

## Asia Pacific Workshop on AMR in 2021

### Session III. Strategies for Improving Antimicrobial Drug Development

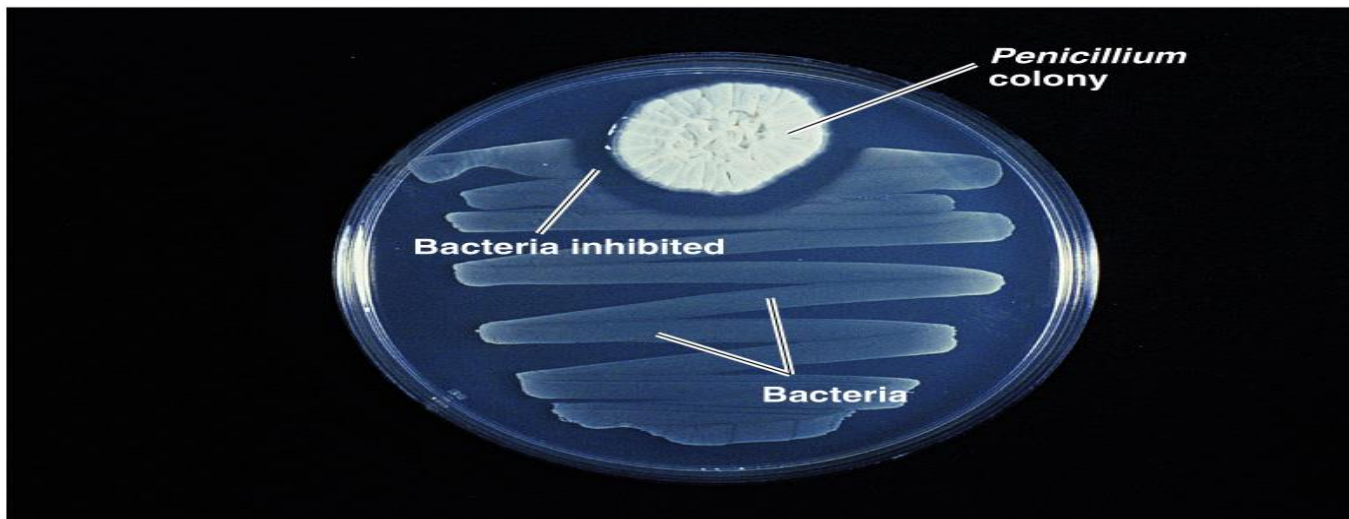
# Antimicrobial Drug Development in Japan

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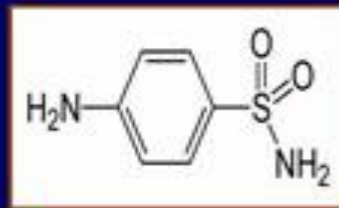
# Discovery of Penicillin by Fleming (1928)



