wwPDB X-ray Structure Validation Summary Report (i)

Jan 30, 2017 – 08:49 PM EST

PDB ID	:	5TQ3
Title	:	Design and Synthesis of a pan-JAK kinase inhibitor clinical candidate (PF-06263276) suitable for the treatment of inflammatory diseases of the lungs and skin
Authors	:	Chrencik, J.; Jones, P.
Deposited on	:	2016-10-23
Resolution	:	2.69 Å(reported)

This is a wwPDB X-ray Structure Validation Summary Report for a publicly released PDB entry.

We welcome your comments at *validation@mail.wwpdb.org*
A user guide is available at
http://wwpdb.org/validation/2016/XrayValidationReportHelp
with specific help available everywhere you see the (i) symbol.

The following versions of software and data (see references (1)) were used in the production of this report:

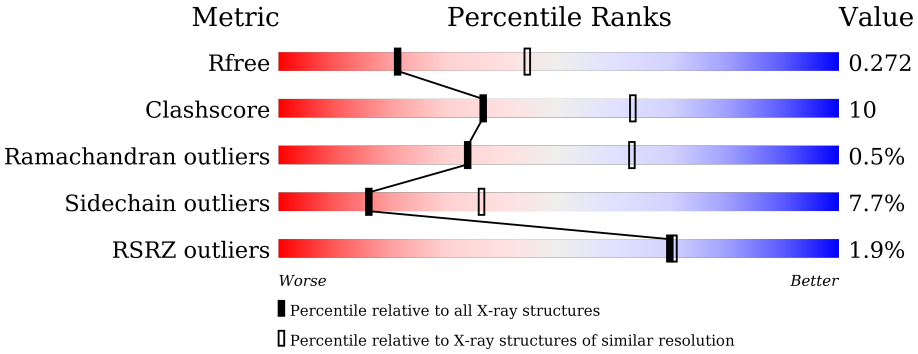
MolProbity	:	4.02b-467
Mogul	:	1.7.1 (RC1), CSD as537be (2016)
Xtriage (Phenix)	:	1.9-1692
EDS	:	rb-20028442
Percentile statistics	:	20151230.v01 (using entries in the PDB archive December 30th 2015)
Refmac	:	5.8.0135
CCP4	:	6.5.0
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	rb-20028442

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
X-RAY DIFFRACTION

The reported resolution of this entry is 2.69 Å.

Percentile scores (ranging between 0-100) for global validation metrics of the entry are shown in the following graphic. The table shows the number of entries on which the scores are based.



Metric	Whole archive (#Entries)	Similar resolution (#Entries, resolution range(Å))
R_{free}	91344	2103 (2.70-2.70)
Clashscore	102246	2422 (2.70-2.70)
Ramachandran outliers	100387	2382 (2.70-2.70)
Sidechain outliers	100360	2382 (2.70-2.70)
RSRZ outliers	91569	2107 (2.70-2.70)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the electron density. The red, orange, yellow and green segments on the lower bar indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria. A grey segment represents the fraction of residues that are not modelled. The numeric value for each fraction is indicated below the corresponding segment, with a dot representing fractions <=5% The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density. The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain
1	A	304	2% 73% 16% • 7%
1	B	304	2% 72% 18% • • 6%

2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 4714 atoms, of which 0 are hydrogens and 0 are deuteriums.

In the tables below, the ZeroOcc column contains the number of atoms modelled with zero occupancy, the AltConf column contains the number of residues with at least one atom in alternate conformation and the Trace column contains the number of residues modelled with at most 2 atoms.

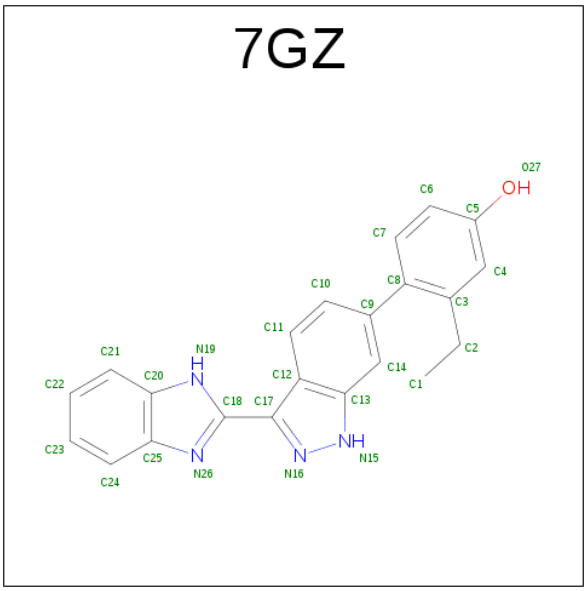
- Molecule 1 is a protein called Tyrosine-protein kinase JAK2.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
			Total	C	N	O	P	S			
1	A	284	2296	1466	391	424	2	13	0	1	0
1	B	287	2311	1472	391	433	2	13	0	0	0

