2021 Antibacterial agents in clinical and preclinical development

World Health Organization

Clinical Antibacterial Pipeline

This overview covers traditional (direct-acting small molecules) and non-traditional antibacterial agents in clinical and preclinical development worldwide. It assesses to what extent the clinical pipeline addresses World Health Organization (WHO) priority pathogens, *Mycobacterium tuberculosis* and *Clostridioides difficile.*

The current clinical antibacterial pipeline contains 77 antibiotics and/or combinations that include at least one new therapeutic entity. Of these, 45 are traditional antibacterial agents and 32 are non-traditional.

In addition there are 1 traditional and 2 non-traditional antibiotics in NDA/MAA stages.

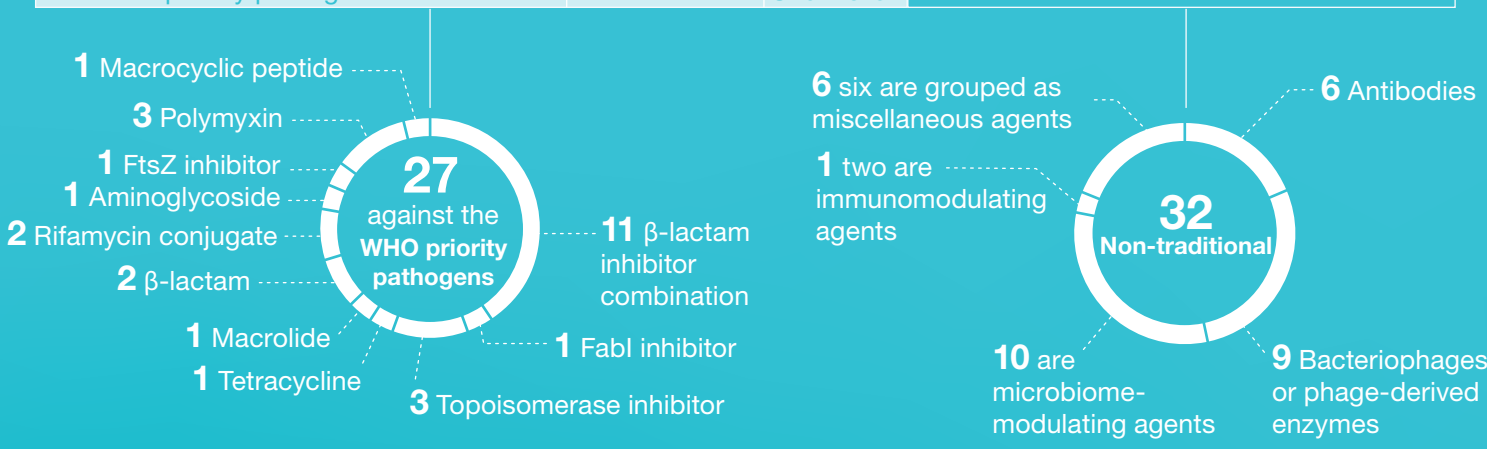
45 Traditional

27 against the WHO priority pathogens

13 against *M. tuberculosis*

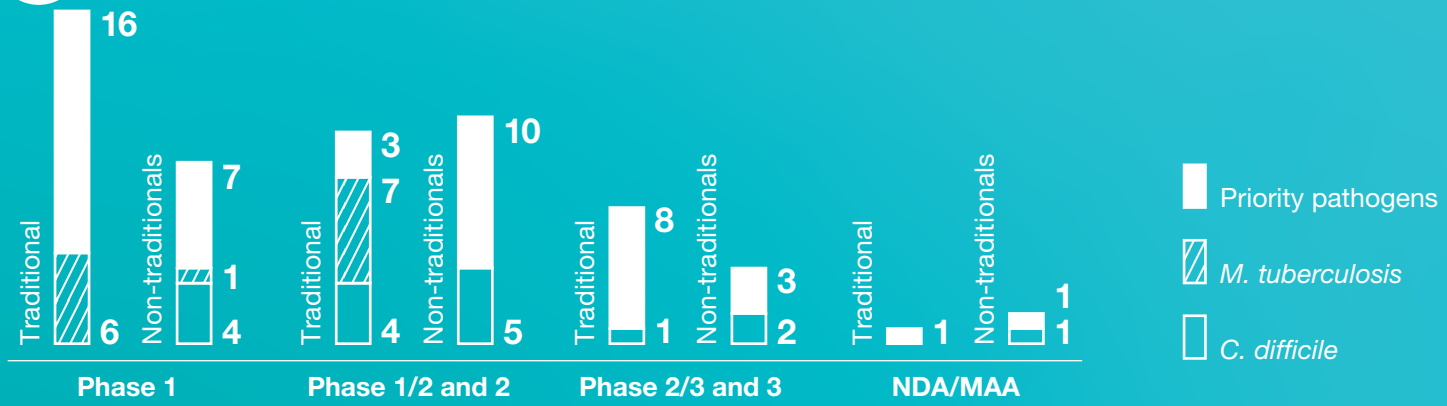
5 against *C. difficile*

32 Non-traditional



17 (40%) meet at least one of the WHO innovation criteria and only 3 of those address WHO critical priority bacteria.

