site Motif A

<400> 30
Asp Tyr Ser Gln Ile Glu Leu Arg
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<210> 31
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> region from polymerase domain of chimeric
        thermostable DNA polymerase CS5

<400> 31
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 1           5           10           15
Ser Arg Ile Leu Phe Glu Lys Leu Gly Ile
        20           25

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<210> 32
 <211> 26
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> region from polymerase domain of chimeric
 thermostable DNA polymerase CS6

 <400> 32
 Tyr Arg Ile Ala Gly Glu Pro Phe Asn Ile Asn Ser Pro Lys Gln Val
 1 5 10 15
 Ser Arg Ile Leu Phe Glu Lys Leu Gly Ile
 20 25

 <210> 33
 <211> 21
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> region from polymerase domain of modified improved
 thermostable DNA polymerase, polymerase domain
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 <221> MOD_RES
 <222> (3)...(3)
 <223> Xaa = His, Glu or Gln

 <221> MOD_RES
 <222> (4)...(4)
 <223> Xaa = any amino acid

 <221> MOD_RES
 <222> (6)...(6)
 <223> Xaa = Asn or His

 <221> MOD_RES
 <222> (7)...(7)
 <223> Xaa = Leu or Ile

 <221> MOD_RES
 <222> (8)...(8)
 <223> Xaa = any amino acid

 <221> MOD_RES
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 <223> Xaa = any amino acid

 <221> MOD_RES
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 <223> Xaa = Asp, Lys or Thr

 <221> MOD_RES
 <222> (13)...(13)
 <223> Xaa = Leu or Val

 <221> MOD_RES
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 <223> Xaa = any amino acid

<221> MOD_RES
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 <223> Xaa = Val, Ile or Leu

<221> MOD_RES
 <222> (18)...(18)
 <223> Xaa = Phe or Tyr

<221> MOD_RES
 <222> (20)...(20)
 <223> Xaa = Lys or Glu

<221> MOD_RES
 <222> (21)...(21)
 <223> Xaa = Leu or Gln

<400> 33
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 1 5 10 15
 Leu Xaa Gly Xaa Xaa
 20