There are 22 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	829	MET	-	initiating methionine	UNP O60674
A	830	GLY	-	expression tag	UNP O60674
A	831	HIS	-	expression tag	UNP O60674
A	832	HIS	-	expression tag	UNP O60674
A	833	HIS	-	expression tag	UNP O60674
A	834	HIS	-	expression tag	UNP O60674
A	835	HIS	-	expression tag	UNP O60674
A	836	HIS	-	expression tag	UNP O60674
A	1073	SER	MET	engineered mutation	UNP O60674
A	1076	THR	PHE	engineered mutation	UNP O60674
A	1126	VAL	ILE	engineered mutation	UNP O60674
B	829	MET	-	initiating methionine	UNP O60674
B	830	GLY	-	expression tag	UNP O60674
B	831	HIS	-	expression tag	UNP O60674
B	832	HIS	-	expression tag	UNP O60674
B	833	HIS	-	expression tag	UNP O60674
B	834	HIS	-	expression tag	UNP O60674
B	835	HIS	-	expression tag	UNP O60674
B	836	HIS	-	expression tag	UNP O60674
B	1073	SER	MET	engineered mutation	UNP O60674
B	1076	THR	PHE	engineered mutation	UNP O60674
B	1126	VAL	ILE	engineered mutation	UNP O60674

- Molecule 2 is 4-[3-(1H-benzimidazol-2-yl)-1H-indazol-6-yl]-3-ethylphenol (three-letter code: 7GZ) (formula: $C_{22}H_{18}N_4O$).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
			Total	C	N	O		
2	A	1	27	22	4	1	0	0
			Total	C	N	O		
2	B	1	27	22	4	1	0	0

- Molecule 3 is water.

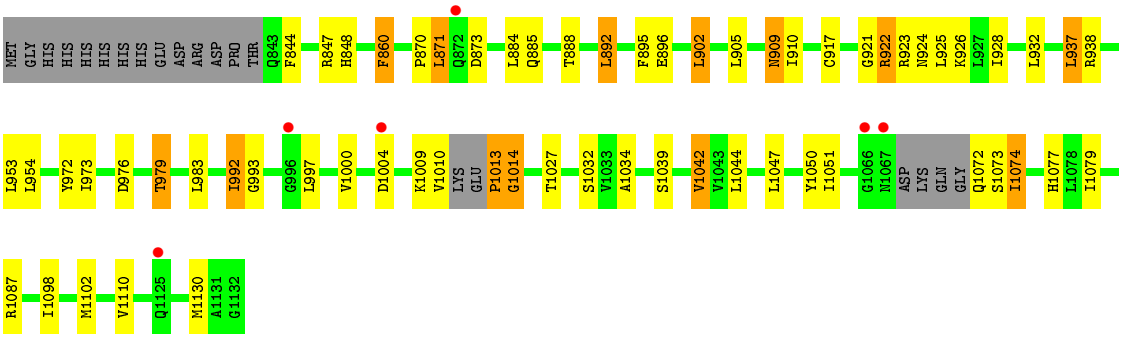
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
			Total	O		
3	A	26	26	26	0	0
			Total	O		
3	B	27	27	27	0	0

3 Residue-property plots (i)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. A red dot above a residue indicates a poor fit to the electron density (RSRZ > 2). Stretches of 2 or more consecutive residues without any outlier are shown as a green connector. Residues present in the sample, but not in the model, are shown in grey.

