Le strategie regolatorie per fronteggiare il fenomeno dell'antibiotico resistenza

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Dichiarazione di trasparenza/interessi*

Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Interessi nell'industria farmaceutica	NO	Attualmente	Da 0 a 3 anni precedenti	oltre 3 anni precedenti
INTERESSI DIRETTI:				
1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica	☒	☐	☐	☐ obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	☒	☐	☐	☐ obbligatorio
1.3 Impiego per una società: altre attività	☒	☐	☐	☐ facoltativo
2. Consulenza per una società	☒	☐	☐	☐ facoltativo
3. Consulente strategico per una società	☒	☐	☐	☐ facoltativo
4. Interessi finanziari	☒	☐	☐	☐ facoltativo
5. Titolarità di un brevetto	☒	☐	☐	☐ facoltativo
INTERESSI INDIRETTI:				
6. Sperimentatore principale	☒	☐	☐	☐ facoltativo
7. Sperimentatore	☒	☐	☐	☐ facoltativo
8. Sovvenzioni o altri fondi finanziari	☒	☐	☐	☐ facoltativo
9. Interessi Familiari	☒	☐	☐	☐ facoltativo

* Enrico Costa, secondo il Regolamento per la disciplina dei conflitti di interesse all'interno dell'Agenzia Italiana del Farmaco approvato dal CdA AIFA con Delibera n. 37 del 13 ottobre 2020.

N.B. <Per questo intervento non ricevo alcun compenso>

The European medicines agencies network strategy 2028

Focus areas for EMANS 2028

- Accessibility
- Leveraging data, digitisation and artificial intelligence
- Regulatory science, innovation and competitiveness
- Antimicrobial resistance and other health threats
- Availability and supply
- Sustainability of the network

To manage the AMR threat, the network must

1) **promote the responsible use of antimicrobials in humans and animals**

2) Further work is also required **to provide incentives for antimicrobial development**

AIFA AGENZIA ITALIANA DEL FARMACO

Challenges and opportunities for incentivising antibiotic research and development in Europe

Michael Anderson,[a,b,*] Dimitra Panteli,[b] Robin van Kessel,[a,c] Gunnar Ljungqvist,[a] Francesca Colombo,[d] and Elias Mossialos[a,b]

What principles are needed for a holistic incentive package for antibiotic research and development?

There is consensus that no single incentive will be sufficient to stimulate antibiotic research and development:

a combination of **push and pull** incentives will be required

The Lancet Regional Health - Europe 2023;33: 100705

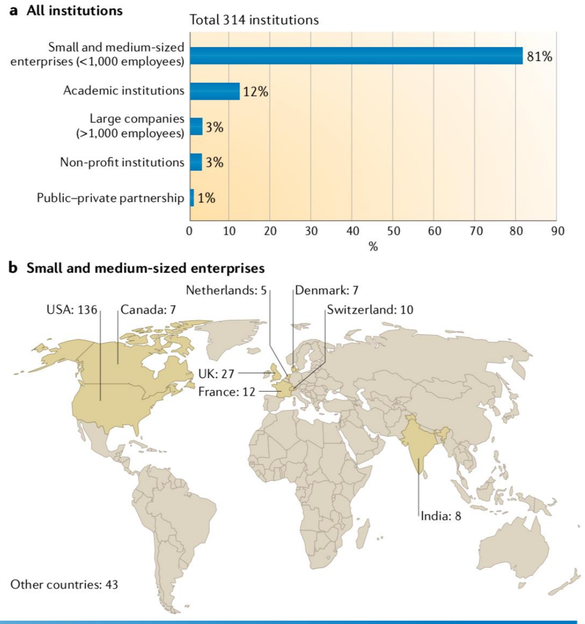
push incentives: funding for antimicrobial research and innovation, primarily via research grants and partnerships

pull incentives (both regulatory and financial) to reward successful development and secure access to effective antimicrobials.

Type and location of institutions that carry out preclinical antibacterial development