# Discovery of Sulfonamide by Domagk (1935)

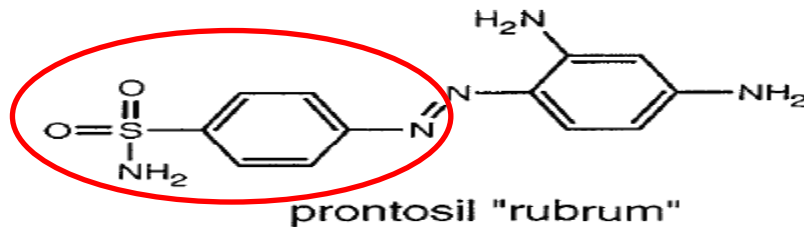


Gerhard Domagk



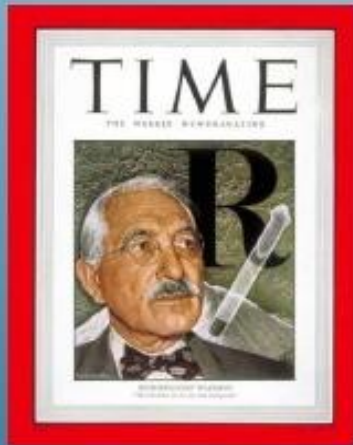
sulfonamide

**Synthetic antibacterial agent**

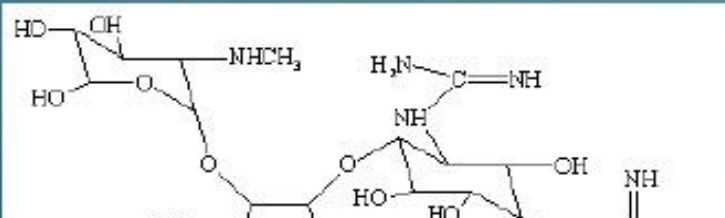
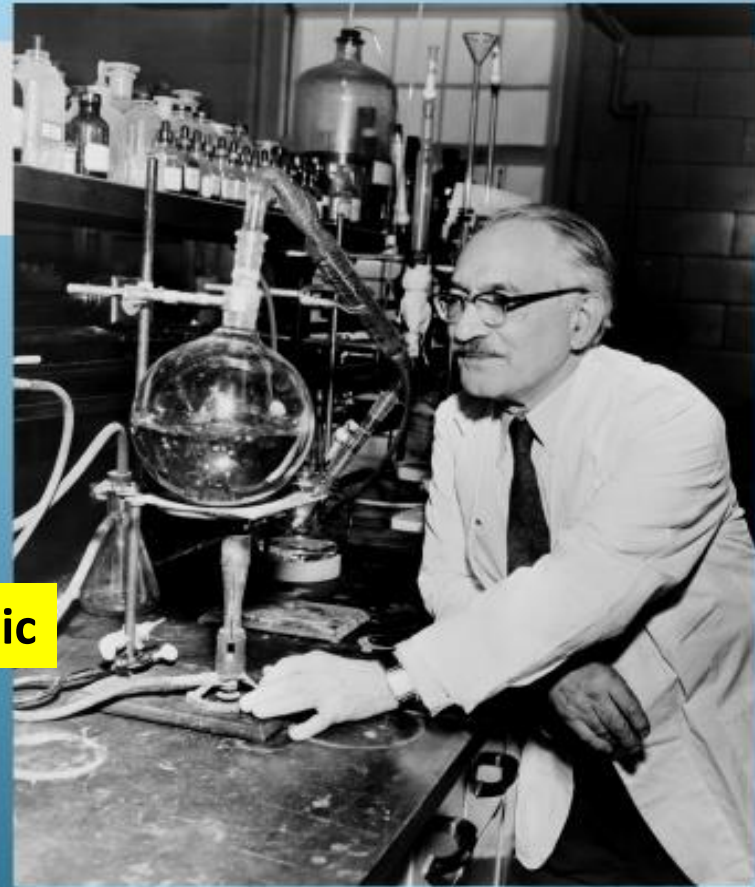


