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FINAL REPORT - DECEMBER 2019

Study of the potential use of an EU Transferable Exclusivity Extension (TEE) to incentivize antibiotic R&D

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ohe.org

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Appendix: Options for Structuring the Market for TEE Vouchers

1. Executive Summary

1. Executive Summary (i)

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Take Away Messages

- A TEE Voucher can be made to work in the EU
- The EMA could oversee the process of issuing TEE Vouchers in response to a list of priority pathogens
- A key uncertainty is how many new drugs are required or likely to qualify and therefore how many TEE Vouchers will be issued. Estimates range from below 1 per annum to 3 per annum.
- A supply of 2 TEE Vouchers per year would generate net revenues of around €500m to the seller but some TEE Vouchers could sell for up to €800m
- TEE Vouchers need to provide income for developers of €280 million for a new product in an existing class of antibiotic product and €440 million for a new class of antibiotic product.
- These results suggest that the TEE Voucher is commercially feasible as an incentive with a TEE period of 9-12 months for new classes of antibiotics and a TEE period of 7-10 months for existing classes of antibiotics
- If 2 TEEs are traded per year, we estimate that the cost for health systems is within the range of €0.35bn to €0.84bn per annum, depending on TEE duration, adjusting for revenue and budget caps operated by some member states
- Guardrails are likely to be required aimed at protecting one or more of the antibiotic product developers, the pharmaceutical companies buying a TEE Voucher, and EU Member State health care systems.

1. Executive Summary (ii)

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Purpose of the Study

- EFPIA wishes to develop and assess a proposal for a new EU pull incentive, Transferable Exclusivity Extensions (TEE), to stimulate antibiotic R&D.
- OHE Consulting was commissioned to work with EFPIA to deliver a proposal with supporting analysis. This report sets out our findings.
- We produced a draft report in April 2019 which was discussed by the EFPIA AMR Task Force. This final report seeks to address the issues raised in discussion.

Process for issuing a TEE Voucher

- The EMA would draw up a list of priority pathogens eligible for a TEE Voucher.
- It would issue designations for molecules addressing these pathogens, and, following a successful licence application, issue a TEE Voucher
- Priority pathogens could be added to, or removed from, the list
- When removed, molecules with a designation would still be entitled to a TEE Voucher if subsequently licensed within the designated indication.

1. Executive Summary (iii)

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Numbers of drugs requiring a TEE Voucher

- A review of existing priority pathogen lists finds 5 as “Critical + Urgent” and a further 13 as “High + Serious” giving **a total of 18 priority pathogens**.
- How many new antibiotics are both needed and able to be developed (and so how many TEEs will be issued) is a matter of debate.
- At the high end, we **assume 3 antibiotics are required for each of the 18 bacteria** giving a total of 15 new antibiotics to address “Critical + Urgent” pathogens and a further 39 to address “High + Serious” pathogens, **a total of 54**.
- Analysis of existing pipelines suggests 15 of the 54 can be expected over the next 6 years, requiring 39 over the period 2027-2036. This requires around 39 designated antibiotics per annum leading to around 4 TEE Vouchers per annum. **Over the period 2021-2036 an annual average of 3 TEE Vouchers would be required** to meet high end expectations
- At the low end, if the eligible pathogen list were **restricted to the “Critical + Urgent” categories,** then, if 3 antibiotics were needed for each of the 5 pathogens, around 15 designated antibiotics are required, leading to **an average of 1 TEE Vouchers per annum**. If fewer than 3 molecules per pathogen were required then the number of TEEs is less than one per annum.
- For modelling purposes **we assume 2 TEE Vouchers per annum**, to understand the pressure on TEE Voucher values.

1. Executive Summary (iv)

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Revenues generated from sale of a TEE Voucher

- We looked at gross sales of the top 30 and top 50 drugs in the EU
- To estimate the willingness to pay for (an illustrative) one-year TEE Voucher, we assumed:
  - Discounting from list price is 30% and the profit margin on net sales is 80%.
  - The expected impact of generic entry in the first year is 47%, i.e. this is the anticipated volume of sales lost
- The results of our modelling suggest
  - A supply of 3 TEE Vouchers per year would generate **net revenues of around €350m** to the seller
  - A supply of 2 TEE Vouchers per year would generate **net revenues of around €500m** to the seller
  - In both cases **some TEE Vouchers could sell for up to €800m**
  - The smaller the number of TEE Vouchers the higher the average price

1. Executive Summary (v)

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Revenues needed by a developer from the sale of a TEE Voucher

- Step 1: We estimate the capitalized R&D costs as follows:
  - For an existing class product €1.24bn
  - For a product establishing a new class €1.81bn
- Step 2: We estimate the EU share of R&D to be 25.2%
  - **The cost of R&D** of a new antibiotic (**existing class**) to be met by EU markets is therefore **€358.1m**
  - **The cost of R&D** of a new antibiotic (**new class**) to be met by EU markets is therefore **€520.4m**

1. Executive Summary (vi)

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Revenues needed by a developer from a TEE Voucher (continued)

