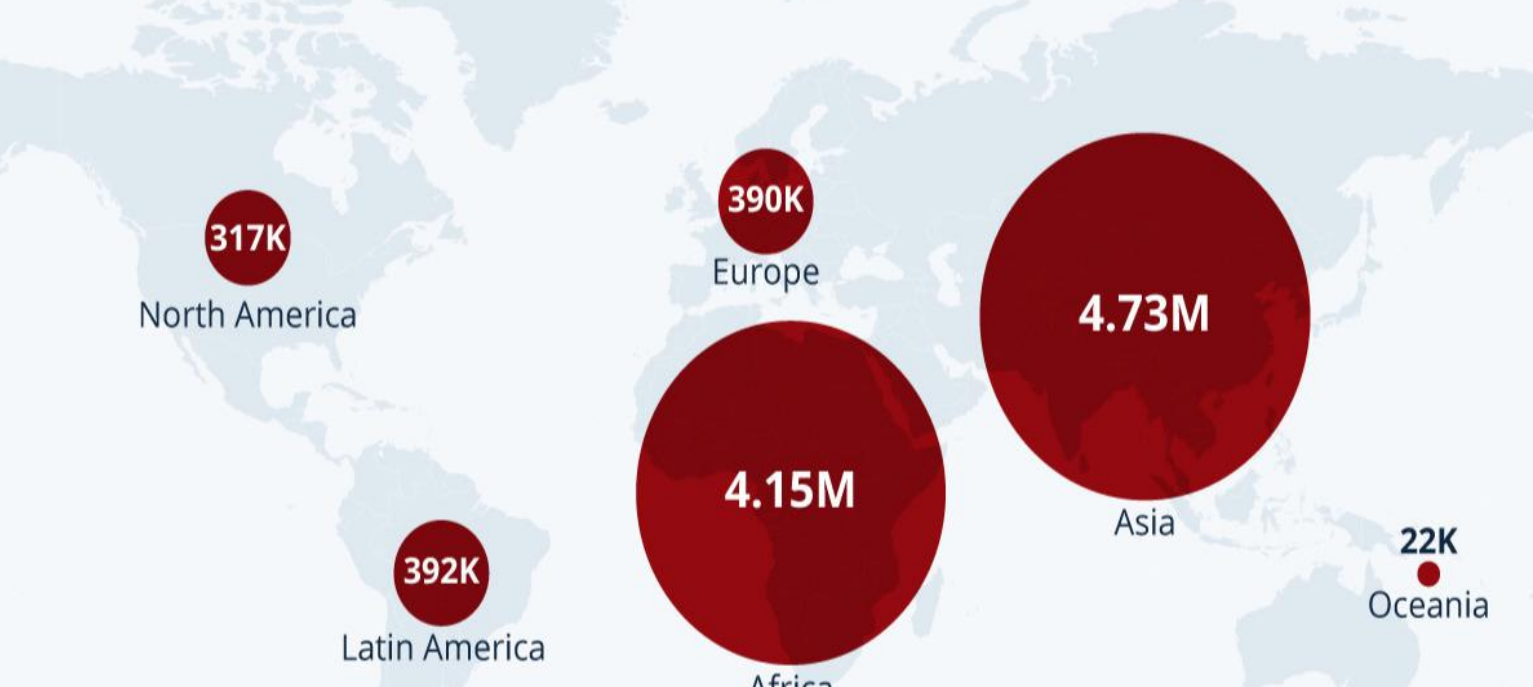


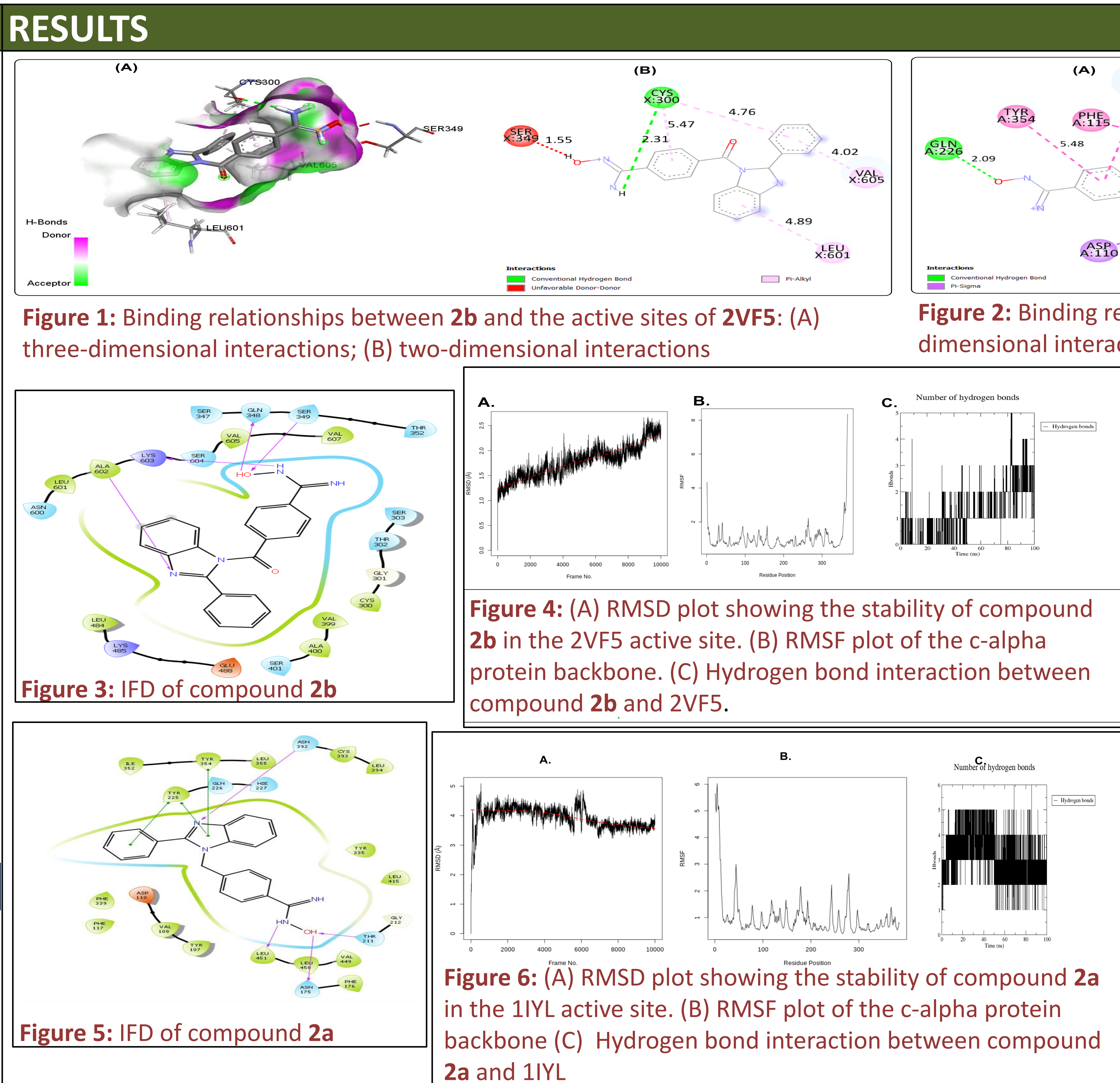
BACKGROUND

- The rise of antibiotic-resistant pathogens including **methicillin-resistant Staphylococcus aureus (MRSA)** driven by overuse of antibiotics has resulted in increased treatment failure, prolonged hospital stays, and higher mortality. Concurrently, fungal infections by opportunistic pathogens such as **Candida species** pose serious threats, particularly in immunocompromised individuals.
- These challenges show the urgent need for novel antimicrobial agents targeting **essential microbial pathways**. Amidoxime-based benzimidazole and benzimidamide derivatives represent a promising chemical class with diverse biological activities, including antimicrobial, antioxidant, and antihypertensive properties.
- Biological Targets used are **Glucosamine-6-phosphate Synthase** which is essential for **cell wall biosynthesis** (PDB ID: 2VF5) and **N-myristoyltransferase** which is important for **fungal survival** (PDB ID: 1IYL)

AMR Could Cause 10 Million Deaths a Year by 2050
Projected annual deaths attributable to antimicrobial resistance by 2050, by region