# Discovery of Streptomycin by Waksman(1943)

Selman Waksman



Antibiotic

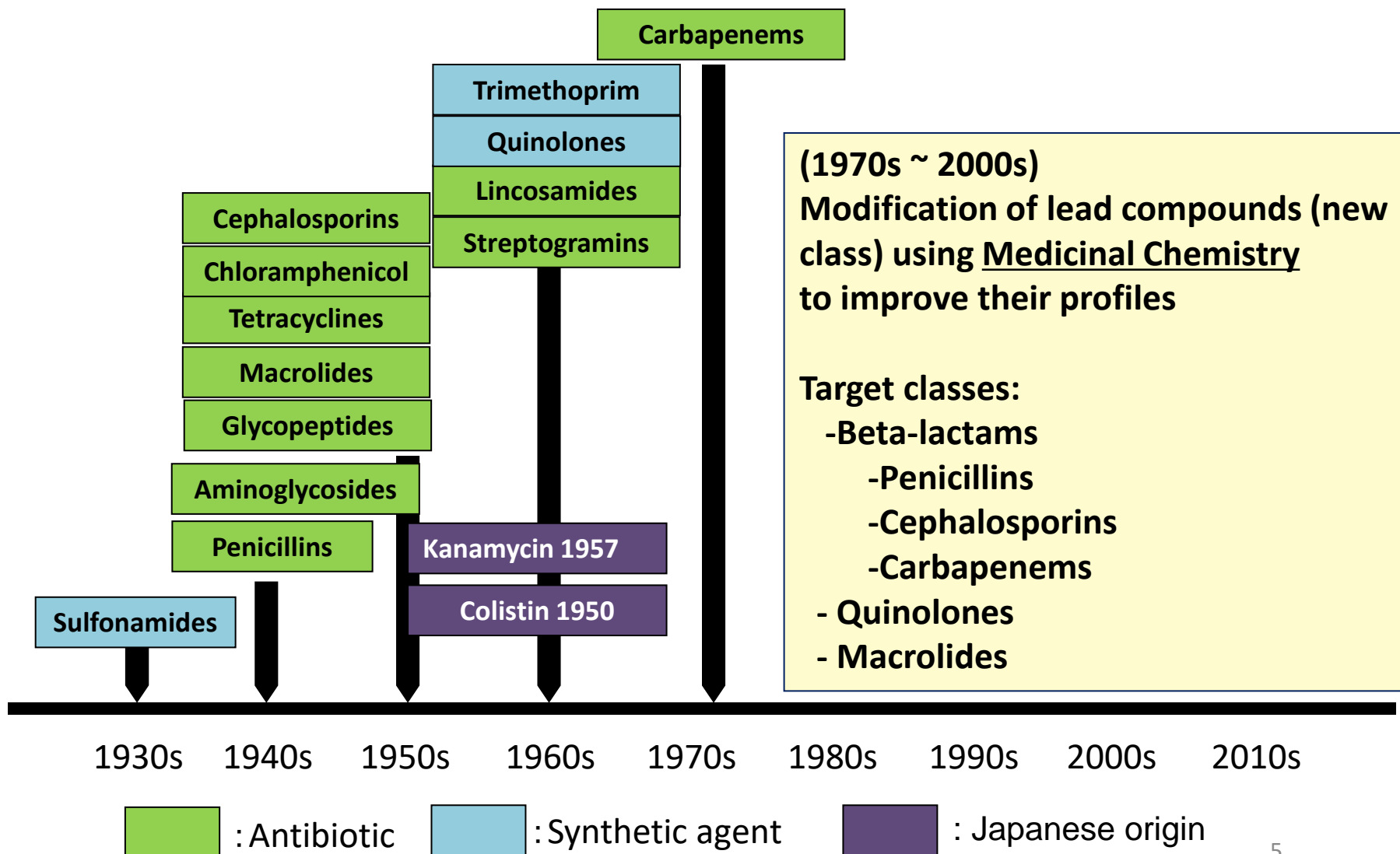


Waksman's method, "screening for antimicrobial activity against test bacteria by detecting zone of growth inhibition", was widely adopted by pharmaceutical industries and produced the major classes of antibiotics over next 20 years.

# Golden era of antibacterial agents discovery

“Discovery of new classes era”