- Step 3: We need to subtract net revenues that will come from sales of the antibiotic.
  - Using information from the top 5 earning antibiotics in 2018, we estimate gross sales of €17.3 million per annum for nine years of exclusivity.
  - With assumptions about net profit and sales after the expiry of patent protection, we estimate, using a cost of capital of 10%, that **the present value of the profits from sales of a new antibiotic in the EU is €78.6m**
  - this sum can be subtracted from the required totals needed to cover the EU share of the capitalised R&D cost of a new antibiotic.
- Step 4: We arrive at the net income needed from a TEE Voucher.**TEE Vouchers need to provide income for developers of**:
  - **€279.5 million** for an existing class of antibiotic product
  - **€441.8 million** for a new class of antibiotic product

1. Executive Summary (vii)

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Organising the market and the impact on the value of TEE Vouchers

- We explored how the organisation of the market for the TEE Vouchers would impact the prices at which vouchers were bought and sold.
- In a separate Appendix we set out the scenarios and the results with:
  - No intermediary, but with two types of market: (i) simultaneous sales (i.e. one market per year for all TEE Vouchers granted in that year) and (ii) a sequential market (each TEE Voucher sold individually at a time of choosing for the seller).
  - An intermediary selling the TEE Vouchers under three types of auction: (i) uniform price (price paid equal to that of the lowest winning bid); (ii) discriminatory price (price paid for each TEE Voucher is the highest bid for that TEE Voucher) (iii) Vickrey auction (winner pays the price of the (losing) second-highest bid).
  - The results differ but not substantially.

1. Executive Summary (viii)

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Duration of a TEE Voucher

- We translated our estimates of the minimum and average WTP of a TEE into required lengths of a TEE Voucher using the minimum and average values of TEE Vouchers expected. These are indicative and highly sensitive to all of the assumptions used.

Scenario	Minimum WTP for a TEE 2018-2026	Average WTP for a TEE 2018-2026[a]	Contribution to R&D cost required from a TEE Voucher	Duration of TEE required Years (in relation to minimum WTP)	Duration of TEE required Years (in relation to average WTP)
Two TEE per year without replacement (new class)	€469.6m	€518.4m	€441.8m	0.94	0.85
Two TEE per year with replacement (new class)	€473.4m	€584.1m	€441.8m	0.93	0.76
Three TEE per year without replacement (existing class)	€349.2m	€445.2m	€279.5m	0.80	0.63
Three TEE per year with replacement (existing class)	€405.1m	€457.4m	€279.5m	0.69	0.61

Sources: IQVIA and OHE Consulting Ltd.
Notes: [a] Averages reported in the table match those reported in the analysis of the Appendix. They are based simultaneous annual sales with price based on the lowest winning WTP.

1. Executive Summary (ix)

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Duration of a TEE Voucher (continued)

- These results suggest that:
  - **A TEE period of 9-12 months** would be needed for new classes of antibiotics
  - **A TEE period of 7-10 months** would be needed for existing classes of antibiotics

Use of an Intermediary

- Selling prices for the TEE Vouchers are similar, but an intermediary is likely to have policy attractions for the EU Commission:
  - It could transfer to developers the agreed required funding, guaranteeing the amount to developers and minimising the impact of TEE Vouchers on health systems.
  - It could make differential rewards to “new class” and “existing class” antibiotics.
- An alternative would be for “new class” and “existing class” antibiotics to have differential TEE periods, i.e. the length of exclusivity attached to the TEE Voucher would differ. However, this could be quite disruptive without an intermediary, as buyers would have to choose whether to wait for a TEE Voucher with a longer TEE to become available. We have not modelled this.

1. Executive Summary (ix)

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Suggested Guardrails

- Guardrails are rules aimed at protecting one or more of the antibiotic product developers, the pharmaceutical companies buying a TEE Voucher, and EU Member State health care systems.
- Products “receiving” a TEE Voucher must have a remaining exclusivity period of at least 2 years to reduce impact on the generic industry.
- Only one TEE Voucher per qualifying molecule (irrespective of the number of licensed indications) and one TEE Voucher per recipient product (irrespective of any bids made).
- TEE Vouchers will only be available for products that address an EMA priority pathogen list. The EMA can add to the list or remove from the list (although when a priority pathogen is removed, molecules with a designation would still be entitled to a TEE Voucher if subsequently licensed within the designated indication).
- TEE Vouchers are freely tradable. A developer can sell a TEE Voucher or use within its business.

1. Executive Summary (x)

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Suggested Guardrails (continued)

- A developer accepting the TEE Voucher for its licensed product will accept obligations to supply or otherwise make the antibiotic available. Further consideration of this issue was not in our Terms of Reference.
- In the event of the antibiotic being withdrawn there could be a requirement to surrender the TEE Voucher if not sold, or to hand over some of the proceeds if it has been sold. However, transfer of the TEE Voucher to the recipient product will be unconditional and irrevocable (e.g., if antibiotic is withdrawn the recipient product will still be entitled to use the TEE Voucher).
- Developers will commit to ensuring appropriate stewardship, for example through an Antibiotic Management Plan agreed with the EMA as part of the RMP. The main obligation for stewardship however rests with the health system.

