



Full wwPDB X-ray Structure Validation Report ⓘ

Aug 29, 2016 – 06:07 PM EDT

PDB ID : 5ITD
Title : Crystal structure of PI3K alpha with PI3K delta inhibitor
Authors : Knapp, M.S.; Elling, R.A.
Deposited on : 2016-03-16
Resolution : 3.02 Å(reported)

This is a Full wwPDB X-ray Structure Validation 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 ⓘ symbol.

The following versions of software and data (see [references ⓘ](#)) 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-20027939
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-20027939

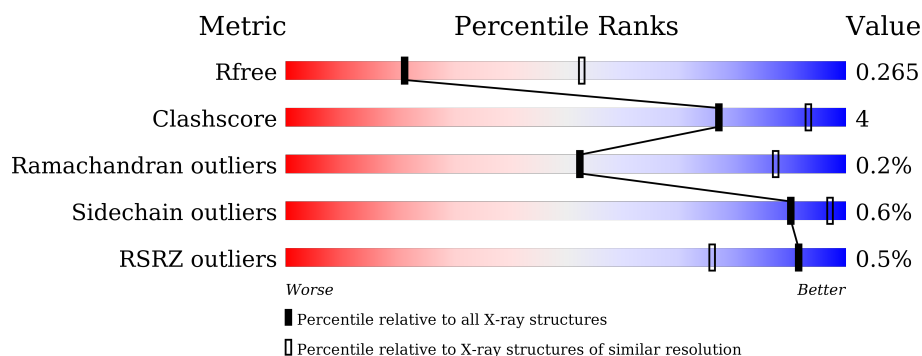
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION



The reported resolution of this entry is 3.02 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	1773 (3.04-3.00)
Clashscore	102246	2117 (3.04-3.00)
Ramachandran outliers	100387	2050 (3.04-3.00)
Sidechain outliers	100360	2053 (3.04-3.00)
RSRZ outliers	91569	1788 (3.04-3.00)

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 $\leq 5\%$. 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	1074	 83% 9% 7%
2	B	323	 % 64% 9% • 27%

The following table lists non-polymeric compounds, carbohydrate monomers and non-standard residues in protein, DNA, RNA chains that are outliers for geometric or electron-density-fit criteria:

Mol	Type	Chain	Res	Chirality	Geometry	Clashes	Electron density
3	6CY	A	1101	-	-	-	X

2 Entry composition

There are 4 unique types of molecules in this entry. The entry contains 9860 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 Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	995	Total	C	N	O	S	0	0	0
			7905	5050	1346	1446	63			

There are 8 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	232	LYS	MET	engineered mutation	UNP P42336
A	233	LYS	LEU	engineered mutation	UNP P42336
A	1069	HIS	-	expression tag	UNP P42336
A	1070	HIS	-	expression tag	UNP P42336
A	1071	HIS	-	expression tag	UNP P42336
A	1072	HIS	-	expression tag	UNP P42336
A	1073	HIS	-	expression tag	UNP P42336
A	1074	HIS	-	expression tag	UNP P42336

- Molecule 2 is a protein called Phosphatidylinositol 3-kinase regulatory subunit alpha.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
2	B	237	Total	C	N	O	S	0	0	0
			1867	1162	330	371	4			

There are 8 discrepancies between the modelled and reference sequences:

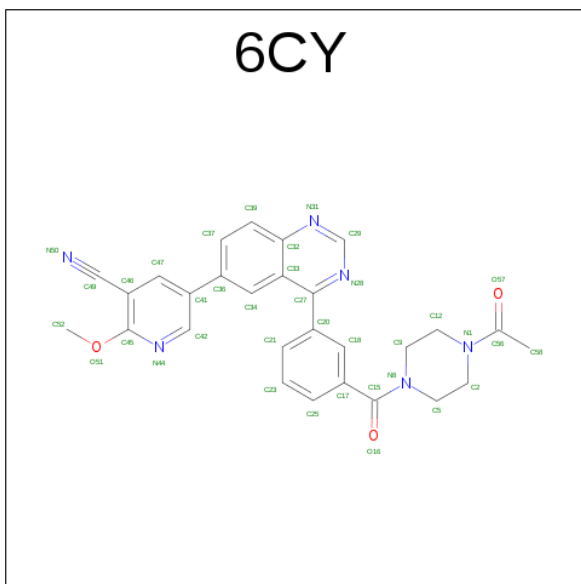
Chain	Residue	Modelled	Actual	Comment	Reference
B	295	MET	-	initiating methionine	UNP P27986
B	296	GLU	-	expression tag	UNP P27986
B	297	TYR	-	expression tag	UNP P27986
B	298	MET	-	expression tag	UNP P27986
B	299	PRO	-	expression tag	UNP P27986
B	300	MET	-	expression tag	UNP P27986
B	301	GLU	-	expression tag	UNP P27986