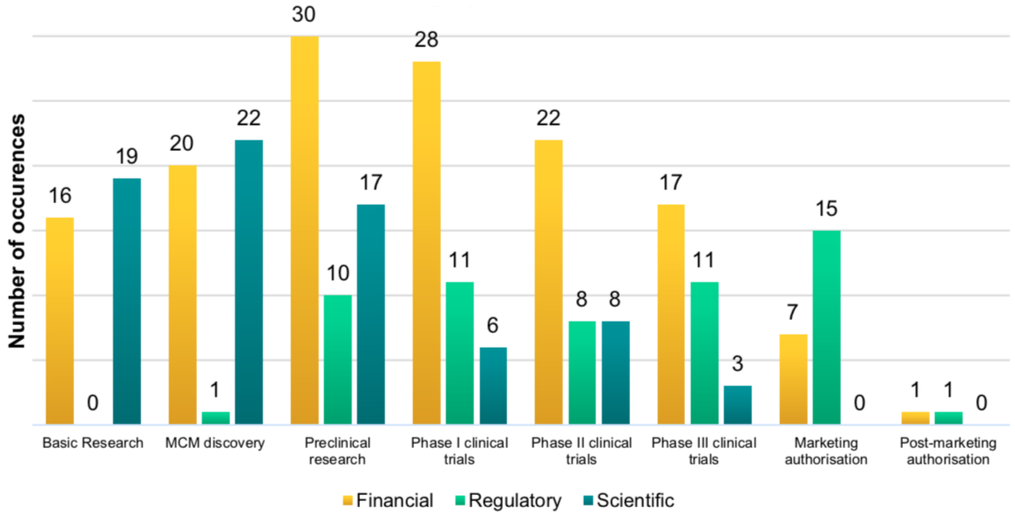
The **large majority** of institutions involved in the preclinical discovery and preclinical development of antibacterials are **small and medium-sized enterprises** (255/ 314).

More than half of the small and medium-sized enterprises are located in **North America**, followed by Europe as the second most prominent continent.



Theuretzbacher, U., Outterson, K., Engel, A. *et al.* The global preclinical antibacterial pipeline. *Nat Rev Microbiol* 18, 275–285 (2020).

Types of challenges faced across the development pipeline



Study on bringing AMR Medical Countermeasures to the Market - Final report *HADEA/2021/OP/0005*

NEWS ANNOUNCEMENT | 3 May 2023 | Health Emergency Preparedness and Response Authority | 3 min read

Bringing AMR medical countermeasures to the market – new study

European Commission
Public Health

Incentives for development of and access to antimicrobials

The Commission is proposing the following **pull incentives**:

1) Temporary mechanism consisting of ***transferable data exclusivity vouchers***, for the development of novel antimicrobials to be granted and used under strict conditions.

2) ***Procurement mechanisms*** for access to new and existing antimicrobials that would guarantee revenue for antimicrobials marketing authorisation holders, regardless of sales volumes.

Reform of the EU pharmaceutical legislation

New Regulation

- Specific rules for the most innovative medicines such as orphans, antimicrobials
- Rules on shortages and security of supply
- EMA governance

New Directive

- Placing on the market of all medicines
- Authorisation and labelling requirements
- Strong incentives for access

Council Recommendation on AMR

transferable data exclusivity voucher
(12 mesi DP > antimicrobico prioritario > ad altro medicinale, utilizzabile una sola volta)

"**antimicrobico prioritario**" se i dati preclinici e clinici confermano un beneficio clinico significativo rispetto alla resistenza antimicrobica e presenta almeno una delle seguenti caratteristiche:

(a) rappresenta una nuova classe di antimicrobici;

(b) il suo meccanismo d'azione è nettamente diverso da quello di qualsiasi antimicrobico autorizzato nell'Unione;

(c) contiene un principio attivo non precedentemente autorizzato in un medicinale nell'Unione che combatte un organismo multiresistente e un'infezione grave o pericolosa per la vita.

Limite all'emissione dei voucher: 15 anni dal momento dell'entrata in vigore del regolamento o la concessione di un totale di 10 voucher, a seconda di quale delle due venga raggiunta prima.

"unpredictably expensive"

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Comment

Transferable exclusivity voucher: a flawed incentive to stimulate antibiotic innovation

As antibiotic resistance increases globally, antibiotic innovation is struggling. WHO states that the antibiotic clinical pipeline is "insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance".[1] To prevent the development of resistance, aim of the 2022 EU Global Health Strategy of "enhanced equity in the access to vaccines and other [medical] countermeasures".[9]

The transferable exclusivity voucher will probably be unpredictably expensive. The cost to European

Commentary

BMJ Global Health

Transferable data exclusivity vouchers are not the solution to the antimicrobial drug development crisis: a commentary on the proposed EU pharma regulation

Astrid Berner-Rodoreda ,[1] Frank Cobelens,[2] Anne-Mieke Vandamme,[3,4] Günter Froeschl,[5] Jolene Skordis,[6] Elil Renganathan,[7] Ellen t'Hoen,[8] Mario Raviglione,[9] Albrecht Jahn,[1] Till Bärnighausen[1,10]

Procurement mechanisms - pull incentives

Subscription Model: fixed annual payments or minimum revenues for a set period in return for sufficient antimicrobial product supply guarantee, delinked from the volumes sold

Market-Entry Reward and Monetary Prizes: one-off or milestone-based payments to reward completed development stages (typically late-stage R&D) or market launch of new antimicrobials

Exclusivity Extension: market protection extensions granted to the successful antimicrobial innovator with applicability to already approved drugs (potentially tradable between firms)