1. Executive Summary (xi)

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The Impact on EU Member State Health Budgets

- The net cost to EU Member State Health Budgets should be estimated by:
  - Estimating the total value of all traded TEE Vouchers, which can be used as a proxy of the **gross cost** of the TEE Vouchers to health systems
  - Subtracting the cost of buying generic versions of the products that are no longer required for the period of the TEE.
  - Adjusting for those health systems with pharmaceutical expenditure caps which means that higher spend on drugs with TEEs is recovered.
- Since adjusting for pharmaceutical expenditure caps requires assumptions about how far spend on drugs with TEEs is recovered, we first estimate the net costs by subtracting expenditure on generic versions of the products benefitting from TEE vouchers
  - If **2 TEEs** are traded per year, we estimate that the gross cost for health systems is within the range of €0.57bn to €1.21bn per annum, depending on TEE duration.
  - If **3 TEEs** are traded per year, we estimate that the gross cost for health systems is within the range of €0.71bn to €1.51bn per annum depending on TEE duration.

1. Executive summary (xii)

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The Impact on EU Member State Health Budgets (continued)

- We then re-model model the net cost for health systems by additionally adjusting for the pharmaceutical expenditure caps in place in the 5 largest EU markets (with the exception of Germany, where there is no such cap)
- For the two cases, 2 and 3 TEEs per year, the estimated net cost of all traded TEE Vouchers are as follows:
  - If 2 TEE Vouchers are traded per year, we estimate that the net cost for health systems is within the range of **€0.35bn to €0.84bn per annum, depending on TEE duration** *(compared to €0.57bn to €1.21bn per annum without adjusting for caps)*
  - If 3 TEE Vouchers are traded per year, we estimate that the net cost for health systems is within the range of **€0.46bn to €0.99bn per annum depending on TEE duration** *(compared to €0.71bn to €1.51bn per annum without adjusting for caps)*

1. Executive Summary (xiii)

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Issues for consideration by the EFPIA AMR TF

- Results are highly sensitive to assumptions.
- The TF has indicated preference for a narrow qualifying list of molecules for a TEE Voucher.
  - Depending on the pathogen list used the numbers of qualifying new drugs could range from less than one per annum to around 3 per annum over time.
  - The option of a differential reward for a first in class versus follower will be difficult to implement without use of an intermediary, which was not supported by the TF
- **The variation in, and potential upper size of, the value of TEE Vouchers may present concerns for Member State health systems (too high) and for antibiotic developers (too low).** Options to address this could include: (i) a cap on the net revenue earned by the recipient of a TEE Voucher; (ii) a variable length of the TEE depending on expected revenues; (iii) use of an intermediary
- We take account of potential sales in our estimate of the size of TEE Voucher needed by developers but of **neither (i) improvements in reimbursement arrangements nor (ii) any push monies received**

2. Purpose of the study and overview of the approach

2. Context: EFPIA's rationale for the study

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- In recent years, the global community has directed a high level of political attention to the crisis of antimicrobial resistance (AMR).
- A decline in AMR product research investment has been observed in the last decades with lower numbers of new antibiotics reaching the market while bacterial infections grow more resistant. There is general but not universal recognition of the need to provide greater incentives to stimulate commercial investment in antibiotic R&D to produce new drugs and vaccines.
- Much emphasis has gone into "push" incentives, and while important, these are not sufficient to incentivise R&D
- Pull incentives have not fared well in debate as they are more complex to design and cost more
- EFPIA wishes to assess the extent to which one pull incentive, Transferable Exclusivity Extensions (TEE), could provide a meaningful incentive by looking at how it could work and what the potential impact would be for industry and for EU health budgets
- An important part of this is understanding potential interaction with other "push" and "pull" incentives and any differential impact on innovators

2. An Overview of OHE's approach (i)

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- **Work with EFPIA's Committees:** We have liaised throughout with Ania Jedrusik, Kristine Peers and members of the EFPIA AMR Incentives Task Force**.** We are grateful for their input and critical review. Errors and misunderstandings remain ours.
- **Estimate numbers of products**: We reviewed the (limited) literature on likely eligibility criteria, and used a range of assumptions about the number of potential first in class and follow-on qualifying antibiotics.
- **Estimate gross value of TEE Vouchers:** We explored, with IQVIA data, the number and distribution of high selling drugs in the EU and, using plausible assumptions about revenue growth, how this might change over time.
- **Set out how the TEE Voucher market would work:** We used simple game theory and auction theory thinking to help us construct plausible scenarios to model the market for TEE Vouchers as between antibiotic innovators and owners of potential recipient products.