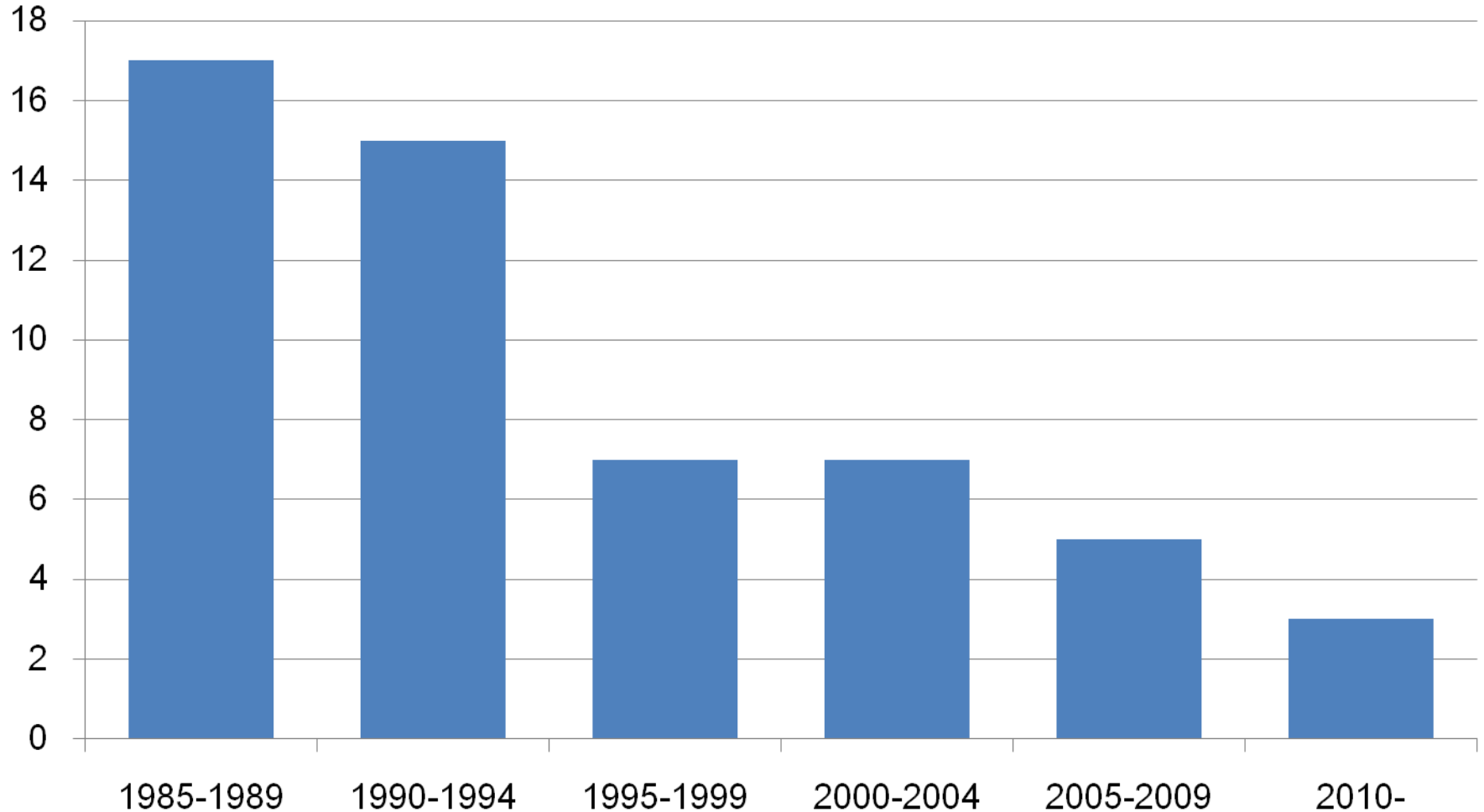
“Chemical modification era”



# Chemical classes of antibacterial agents and the agents of Japanese origin in the golden era

Chemical class	Original lead compounds	Japanese origin
[Natural product]		
$\beta$ -Lactams		
• Penicillins	Penicillin G	<b>Piperacillin (1976)</b>
• Cephalosporins	Cephalosporin C	<b>Cefazolin (1969)</b>
• Carbapenems	Thienamycin	<b>Meropenem (1987)</b>
• $\beta$ -Lactamase inhibitor	Clavulanic acid	<b>Tazobactam (1984)</b>
Aminoglycosides	Streptomycin	<b>Kanamycin (1957)</b> <b>Amikacin (1972)</b>
Tetracyclines	Tetracycline	
Chloramphenicols	Chloramphenicol	
Macrolides	Erythromycin	<b>Clarithromycin (1984)</b>
Glycopeptides	Vancomycin, Teicoplanin	
Polypeptides	Polymixin B	<b>Colistin (1950)</b>
Lipopeptides	Daptomycin	
[Synthetic chemical]		
Sulfonamides	Sulfanilamide	<b>Sulfamethoxazole (1959)</b>
Quinolones	Nalidixic acid	<b>Norfloxacin (1977)</b> <b>Levofloxacin (1987)</b>
Oxazolidinones	Linezolid	