Accelerated Approval and Priority Review Vouchers: vouchers for accelerated assessment and approval of antibiotics or other products under development by the same company (typically tradable between firms)

Tax credits: to reduce the cost of development and provides a financial incentive for companies to invest in antibiotic research

High unit price model: to ensure high revenues despite low volumes analogous to orphan drugs

Articolo 49
(Misure in materia di farmaci innovativi, antibiotici reserve e farmaci ad innovatività condizionata)

Legge n.232/2016: Fondo farmaci innovativi **>>> 1.000 milioni** di euro/annuo

- ***Anno 2022****: + 100 milioni di euro*
- ***Anno 2023****: + 200 milioni di euro*
- ***Anno 2024****: + 300 milioni di euro*

(Legge n.234/2021)

Dal 1° gennaio 2025: gli agenti antinfettivi per infezioni da germi multiresistenti già inseriti nel prontuario farmaceutico nazionale, e classificati come **"reserve"** secondo la nomenclatura **AWaRe (Access, Watch, Reserve) dell'Oms**, potranno accedere al fondo per un importo comunque non superiore a **100 milioni** di euro annui

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Council Recommendation on AMR

- concrete **targets to reduce antimicrobial use by 2030** *(-20% humans; -50% farm animals and aquaculture)*
- **strengthening of national action plans: surveillance of AMR and antimicrobial consumption** (monitor the use, including indicators to assess progress)
- **improve the health and welfare of food-producing animals** to decrease the spread of infectious diseases in farming
- **awareness raising** among the public and professionals working in the human health and veterinary sectors,
- **training** for health professionals and communication campaigns

Misure per l'uso prudente di antibiotici

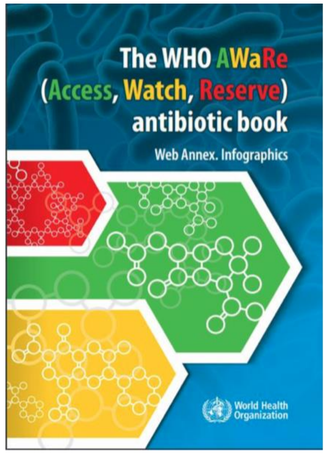
European Commission
Public Health

Attraverso la riforma della legislazione farmaceutica, le misure per un uso prudente entreranno a far parte del processo stesso di autorizzazione all'immissione in commercio

- Modalità prescrittive
- Adeguate dimensioni delle confezionei
- Informazioni specifiche sul paziente/operatore sanitario
- Piano di gestione antimicrobica che includa misure di mitigazione del rischio monitoraggio e segnalazione della resistenza all'antimicrobico

WHO AWaRe (Access, Watch, Reserve) antibiotic book

> guida evidence-based per una scelta ottimale degli antibiotici, della dose, della via di somministrazione e della durata del trattamento per oltre 30 delle più comuni infezioni cliniche nei bambini e negli adulti

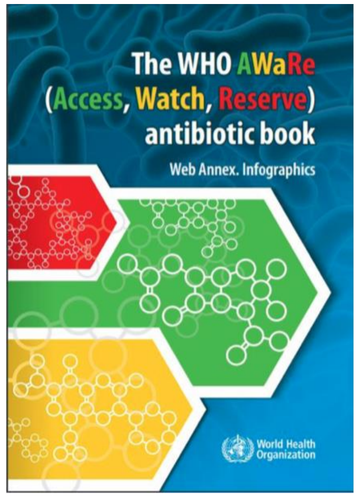


Access - antibiotici che hanno uno spettro di attività ristretto e un buon profilo di sicurezza in termini di reazioni avverse, da usare preferibilmente nella maggior parte delle infezioni più frequenti quali ad esempio le infezioni delle vie aeree superiori **(>60%)**

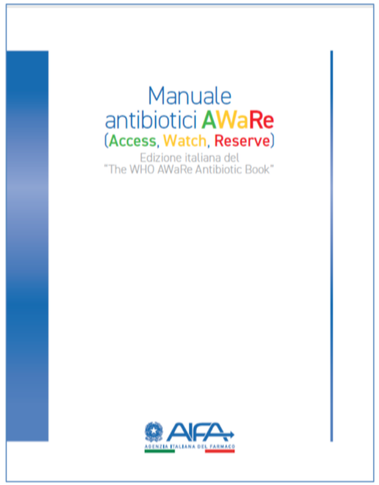
Watch - antibiotici a spettro d'azione più ampio, raccomandati come opzioni di prima scelta solo per particolari condizioni cliniche

Reserve - antibiotici da riservare al trattamento delle infezioni da germi multiresistenti

WHO AWaRe (Access, Watch, Reserve) antibiotic book



Versione italiana



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