2. An Overview of OHE's approach (ii)

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- **Estimate what a TEE Voucher needs to be worth:** We generated estimates of:
  - R&D cost using established R&D models;
  - Share of global R&D costs to be met by the EU;
  - Potential impact of other EU push and pull initiatives on the costs to be recovered.
- **Consider Impact on Member State Health Systems:** We have produced an initial estimate of the effect.
- **Examine the implications for public policy:** In particular we have explored issues around "guardrails", i.e. protection for the sellers and buyers of TEE Vouchers and protections for the health systems funding them.
- **Write up the results:** This report sets out our assumptions, the analysis supporting them, our estimates of the range of values of TEE Vouchers, and the policy implications.

2. An Overview of OHE's approach (iii)

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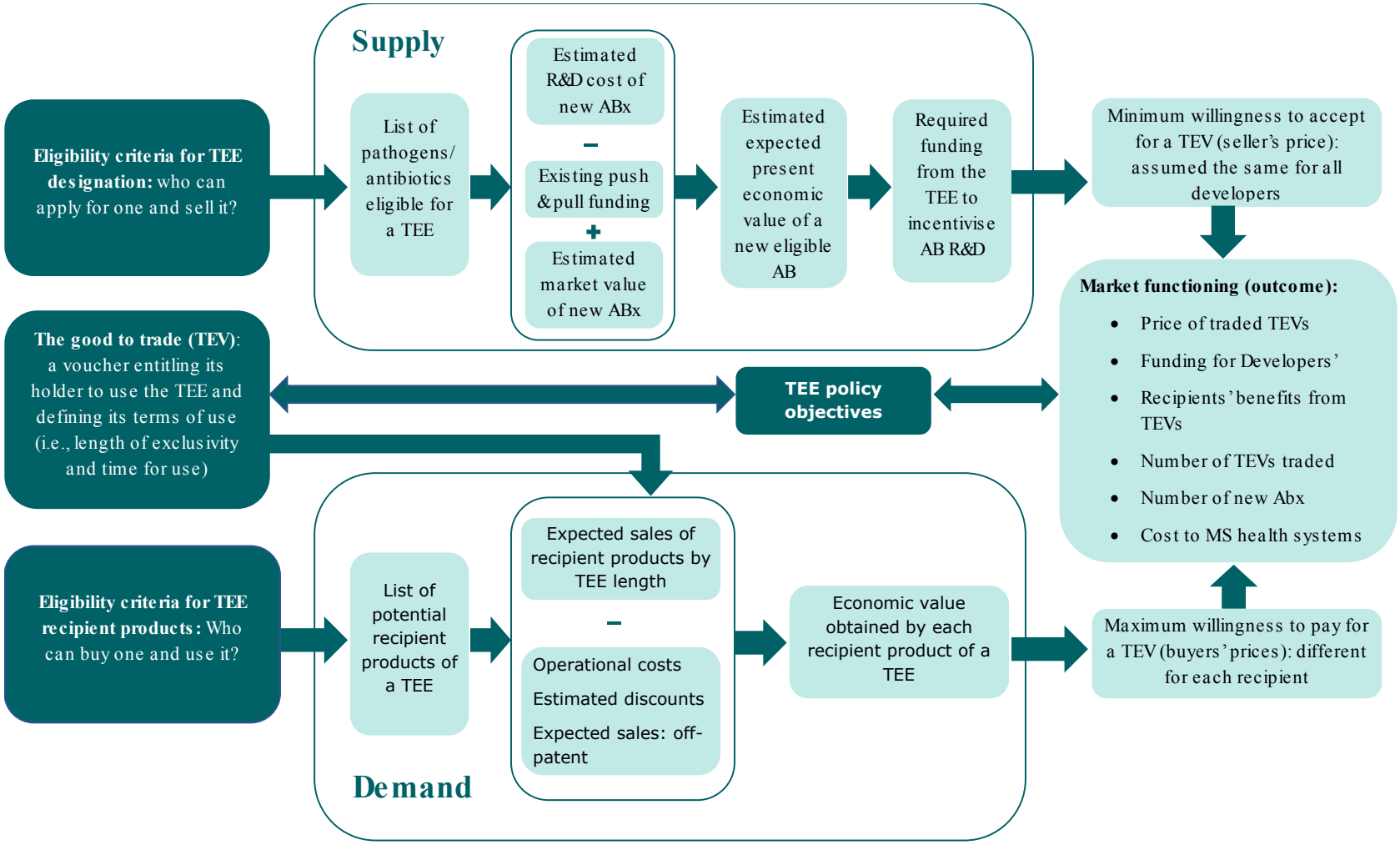
This diagram summarises OHE's conceptualisation of the market for TEE Vouchers



3. Eligibility criteria and analysis of the number of qualifying antibiotics required

3. Eligibility criteria: role of the EMA (i)

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- Assume the EU introduces a TEE for qualifying antibiotics from (say) 1st January 2021
- The EMA would be responsible for drawing up a list of priority lists of categories of antibiotics needed based on the pathogens that they would tackle:
  - The EMA could set up an Expert Advisory Group to support it, including ECDC members. Alternatively, the ECDC could be required to draw up the list;
  - In recognition that R&D is a global activity and resistance patterns are a global phenomena, the EMA would be expected to have reference to work done elsewhere (notably in the US and by WHO) on priority pathogen lists.
- The criteria for EMA designation would need to be set out, but, there would be no limit to the potential number of antibiotic categories identified as priorities.
- The EMA would be given (say) 6 months to draw up the initial priority pathogen list.
- The EMA would accept applications for TEE designation for drugs from (say) 1st July 2021. The process of designation to be modelled on that for orphan drug designation.