# Approved New Antibacterial Agents in Japan (1985 – 2016)



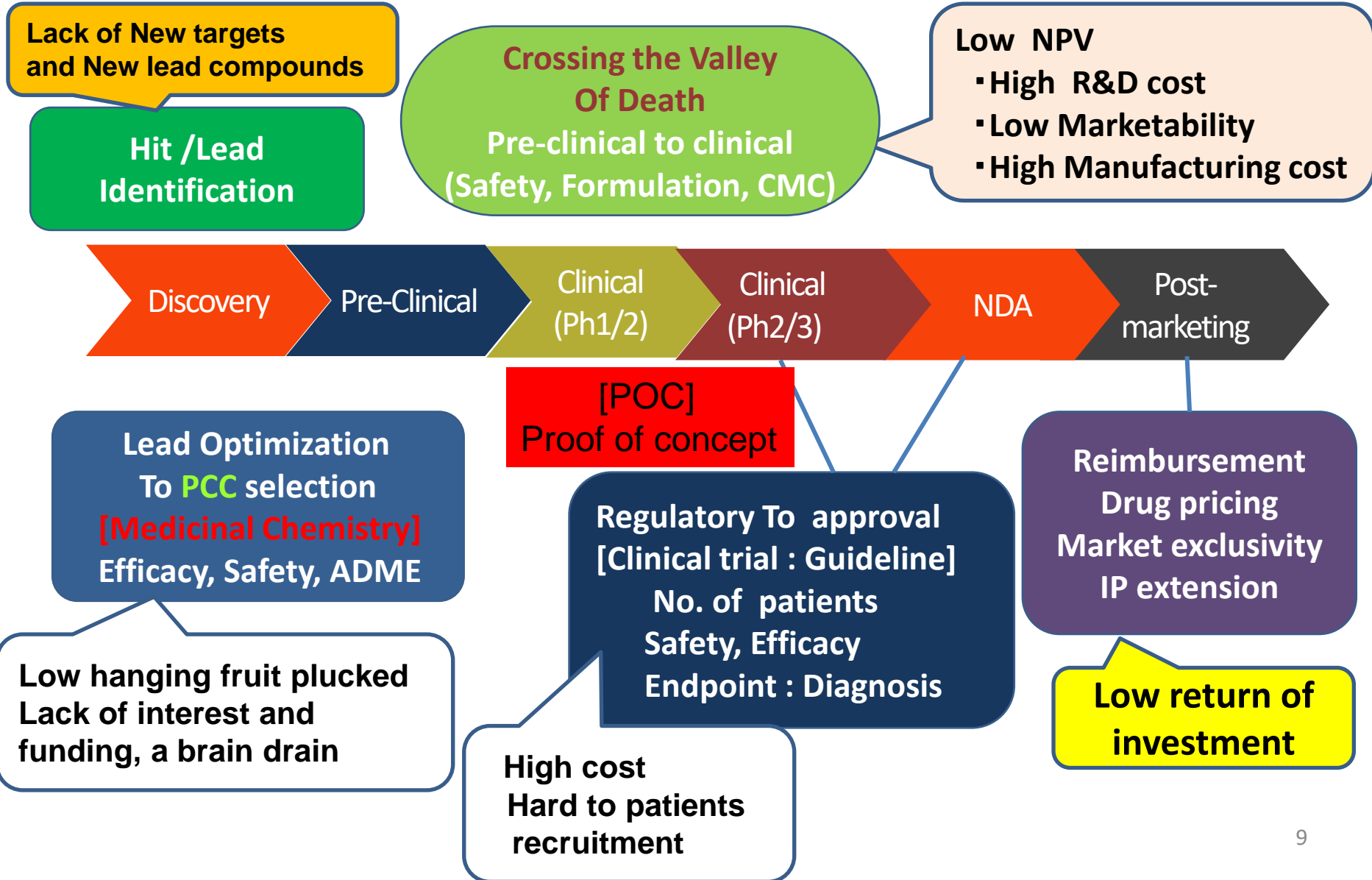
# Why the R&D pipeline is dry?