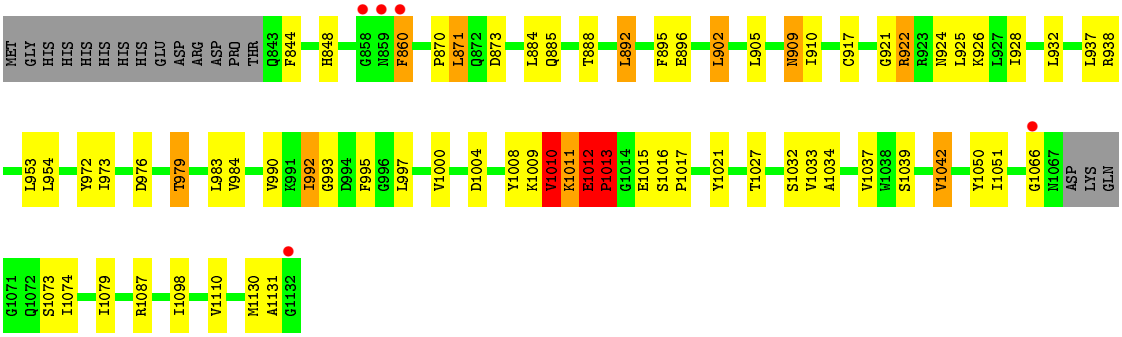
- Molecule 1: Tyrosine-protein kinase JAK2

Chain A:



- Molecule 1: Tyrosine-protein kinase JAK2

Chain B:



4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants a, b, c, α, β, γ	36.85Å 182.73Å 52.77Å 90.00° 110.41° 90.00°	Depositor
Resolution (Å)	34.54 – 2.69 34.54 – 2.69	Depositor EDS
% Data completeness (in resolution range)	90.9 (34.54-2.69) 90.9 (34.54-2.69)	Depositor EDS
R_{merge}	0.12	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	3.01 (at 2.68Å)	Xtriage
Refinement program	REFMAC 5.8.0073	Depositor
R, R_{free}	0.216 , 0.271 0.217 , 0.272	Depositor DCC
R_{free} test set	857 reflections (5.45%)	DCC
Wilson B-factor (Å^2)	37.4	Xtriage
Anisotropy	0.185	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.30 , 5.4	EDS
L-test for twinning[2]	$< \|L\| > = 0.49$, $< L^2 > = 0.32$	Xtriage
Estimated twinning fraction	0.406 for h,-k,-h-l	Xtriage
F_o,F_c correlation	0.91	EDS
Total number of atoms	4714	wwPDB-VP
Average B, all atoms (Å^2)	37.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 6.63% of the height of the origin peak. No significant pseudotranslation is detected.*

[1] Intensities estimated from amplitudes.

[2] Theoretical values of $< |L| >$, $< L^2 >$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.

5 Model quality (i)

5.1 Standard geometry (i)

Bond lengths and bond angles in the following residue types are not validated in this section: PTR, 7GZ

The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 5$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Chain	Bond lengths		Bond angles	
		RMSZ	$\#\|Z\| >5$	RMSZ	$\#\|Z\| >5$
1	A	0.49	0/2310	0.72	7/3112 (0.2%)
1	B	0.55	2/2326 (0.1%)	0.73	5/3136 (0.2%)
All	All	0.52	2/4636 (0.0%)	0.72	12/6248 (0.2%)

Chiral center outliers are detected by calculating the chiral volume of a chiral center and verifying if the center is modelled as a planar moiety or with the opposite hand. A planarity outlier is detected by checking planarity of atoms in a peptide group, atoms in a mainchain group or atoms of a sidechain that are expected to be planar.

Mol	Chain	#Chirality outliers	#Planarity outliers
1	A	0	6
1	B	0	6
All	All	0	12

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	B	1013	PRO	N-CD	5.29	1.55	1.47
1	B	1017	PRO	N-CD	5.24	1.55	1.47

The worst 5 of 12 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	A	1013	PRO	CB-CA-C	-10.93	84.69	112.00
1	A	1013	PRO	N-CA-C	9.68	137.27	112.10
1	B	922	ARG	N-CA-CB	-8.64	95.05	110.60
1	B	1131	ALA	CB-CA-C	-7.79	98.42	110.10
1	B	1074	ILE	N-CA-C	-7.45	90.89	111.00

There are no chirality outliers.