3. Eligibility criteria: role of the EMA (ii)

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- The EMA would determine if a particular product is expected to address a pathogen on its priority list and so is entitled to a TEE designation.
- Designation entitles the holder to benefit from EMA regulatory facilitation through protocol assistance and scientific advice on clinical development and on licensing routes and applications.
- Within a listed category there is no restriction on the number of products that can obtain a TEE designation.
- Within a priority listed category there is no restriction on the number of products that can obtain a Transferable Exclusivity Extension Voucher (TEE Voucher).
- The EMA determines if a new antibiotic meets the requirements for an EU licence and then whether the licenced product indication is in line with the TEE designated indication and so meets the requirement for a TEE Voucher.
- EMA can recommend additions and removals from the priority pathogen list. Criteria will be needed for removals. These could include: (i) the numbers of new products licensed; (ii) the number of TEE Vouchers designated; or (iii) reduced trends in resistance.

3. Eligibility criteria: Comparison of the three priority lists (i)

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- Priority lists aim to prioritise funding and facilitate global coordination of R&D strategies for the discovery of new active agents against bacteria with acquired resistance to antibiotics
- We compare three priority lists (all global):

  - WHO (2017) – ranks antibiotic-resistant bacterium into critical, high and medium

    * Criteria: treatability, mortality, healthcare burden and 10-year trend of resistance

  - CDC (2013) – ranks antibiotic-resistant bacterium into urgent, serious and concerning

    * Criteria: burden of illness, level of concern and antibiotics left to defend against these infections

  - ESKAPE (2008/9) –classifies antibiotic-resistant bacterium only as ‘of interest’

- Priority lists help to identify the most plausible set of criteria to be applied to establish priorities

3. Eligibility criteria: Comparison of the three priority lists (ii)

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Bacteria (WHO category)	WHO (2017)	CDC (2013)	ESKAPE (2008-9)
Acinetobacter baumannii, carbapenem-R	Critical	Serious (MDR)	Yes
Pseudomonas aeruginosa, carbapenem-R	Critical	Serious (MDR)	Yes
Enterobacteriaceae, carbapenem-R, 3rd-gen ceph-R (ESBL+)	Critical	Urgent (carbapenem-R) Serious (ESBL+)	Yes
Enterococcus faecium, vancomycin-R	High	Serious (VRE)	Yes
Staphylococcus aureus, methicillin-R, vancomycin-I/R	High	Serious (MRSA) Concerning (VRSA)	Yes
Helicobacter pylori, clarithromycin-R	High		
Campylobacter spp., fluoroquinolone-R	High	Serious (drug-R)	
Salmonellae spp., fluoroquinolone-R	High	Serious (drug-R)	
Neisseria gonorrhoeae, 3rd-gen ceph-R, fluoroquinolone-R	High	Urgent (drug-R)	
Streptococcus pneumoniae, penicillin-NS	Medium	Serious (drug-R)	
Haemophilus influenzae, ampicillin-R	Medium		
Shigella spp., fluoroquinolone-R	Medium	Serious	
Clostridium difficile		Urgent	
Candida spp. fluconazole-R		Serious (Flu-R)	
M. tuberculosis		Serious (drug-R)	
Group A *Streptococcus*		Concerning (erythro-R)	
Group B *Streptococcus*		Concerning (clinda-R)	

WHO PPL, CDC, & ESKAPE

Source: Rex, 2017 (http://amr.solutions/blog/who-priority-pathogens-list)

3. Eligibility criteria: Comparison of the three priority lists (iii)

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Pathogens listed as (WHO + CDC; total (*with no overlap*)):

1. Critical + Urgent = 3 + 3; 5 in total
2. High + Serious = 6 + 11; 13 in total
3. Medium + Concerning = 3 + 3; 6 in total

In total:

- **5 pathogens in the "Critical + Urgent"**
- **13 pathogens in the "High + Serious"**
- **18 pathogens in "Critical + Urgent" or "High + Serious"**

3. Eligibility criteria: Current pipelines (i)

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We collected information about what is currently in the pipeline by looking at three sources:

1. PEW Charitable Trusts: https://www.pewtrusts.org/en/research-and-analysis/data-visualizations/2014/antibiotics-currently-in-clinical-development
2. World Health Organization (WHO): https://apps.who.int/iris/bitstream/handle/10665/258965/WHO-EMP-IAU-2017.11-eng.pdf?sequence=1
3. Access to Medicine Foundation: https://amrbenchmark.org/research-areas/rd/