Projections from 2019 based on a scenario where no actions against AMR are taken
Sources: HM Government, Murray et al. Global burden of bacterial antimicrobial resistance. The Lancet (2022), OECD, Wellcome Trust



CONCLUSION

Amidoxime-based benzimidazole derivatives demonstrated promising *in silico* antimicrobial potential. Compound **2b** showed the highest antibacterial binding affinity (−8.0 kcal/mol), while compound **2a** showed the highest antifungal binding affinity (−11.7 kcal/mol). MM-GBSA, IFD, and MD simulations confirmed stable and favorable protein-ligand interactions for both compounds. ADMET profiling indicated acceptable drug-likeness and low toxicity. Compounds **2a** and **2b** are recommended as lead candidates for preclinical antimicrobial drug development.

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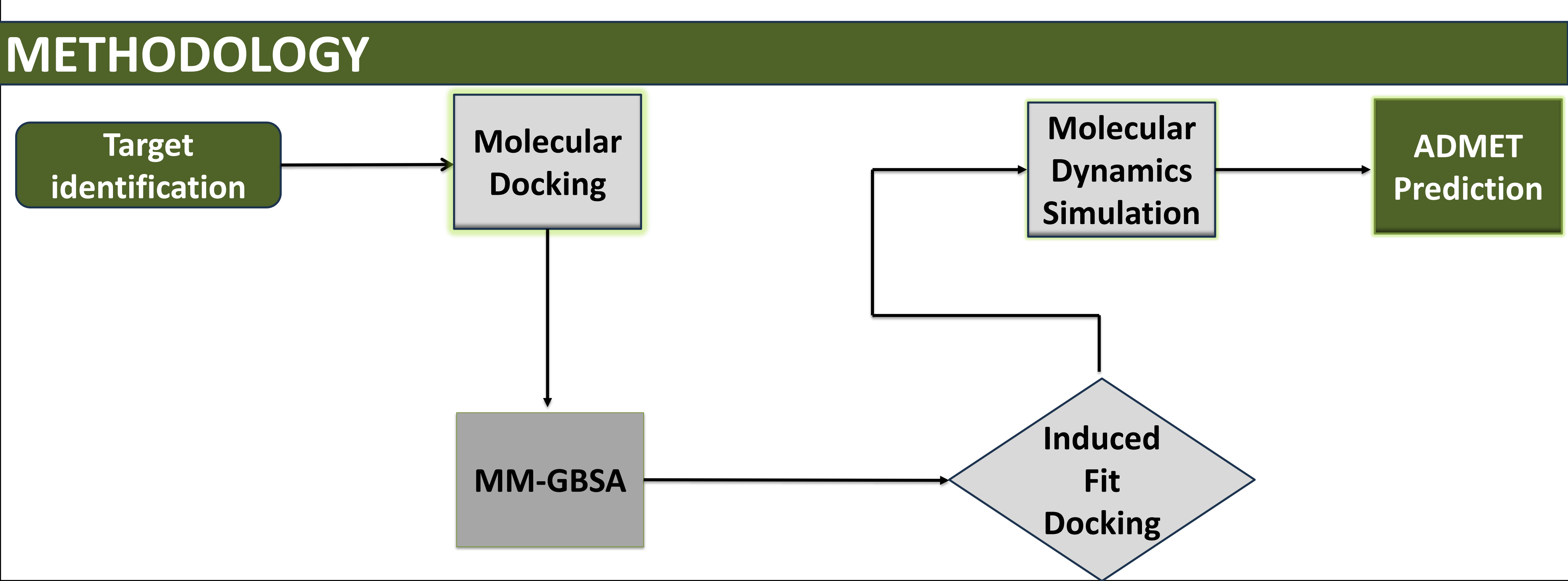


Table 1. Predicted Pharmacokinetic Properties and Toxicity Risks of Designed Compounds

Cpds	Physicochemical properties							Toxicity risks		
	MW	cLogP	TPSA (Å²)	Solubility Prediction	Drug likeness	Drug score	Mutagenic	Tumorigenic	Irritant	Reproductive effective
2a	342.0	2.96	73.93	-3.89	3.96	0.76	No	No	No	No
2b	356.0	3.36	91.00	-5.59	0.05	0.44	No	No	No	No