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Chain	Residue	Modelled	Actual	Comment	Reference
B	306	TYR	THR	conflict	UNP P27986

- Molecule 3 is 5-{4-[3-(4-acetylpiperazine-1-carbonyl)phenyl]quinazolin-6-yl}-2-methoxypyridine-3-carbonitrile (three-letter code: 6CY) (formula: C₂₈H₂₄N₆O₃).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
3	A	1	Total	C	N	O	0	0
			37	28	6	3		

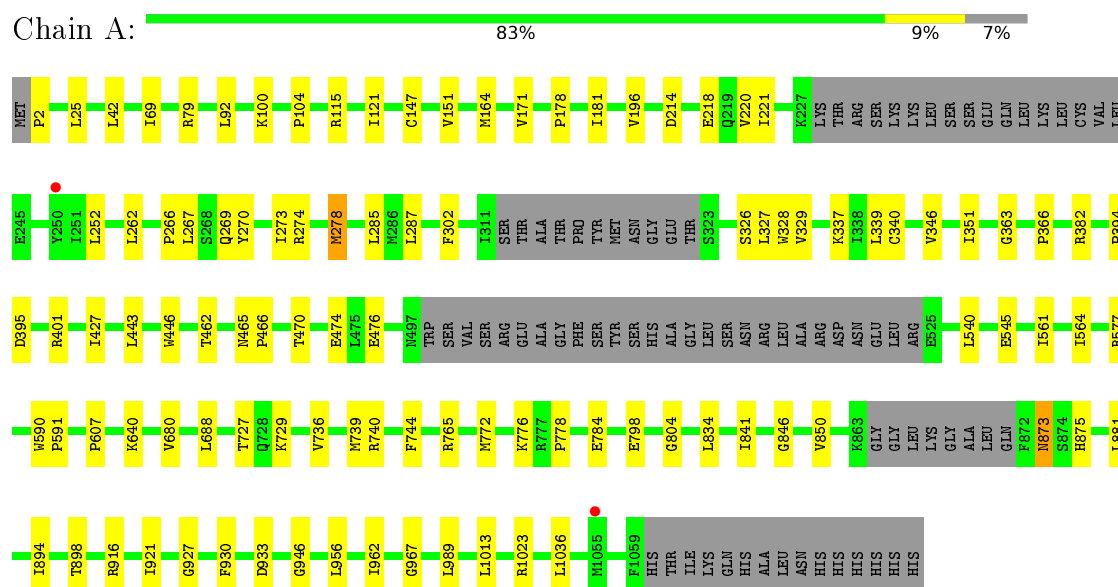
- Molecule 4 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	51	Total	O	0	0
			51	51		