3. Eligibility criteria: Current pipelines (ii)

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PEW (2018)					WHO (2017)					Access to Medicine Foundation				
Distribution per phase of development	I	II	III	Reg	Distribution per phase of development	I	II	III	Reg	Distribution per phase of development	I	II	III	Reg
	15	12	11	4		23	11	13	2		*Information not available*			
Total	42				Total	59[a]				Total	87 projects			
Active by priority lists: • CDC: 21 are active against the urgent pathogen lists • WHO: 21 active to priority pathogens • ESKAPE: 19 are active to pathogens considered of special interest					Active by priority lists: • WHO: 42 are new therapeutic entities active against priority pathogens [a]*Includes biologicals*					Active by priority lists: • 28 antibiotics in clinical development that target pathogens posing significant threats due to AMR (according to WHO and CDC)				

The objective of this section is to try to estimate the expected number of future antibiotics over the next 5-10 years, and within those, how many could be eligible for a TEE:

- Two methods have been used:
  1. **Based on current pipeline** (PEW, WHO), apply “average” (industry) success rates and duration to estimate expected launches, by when - we focus also on antibiotics active against “critical” priority pathogens
  2. **Based on the number of approved QIDP-antibiotics** as proxy for future QIDP-antibiotics

3. Eligibility criteria: Current pipelines (iii)

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- We have estimated expected future launches, based on PEW's pipeline information, and applying "average" (industry):
  - Success rates, and
  - Duration per phase
- Our method assumes all projects in each phase are half-way through their respective development phase. One implication is that future antibiotics will be expected in "blocks"
- Our method implies that from each project in the pipeline, we will get a share of that project approved (e.g. the probability of progressing from phase 1 to approval is 0.12 (see next slide); thus, for each project currently in phase 1, we will get a 12/100th of a project)
- Next slide shows assumptions on success rates and durations (average from 3 sources), and expected launches, in which year, based on PEW's pipeline information (42 antibiotics in the pipeline)

3. Eligibility criteria: Current pipelines (iv)

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Assumptions: Success rates & Durations

	Individual				Cumulative* (from phase to launch)			
	Phase I	Phase II	Phase III	Registration	Phase I	Phase II	Phase III	Registration
Success rates	0,44	0,47	0,68	0,86	0,12	0,27	0,58	0,86
Duration (months)	15	25	30	11	73,8	53,7	26,0	5,5
Projects in pipeline	15	12	11	4	**42**			

* For cumulative duration, we assume all projects are half way through their respective phase (total duration = 81 months)

Expected launches

	Year of launch				
	2019	2021	2023	2025	**Total**
Expected number of launches	2,57	6,68	3,87	1,82	***14,94***

- Using the PEW assumptions the current pipeline (with no changes) would give us nearly **15 antibiotics**, launched between 2019 and 2025 (implying **slightly over 2 antibiotics per year**).
- Analysis based on **QIPD designations and approvals** from 2012 until 2017 shows that **FDA has approved 12 antibiotics with QIPD over the last five years** – this implies **2.4 drugs with QIDP designation come to market per year.** We take this as supporting our expectation of **slightly over 2 antibiotics per year.**
- For the **critical 3 pathogens**, our analysis estimates **around 5-6 antibiotics in total over 6-7 years (circa 1 per year)**
  - Note that WHO report states a slightly lower number (“*only one to two could probably make it to the market”)*

3. Eligibility criteria: The gap - numbers of products needed (i)

We now estimate the number of new antibiotics needed to cover the "gap" between the current pipeline and "needs" (as per the priority lists)

As noted earlier, the pathogens listed as (WHO + CDC; total (*with no overlap*)):

1. **Critical + Urgent** = 3 + 3; **5 in total**
2. **High + Serious** = 6 + 11; **13 in total**
3. **Medium + Concerning** = 3 + 3; **6 in total**

- In total, **18 pathogens deemed as "Critical + Urgent " or "High +Serious"**
- We **assume 3 antibiotics required for each bacteria**, requiring **54 antibiotics to address "Critical/High" + "Urgent/Serious" priority areas.** 18 are expected from current pipelines, **an additional 36 are required (3 per year over a 10 year period)**
- Focusing only on "**Critical + Urgent" priority areas**, 5 pathogens will require **15 new antibiotics** (3 per pathogen). 5 of the 15 from current pipelines are expected in these priority areas, **an additional 10 are required (1 per year over a 10 year period)**

3. Eligibility criteria: The gap - numbers of products needed (ii)

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Given development times, we assume that:

- A TEE policy implemented in 2021 will increase the number of projects starting in phase-I in the same year of implementation
- A TEE implemented in 2021 will bring first additional antibiotics to the market with a delay of around six years - say from 2027 onwards

We work with the following two scenarios for the number of antibiotics needed to cover the gap for AMR:

- Scenario 1: increase the number of antibiotics to tackle the 18 pathogens within **"Critical/Urgent"** or **"High/Serious"** categories of WHO and CDC to over 3 per year between 2027-2036
- Scenario 2: increase the number of **new class** antibiotics to tackle the 5 pathogens within **"Critical/Urgent"** categories of WHO and CDC to 1 per year between 2027-2036

3. Eligibility criteria: The gap - numbers of products needed (iii)

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Pipeline Estimate in 2027 to meet the objective of each scenario