Traditional and non-traditional antibacterials in clinical development (Phases 1–3)



Overall, the clinical pipeline and recently approved antibiotics are insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance.

2021 Preclinical Antibacterial Pipeline

World Health Organization

There are 121 commercial and non-commercial entities developing 217 antibacterial agents/programs that are in the preclinical stage.

Categorization of preclinical agents

1. Small molecule - direct acting	**90**	(41.5%)	7. Bacteriophage/Bacteriophage products	**28**	(12.9%)
2. Small molecule - indirect acting	**23**	(10.6%)	8. Biologic (Antibody or other biotherapeutic)	**8**	(3.7%)
3. Peptide - direct acting	**33**	(15.2%)	9. Nucleic acid based product	**4**	(1.8%)
4. Peptide - indirect acting	**2**	(0.9%)	10. Immunomodulators	**7**	(3.2%)
5. Large molecule - direct acting	**15**	(6.9%)	11. Microbiome modifying agents	**1**	(0.5%)
6. Large molecule - indirect acting	**4**	(1.8%)	12. Decolonization agents	**2**	(0.9%)

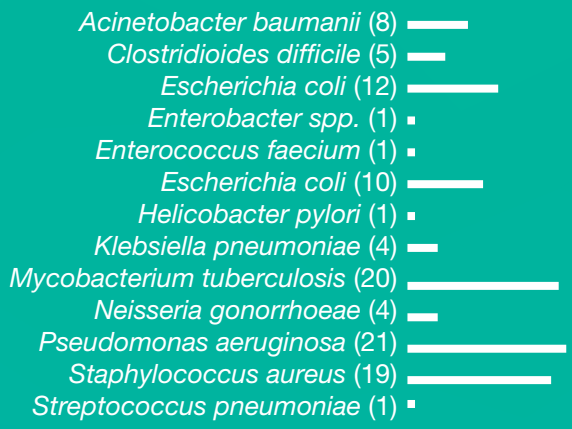
Mode of action and development stages

	Development stage		
Mode of action	**LO**	**PCC**	**IND**
Anti-virulence	19	3	2
Cell wall synthesis - BL and/or BLI	0	2	6
Cell wall synthesis - Other	14	14	1
Central metabolism	2	4	1
Direct membrane effect	17	25	14
DNA replication/synthesis	6	5	1
Protein synthesis	7	7	4
RNA synthesis	2	1	0
Immunomodulation	3	7	0
Other cellular function	9	5	2
Potentiator or Enabling agent	5	4	1
Not disclosed	5	4	0
Unknown	10	2	0
De-colonisation	0	1	2
Total	**99**	**84**	**34**

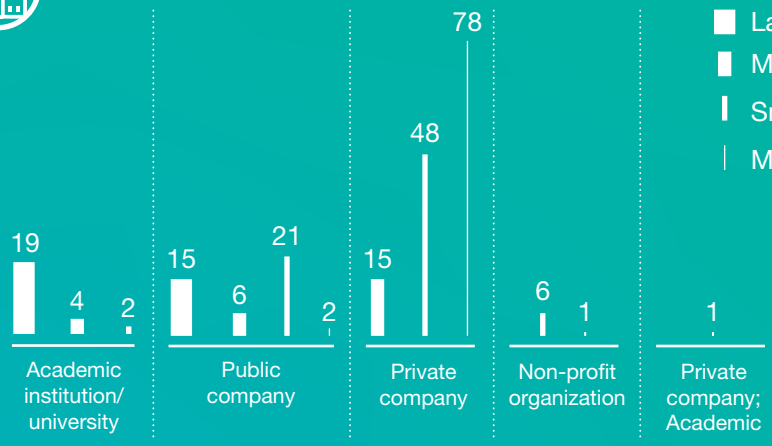
LO=lead optimization; PCC=preclinical candidate; CTA/IND=CTA/IND-enabling studies

Pathogens targeted by a single pathogen target product

A total of 95 agents (43.8%) have been classified by the product developers as species specific.



Developers' type and size



The majority (50.4%) of preclinical developmental research projects are being conducted in the European Region, followed by 37.2% in the Region of the Americas (mostly the USA and Canada), 9.3% in the Western Pacific Region and 4.1% in the South-East Asia Region

The preclinical and clinical antibacterial pipeline data is available in an interactive database and downloadable on the WHO Global R&D Health Observatory. Clinical: https://bit.ly/37B9tHT Preclinical: https://bit.ly/2Mvq5Jc

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