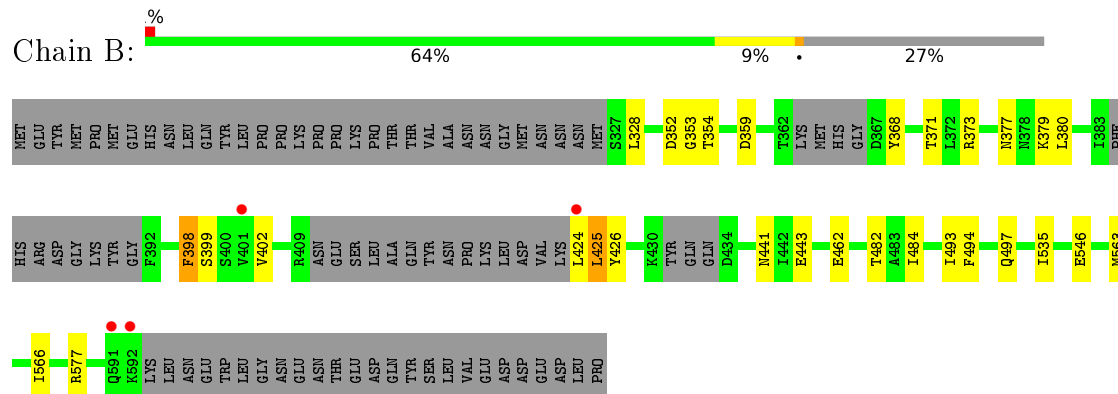
3 Residue-property plots

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 ($\text{RSRZ} > 2$). 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: Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform



- Molecule 2: Phosphatidylinositol 3-kinase regulatory subunit alpha



4 Data and refinement statistics

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α , β , γ	104.64Å 107.35Å 134.50Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	48.76 – 3.02 48.76 – 2.82	Depositor EDS
% Data completeness (in resolution range)	98.1 (48.76-3.02) 98.5 (48.76-2.82)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.16 (at 2.81Å)	Xtriage
Refinement program	BUSTER-TNT	Depositor
R, R_{free}	0.193 , 0.253 0.202 , 0.265	Depositor DCC
R_{free} test set	1463 reflections (5.16%)	DCC
Wilson B-factor (Å ²)	69.6	Xtriage
Anisotropy	0.109	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.29 , 54.1	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	0.015 for k,h,-l	Xtriage
F_o, F_c correlation	0.94	EDS
Total number of atoms	9860	wwPDB-VP
Average B, all atoms (Å ²)	71.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.23% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

²Theoretical values of $\langle |L| \rangle$, $\langle L^2 \rangle$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.

5 Model quality

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: 6CY

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	0.48	0/8084	0.67	0/10970
2	B	0.47	0/1892	0.67	0/2556
All	All	0.48	0/9976	0.67	0/13526

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

There are no planarity outliers.

5.2 Too-close contacts

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	7905	0	7671	57	0
2	B	1867	0	1702	20	0
3	A	37	0	0	1	0
4	A	51	0	0	0	0
All	All	9860	0	9373	71	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 4.

All (71) 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)
2:B:563:MET:HA	2:B:566:ILE:HG22	1.74	0.69
1:A:69:ILE:HG12	1:A:104:PRO:HG3	1.75	0.68
2:B:441:ASN:HD22	2:B:443:GLU:HB3	1.59	0.66
1:A:881:LEU:HD11	1:A:927:GLY:HA2	1.77	0.65
2:B:328:LEU:H	2:B:402:VAL:HG21	1.63	0.63
1:A:252:LEU:HD13	1:A:285:LEU:HD13	1.82	0.61
1:A:121:ILE:HG12	1:A:688:LEU:HB3	1.83	0.61
2:B:494:PHE:HB3	2:B:535:ILE:HG12	1.83	0.60
1:A:2:PRO:HG2	2:B:482:THR:HG23	1.88	0.56
1:A:427:ILE:HD11	1:A:443:LEU:HD22	1.88	0.55
2:B:359:ASP:HA	2:B:368:TYR:HD1	1.72	0.55
1:A:164:MET:HE2	1:A:262:LEU:HB2	1.90	0.53
1:A:346:VAL:HB	1:A:351:ILE:HD13	1.89	0.53
1:A:269:GLN:HA	1:A:274:ARG:HH21	1.73	0.53
2:B:484:ILE:HD12	2:B:546:GLU:HG3	1.90	0.53
1:A:147:CYS:O	1:A:151:VAL:HG23	2.10	0.52
1:A:640:LYS:HE2	1:A:680:VAL:HG11	1.90	0.52
1:A:151:VAL:HG21	1:A:302:PHE:HB2	1.92	0.52
1:A:946:GLY:HA3	2:B:577:ARG:HH12	1.75	0.52
1:A:328:TRP:HA	1:A:394:PRO:HB3	1.92	0.51
1:A:178:PRO:HD2	1:A:181:ILE:HB	1.92	0.51
1:A:446:TRP:CH2	1:A:466:PRO:HD2	2.46	0.51
1:A:834:LEU:HD23	1:A:930:PHE:CD1	2.45	0.51
1:A:989:LEU:HD11	1:A:1036:LEU:HD22	1.93	0.50
1:A:894:ILE:O	1:A:898:THR:HG23	2.11	0.50
1:A:873:ASN:HD21	1:A:875:HIS:HB2	1.76	0.50
1:A:181:ILE:HG12	1:A:278:MET:HB2	1.94	0.50
1:A:401:ARG:HD2	1:A:462:THR:HG21	1.94	0.50
1:A:337:LYS:HB3	1:A:476:GLU:HB3	1.94	0.49
1:A:164:MET:CE	1:A:262:LEU:HB2	2.42	0.49
1:A:776:LYS:HD2	1:A:804:GLY:HA3	1.95	0.48
1:A:25:LEU:HD22	2:B:497:GLN:HG2	1.95	0.47
1:A:540:LEU:HB2	1:A:1023:ARG:HD2	1.97	0.47
1:A:100:LYS:HD3	2:B:493:ILE:HG23	1.97	0.46
1:A:727:THR:HG22	1:A:729:LYS:H	1.80	0.46
1:A:79:ARG:HG3	2:B:493:ILE:HD11	1.98	0.46
2:B:354:THR:HA	2:B:426:TYR:O	2.15	0.46
1:A:220:VAL:HG23	1:A:252:LEU:HD11	1.98	0.46
1:A:363:GLY:N	1:A:607:PRO:HG3	2.31	0.46
2:B:371:THR:HA	2:B:379:LYS:O	2.16	0.46
1:A:561:ILE:O	1:A:564:ILE:HG22	2.15	0.46
2:B:462:GLU:HG3	2:B:566:ILE:HD11	1.98	0.45