**Three big challenges to development of new antibacterial agents**

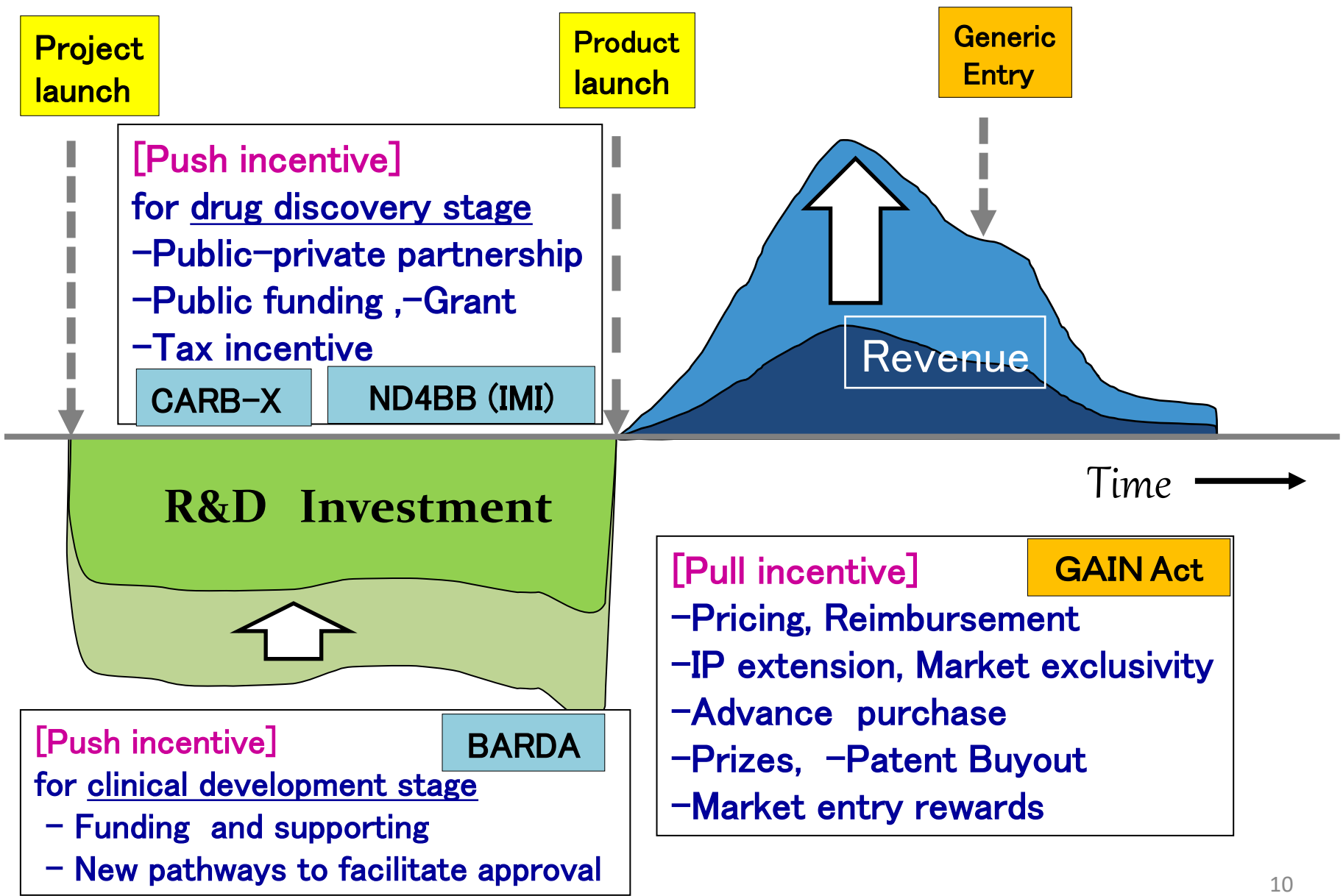
- Hard to discovery**
- Hard to development/Regulatory**
- Low return on investment**



# Bottlenecks in the value chain of R&D of antibacterial agents.



# “Push” and “Pull” Incentive for R&D



## Current situation to promote antimicrobials R&D against AMR in Japan

- Establish new “Public- private partnership (PPP)” for discovery research and development for novel antimicrobials against AMR
  - Collaborations of AMED, Industry (JPMA), and academia were started and AMED PPP for Infectious Diseases R&D was established in Sep. 2018.
  - AMED supports and promotes R&D activities, such as drug discovery researches for AMR.
  
- Develop incentives for new antimicrobials against AMR
  - “Pull-incentives” : JPMA submitted to MHLW “Suggestion from the JPMA on the introduction of Pull incentive\* to facilitate of R&D for AMR” in 2019.

\*model delinked from sales :

  - Market entry rewards -Transferable Exclusivity Extensions

**Well balanced push and pull incentives  
are necessary to promote antimicrobials  
R&D against AMR**