	Development phase					
	PCRD	Phase I	Phase II	Phase III	Registration	Overall
Success rates of antibiotics	0.35	0.44	0.47	0.68	0.86	0.042
Scenario 1: number of projects per phase of development	94.5	33.1	14.6	6.8	4.7	4
Success rates of "new class" antibiotics	0.175	0.67	0.46	0.7	0.87	0.032
Scenario 2: number of projects per phase of development	30.4	5.3	3.6	1.6	1.2	1

Sources: OHE consulting Ltd; Towse et al. (2017); O'Neill (2015)

- The table shows, per scenario, the number of projects needed to start within each phase of development to meet the objective of the number of antibiotics:
  - Designation criteria should be defined to grant candidates that meet the objective (e.g. critical, urgent, new class) of each scenario. We assume designation occurs prior to entry into Phase 1
  - Around 33 new designated antibiotics would be required per year in Scenario 1 and around 5 per year in Scenario 2
  - Such numbers of designated antibiotics will produce 4 TEEs per year in Scenario 1, and 1 per year in Scenario 2, in both cases from 2027 onwards

3. Eligibility criteria: The gap - numbers of products needed (iv)

OHE

We assume therefore that, for a TEE implemented from 2021

- If the TEE is targeted at **"Critical/Urgent"** and **"High/Serious"** pathogens, then:
  - 13 products would obtain TEE Vouchers in the period 2021-2026, and a further 36 over the period 2027-2036. (This **an average of 3 per annum** over the period 2021-2036)
- If the TEE is targeted only at **"Critical/Urgent"** pathogens, for which we assume new classes of products are needed, then:
  - 5 products would obtain TEE Vouchers in the period 2021-2026 and a further 10 over the period 2027-2036. (This is **an average of 1 per annum** over the period 2021-2036. However, **for modelling purposes we assume 2 per annum**, so that we can understand the pressure on TEE values.)

4. Value of a TEE to a recipient

4. Value of a TEE: eligible candidates to “purchase” a TEE

OHE

- We begin with the top-30 on-patent products by sales in the EU/EEA in 2018
- We reduce the list to 13 products by removing from the top-30 those products losing the exclusivity in less than 2 years time – an EFPIA suggested qualifying condition for a TEE buyer
- For the forecast analysis of gross values of TEEs and WTP we use the top-50 list, which after excluding < 2 years exclusivity products, is reduced to 18 products

4. Value of a TEE Voucher: 13 eligible candidates from top 30 to "purchase" a TEE Voucher

OHE

List of eligible candidates to "purchase" a TEE based on top-30 products by sales in EU/EEA

Ranking	From Top 30 - 2018	Date 1st EU launch	Date 1 patent expiry EU5	2018	2017	2016	2015	2014
2	P-1	ago-2016	mar-2028	€ 2.248.421.237	€ 1.617.034.320			
5	P-2	jun-2011	may-2026	€ 1.917.999.323	€ 1.917.999.323	€ 920.056.776	€ 486.895.508	
6	P-3	may-2015	jun-2026	€ 1.787.076.048	€ 1.316.171.460	€ 695.911.980		
7	P-4	jul-2015	jun-2028	€ 1.611.421.923	€ 792.821.433			
8	**P-5**	ago-2017	sep-2031	€ 1.597.593.586				
9	P-6	dic-2012	may-2025	€ 1.558.977.404	€ 1.332.645.378	€ 1.138.365.697	€ 872.221.467	€ 532.714.473
15	P-7	jun-2013	mar-2026	€ 1.073.875.309	€ 951.843.115	€ 794.405.954	€ 514.713.506	
18	P-8	oct-2014	dic-2026	€ 1.035.132.395	€ 738.222.979			
20	P-9	sep-2014	sep-2024	€ 876.412.570	€ 757.257.808	€ 560.824.675		
22	P-10	mar-2014	feb-2028	€ 874.208.290	€ 793.678.817	€ 686.254.427	€ 548.645.458	
25	P-11	nov-2009	oct-2024	€ 768.706.785	€ 745.688.386	€ 711.585.184	€ 617.788.664	€ 471.632.000
27	**P-12**	nov-2015	jul-2027	€ 743.594.976				
29	**P-13**	mar-2015	ene-2026	€ 741.374.011				

Note: in **BOLD** new product in top 30 in 2018
Source: IQVIA

4. Value of a TEE Voucher: Estimated generic impact in the first year after loss of exclusivity

OHE

- We have the date of 1st patent expiry in EU5 for all branded medicines in our database
- However, that is not enough information to know when exactly generic/biosimilar versions of branded entered the market
- We identify the highest reduction in sales any one year, and then we calculate the average of:
  - i. All of them (n = 18)
  - ii. Top 5 largest
  - iii. Top 3 largest (the one used, **47%**)
- Impact of generic competition has been calculated both, in percentage terms and in absolute value

Average reductions (n = 18)	
Percentages	Sales
-23,0%	260.018.403 €

Average reductions (N = top 5)	
Percentages	Sales
-38,9%	499.957.203 €

Average reductions (N = top 3)	
Percentages	Sales
-46,7%	599.071.787 €

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: Estimates of gross and net revenues - profit margins and willingness-to-pay for a TEE