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
2:B:353:GLY:HA3	2:B:425:LEU:HB2	1.98	0.45
1:A:196:VAL:HG12	1:A:287:LEU:HB3	1.99	0.45
1:A:765:ARG:HD3	1:A:784:GLU:HG3	1.98	0.45
1:A:962:ILE:HG23	1:A:967:GLY:HA2	1.99	0.44
1:A:465:ASN:ND2	1:A:470:THR:HG21	2.33	0.44
1:A:218:GLU:HA	1:A:221:ILE:HD12	2.00	0.43
2:B:352:ASP:HA	2:B:373:ARG:O	2.17	0.43
1:A:42:LEU:HD21	1:A:92:LEU:HD11	2.01	0.43
1:A:916:ARG:HB3	1:A:921:ILE:HD11	2.01	0.43
1:A:220:VAL:CG2	1:A:252:LEU:HD11	2.49	0.42
1:A:366:PRO:HD2	2:B:377:ASN:OD1	2.19	0.42
2:B:398:PHE:HB3	2:B:399:SER:H	1.63	0.42
1:A:545:GLU:CD	2:B:379:LYS:HD2	2.40	0.42
1:A:590:TRP:HD1	1:A:591:PRO:O	2.02	0.42
1:A:841:ILE:HG12	1:A:846:GLY:HA2	2.01	0.42
2:B:371:THR:HG22	2:B:380:LEU:HD23	2.00	0.42
1:A:798:GLU:HB2	1:A:850:VAL:HB	2.02	0.41
1:A:214:ASP:HA	1:A:266:PRO:HB3	2.01	0.41
1:A:171:VAL:HG12	1:A:270:TYR:HA	2.02	0.41
1:A:736:VAL:HG12	1:A:740:ARG:HH11	1.86	0.41
3:A:1101:6CY:C5	3:A:1101:6CY:C25	2.98	0.41
1:A:339:LEU:HB2	1:A:474:GLU:HB2	2.03	0.41
1:A:772:MET:HB2	1:A:778:PRO:HD2	2.02	0.41
1:A:267:LEU:HG	1:A:273:ILE:HG13	2.02	0.41
1:A:739:MET:HA	1:A:744:PHE:CD1	2.55	0.41
1:A:1013:LEU:HD12	1:A:1013:LEU:HA	1.96	0.40
1:A:395:ASP:OD1	1:A:577:ARG:HG2	2.21	0.40
1:A:340:CYS:HB3	1:A:382:ARG:HD3	2.03	0.40
1:A:326:SER:O	1:A:329:VAL:HG22	2.21	0.40

There are no symmetry-related clashes.