5 of 12 planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	A	1014	GLY	Peptide
1	A	873	ASP	Peptide
1	A	921	GLY	Peptide
1	A	922	ARG	Peptide
1	A	992	ILE	Peptide

5.2 Too-close contacts (i)

In the following table, the Non-H and H(model) columns list the number of non-hydrogen atoms and hydrogen atoms in the chain respectively. The H(added) column lists the number of hydrogen atoms added and optimized by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, whereas Symm-Clashes lists symmetry related clashes.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	2296	0	2224	38	0
1	B	2311	0	2234	49	0
2	A	27	0	0	1	0
2	B	27	0	0	1	0
3	A	26	0	0	0	0
3	B	27	0	0	0	0
All	All	4714	0	4458	87	0

The all-atom clashscore is defined as the number of clashes found per 1000 atoms (including hydrogen atoms). The all-atom clashscore for this structure is 10.

The worst 5 of 87 close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:B:1010:VAL:HA	1:B:1011:LYS:CB	1.77	1.13
1:B:1011:LYS:H	1:B:1012:GLU:HG2	1.18	1.07
1:B:1015:GLU:N	1:B:1015:GLU:OE2	1.87	1.06
1:B:1010:VAL:HA	1:B:1011:LYS:HB3	1.38	1.05
1:B:1011:LYS:HA	1:B:1012:GLU:HB2	1.55	0.86

There are no symmetry-related clashes.

5.3 Torsion angles (i)

5.3.1 Protein backbone (i)

In the following table, the Percentiles column shows the percent Ramachandran outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the backbone conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles	
1	A	277/304 (91%)	264 (95%)	13 (5%)	0	100	100
1	B	281/304 (92%)	262 (93%)	16 (6%)	3 (1%)	17	42
All	All	558/608 (92%)	526 (94%)	29 (5%)	3 (0%)	34	63

All (3) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	B	1011	LYS
1	B	1012	GLU
1	B	1013	PRO

5.3.2 Protein sidechains (i)

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the sidechain conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles	
1	A	238/275 (86%)	220 (92%)	18 (8%)	16	37
1	B	242/275 (88%)	223 (92%)	19 (8%)	15	34
All	All	480/550 (87%)	443 (92%)	37 (8%)	16	36

5 of 37 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	1087	ARG
1	B	888	THR
1	B	1042	VAL

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Mol	Chain	Res	Type
1	A	1130	MET
1	B	860	PHE

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 8 such sidechains are listed below:

Mol	Chain	Res	Type
1	A	1077	HIS
1	B	1077	HIS
1	B	885	GLN
1	A	924	ASN
1	B	853	GLN

5.3.3 RNA (i)

There are no RNA molecules in this entry.

5.4 Non-standard residues in protein, DNA, RNA chains (i)

4 non-standard protein/DNA/RNA residues are modelled in this entry.

In the following table, the Counts columns list the number of bonds (or angles) for which Mogul statistics could be retrieved, the number of bonds (or angles) that are observed in the model and the number of bonds (or angles) that are defined in the chemical component dictionary. The Link column lists molecule types, if any, to which the group is linked. The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\| > 2$	Counts	RMSZ	$\#\|Z\| > 2$
1	PTR	A	1007	1	13,16,17	2.02	1 (7%)	19,22,24	0.78	0
1	PTR	A	1008	1	13,16,17	1.94	1 (7%)	19,22,24	0.84	0
1	PTR	B	1007	1	13,16,17	2.07	1 (7%)	19,22,24	0.68	0
1	PTR	B	1008	1	13,16,17	2.03	1 (7%)	19,22,24	0.85	0

In the following table, the Chirals column lists the number of chiral outliers, the number of chiral centers analysed, the number of these observed in the model and the number defined in the chemical component dictionary. Similar counts are reported in the Torsion and Rings columns. '-' means no outliers of that kind were identified.

Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
1	PTR	A	1007	1	-	0/9/11/13	0/1/1/1
1	PTR	A	1008	1	-	0/9/11/13	0/1/1/1
1	PTR	B	1007	1	-	0/9/11/13	0/1/1/1
1	PTR	B	1008	1	-	0/9/11/13	0/1/1/1

All (4) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	B	1007	PTR	OH-CZ	-7.06	1.23	1.40
1	A	1007	PTR	OH-CZ	-6.87	1.24	1.40
1	B	1008	PTR	OH-CZ	-6.83	1.24	1.40
1	A	1008	PTR	OH-CZ	-6.78	1.24	1.40

There are no bond angle outliers.