5.3 Torsion angles ⓘ

5.3.1 Protein backbone ⓘ

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	985/1074 (92%)	936 (95%)	47 (5%)	2 (0%)	52	87
2	B	227/323 (70%)	212 (93%)	14 (6%)	1 (0%)	39	79
All	All	1212/1397 (87%)	1148 (95%)	61 (5%)	3 (0%)	52	87

All (3) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
2	B	425	LEU
1	A	933	ASP
1	A	327	LEU

5.3.2 Protein sidechains ⓘ

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	855/980 (87%)	851 (100%)	4 (0%)	92	97
2	B	186/301 (62%)	184 (99%)	2 (1%)	80	94
All	All	1041/1281 (81%)	1035 (99%)	6 (1%)	90	97

All (6) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	115	ARG
1	A	278	MET
1	A	873	ASN
1	A	956	LEU
2	B	398	PHE
2	B	424	LEU

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. There are no such sidechains identified.

5.3.3 RNA ⓘ

There are no RNA molecules in this entry.

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

There are no non-standard protein/DNA/RNA residues in this entry.

5.5 Carbohydrates [i](#)

There are no carbohydrates in this entry.

5.6 Ligand geometry [i](#)

1 ligand is 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	$\# Z > 2$
3	6CY	A	1101	-	41,41,41	1.27	4 (9%)	55,58,58	2.66	15 (27%)

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
3	6CY	A	1101	-	-	0/23/34/34	0/5/5/5

All (4) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	1101	6CY	C39-C37	2.09	1.41	1.36
3	A	1101	6CY	C17-C15	2.15	1.53	1.50
3	A	1101	6CY	C27-N28	2.88	1.35	1.32
3	A	1101	6CY	O51-C45	3.15	1.40	1.35

All (15) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
3	A	1101	6CY	N31-C29-N28	-11.02	120.22	128.87
3	A	1101	6CY	C33-C27-N28	-6.66	118.51	123.01
3	A	1101	6CY	C46-C45-N44	-5.91	119.79	124.01
3	A	1101	6CY	O57-C56-C58	-3.04	111.37	122.02
3	A	1101	6CY	O16-C15-C17	-2.64	115.14	120.16
3	A	1101	6CY	C41-C42-N44	-2.47	120.31	124.31
3	A	1101	6CY	C5-C2-N1	-2.26	105.69	110.44
3	A	1101	6CY	C29-N28-C27	2.63	122.10	117.47
3	A	1101	6CY	C17-C15-N8	2.66	122.30	118.77
3	A	1101	6CY	C42-N44-C45	2.67	122.59	116.47
3	A	1101	6CY	C5-N8-C9	2.77	117.65	112.57
3	A	1101	6CY	C52-O51-C45	3.07	120.63	117.33
3	A	1101	6CY	O51-C45-C46	3.91	118.25	115.98
3	A	1101	6CY	C58-C56-N1	5.57	125.55	118.21
3	A	1101	6CY	C29-N31-C32	5.82	120.45	115.19

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
3	A	1101	6CY	1	0

5.7 Other polymers ⓘ

There are no such residues in this entry.

5.8 Polymer linkage issues ⓘ

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	995/1074 (92%)	-0.52	2 (0%) 95 87	36, 66, 103, 145	0
2	B	237/323 (73%)	-0.41	4 (1%) 73 44	48, 81, 127, 147	0
All	All	1232/1397 (88%)	-0.50	6 (0%) 91 76	36, 68, 113, 147	0

All (6) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
2	B	591	GLN	2.7
1	A	1055	MET	2.6
2	B	592	LYS	2.5
2	B	401	VAL	2.5
2	B	424	LEU	2.3
1	A	250	TYR	2.2

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

There are no non-standard protein/DNA/RNA residues in this entry.

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(\AA^2)	Q<0.9
3	6CY	A	1101	37/37	0.90	0.27	3.09	51,56,109,109	0

6.5 Other polymers [i](#)

There are no such residues in this entry.