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
1	B	1008	PTR	1	0

5.5 Carbohydrates (i)

There are no carbohydrates in this entry.

5.6 Ligand geometry (i)

2 ligands are modelled in this entry.

In the following table, the Counts columns list the number of bonds (or angles) for which Mogul statistics could be retrieved, the number of bonds (or angles) that are observed in the model and the number of bonds (or angles) that are defined in the chemical component dictionary. The Link column lists molecule types, if any, to which the group is linked. The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\| > 2$	Counts	RMSZ	$\#\|Z\| > 2$
2	7GZ	A	4000	-	27,31,31	0.82	1 (3%)	30,45,45	0.87	2 (6%)

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\| > 2$	Counts	RMSZ	$\#\|Z\| > 2$
2	7GZ	B	4001	-	27,31,31	0.82	1 (3%)	30,45,45	0.88	2 (6%)

In the following table, the Chirals column lists the number of chiral outliers, the number of chiral centers analysed, the number of these observed in the model and the number defined in the chemical component dictionary. Similar counts are reported in the Torsion and Rings columns. '-' means no outliers of that kind were identified.

Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
2	7GZ	A	4000	-	-	0/6/18/18	0/5/5/5
2	7GZ	B	4001	-	-	0/6/18/18	0/5/5/5

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	4000	7GZ	C17-C18	-3.23	1.46	1.53
2	B	4001	7GZ	C17-C18	-3.18	1.46	1.53

All (4) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	B	4001	7GZ	C25-N26-C18	-2.34	104.70	108.76
2	A	4000	7GZ	C25-N26-C18	-2.33	104.73	108.76
2	B	4001	7GZ	C21-C20-N19	2.90	132.53	127.74
2	A	4000	7GZ	C21-C20-N19	2.91	132.54	127.74

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

2 monomers are involved in 2 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	4000	7GZ	1	0
2	B	4001	7GZ	1	0

5.7 Other polymers (i)

There are no such residues in this entry.

5.8 Polymer linkage issues (i)

There are no chain breaks in this entry.

6 Fit of model and data (i)

6.1 Protein, DNA and RNA chains (i)

In the following table, the column labelled '#RSRZ> 2' contains the number (and percentage) of RSRZ outliers, followed by percent RSRZ outliers for the chain as percentile scores relative to all X-ray entries and entries of similar resolution. The OWAB column contains the minimum, median, 95th percentile and maximum values of the occupancy-weighted average B-factor per residue. The column labelled 'Q< 0.9' lists the number of (and percentage) of residues with an average occupancy less than 0.9.

Mol	Chain	Analysed	<RSRZ>	#RSRZ>2			OWAB(Å^2)	Q<0.9
1	A	282/304 (92%)	0.10	6 (2%)	67	68	21, 34, 63, 91	0
1	B	285/304 (93%)	-0.00	5 (1%)	71	72	22, 34, 64, 90	0
All	All	567/608 (93%)	0.05	11 (1%)	70	70	21, 34, 64, 91	0

The worst 5 of 11 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	1132	GLY	8.1
1	B	860	PHE	3.7
1	A	1125	GLN	2.9
1	B	859	ASN	2.8
1	A	1067	ASN	2.6

6.2 Non-standard residues in protein, DNA, RNA chains (i)

In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	LLDF	B-factors(Å^2)	Q<0.9
1	PTR	B	1008	16/17	0.85	0.20	-	39,49,57,64	0
1	PTR	A	1008	16/17	0.84	0.20	-	39,49,59,68	0
1	PTR	A	1007	16/17	0.88	0.15	-	43,55,62,65	0
1	PTR	B	1007	16/17	0.89	0.17	-	42,55,64,68	0

6.3 Carbohydrates (i)

There are no carbohydrates in this entry.

6.4 Ligands (i)

In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	LLDF	B-factors(Å^2)	Q<0.9
2	7GZ	B	4001	27/27	0.92	0.19	0.71	21,24,29,32	0
2	7GZ	A	4000	27/27	0.94	0.16	-0.97	20,23,28,29	0

6.5 Other polymers (i)

There are no such residues in this entry.