OHE

We followed a stepped approach to estimate the willingness-to-pay (WTP) for a TEE Voucher of one year:

- **Step 1:** apply 30% reduction to (gross) sales due to discounting [**net sales = gross sales * 0.7**]
- **Step 2:** assume 80% profit margin [**profit = 80% * net sales**]
- **Step 3:** from the generics entry analysis (see later), we estimate a 47% reduction in gross sales as a result of generic entry, applying this reduction to net sales [**"Lost net sales after generic entry" = net sales * 0.47**] we obtain the WTP for a TEE
  - **Note:** we assume for simplicity that "**Lost net sales after generic entry"** are equivalent to "**Lost net profit after generic entry"** i.e. operational costs are assumed to remain the same**.**

4. Value of a TEE Voucher: Estimates of gross and net revenues - estimated WTP for a one year TEE in respect of 13 products

OHE

WTP for a TEE	
P-1	€ 734.715.779
P-2	€ 626.743.932
P-3	€ 583.962.181
P-4	€ 526.563.748
P-5	€ 522.045.067
P-6	€ 509.426.472
P-7	€ 350.909.839
P-8	€ 338.249.831
P-9	€ 286.385.012
P-10	€ 285.664.721
P-11	€ 251.190.033
P-12	€ 242.984.256
P-13	€ 242.258.512

Sources: IQVIA and OHE Consulting Ltd.

Source: Authors' calculations

Results: highest WTP for a 1 year TEE is €734K, followed by €626K and €584K. By the 11th product the WTP has fallen to €251K, 34% of the WTP of the highest value product.

- Results should be interpreted with caution as calculations are based on 2018 sales
  - Some of these medicines are relatively new products, there is still scope that sales will be higher in the future (increasing the WTP for a TEE Voucher)

4. Value of a TEE Voucher: Estimates of gross and net revenues - evolution of gross sales from a TEE Voucher and WTP for a TEE Voucher over time

OHE

- Our analysis indicates that if “Critical + Urgent” and “High + Serious” pathogens are targeted, then:

  - 2 TEE Vouchers per year may be needed for the period 2021-6;

  - 4 TEE Vouchers may be needed per year 2027-2036

- If only “Critical + Urgent” pathogens are targeted then:

  - 1 TEE Voucher per year may be needed for the period 2021-2036

- In practice there may be fewer or more TEE Vouchers. For ease of initial modelling **we set out the impact of 2 and 3 TEE Vouchers being sold per year** under the circumstances of (i) no replenishment and (ii) replenishment, i.e. new products entering the top 50.

4. Value of a TEE: The results of the modelling

OHE

In the following slides we set out:

- The assumptions we use in the modelling
- Value of a TEE (2 per year): Evolution of WTP of the two potential buyers with highest gross sales

  - With and without replacement “best selling” drugs
- Value of a TEE (3 per year): Evolution of WTP of the three potential buyers with highest gross sales

  - With and without replacement “best selling” drugs
- A summary of the results

4. Value of a TEE: The results of the modelling – Assumptions (i)

OHE

We analyse how the sales of potential buyers of a TEE Voucher will evolve over time.

For this, we:

1. **Estimate sales of remaining potential buyers (as actual buyers are "eliminated" from the pool)**

- We take the list of top-50 products by sales in 2018 as the starting point
- We use the three TEE per year scenario to see how the gross value of TEE Vouchers and WTP of buyers evolve over time
- We assume no replacement of buyers leaving the list of eligible products
- We assume, for products with no history (new in the list in 2018), that they grow at the average CAGR of the bottom 4 products of top-30 with available data (e.g., 18, 20, 22, 25)

2. **Assessed the impact of new entries to the top-30 list**

- We have identified the new entries in the top-30 list between 2014-2018 to assess how likely is that new entries can replace buyers of TEE who leave the market
- For the highest and the second highest we have identified the entry position and gross sales

3. **Based in the new entries analysis we assume one/two "average" new entrant(s) in the list which change the WTP of potential buyers**

4. Value of a TEE Voucher: The results of the modelling - Assumptions (ii)

OHE

- We assume same CAGR for 2019 onwards as for the historic period
- In both cases analysed, 2 and 3 TEE Vouchers per year, we assume no replacement to estimate next year's highest gross sales and WTP products still in the list
- Based on our analyses, over the following 5-8 years:
  - Gross sales for the 2 highest selling medicines decrease overall over time (2018-2026) ranging between €1.4bn and €2.4bn
  - WTP for the 2 highest selling medicines decreases overall over time (2018-2026) ranging between €802m and €455m
  - Gross sales for the 3 highest selling medicines decrease overall over time (2018-2023) ranging between €2.3bn and €1.0bn
  - WTP for the 3 highest selling medicines decreases overall over time (2018-2023) ranging between €750m and €349m

4. Value of a TEE Voucher: The results of the modelling - impact of potential new entries to the top-30 list

OHE

- We have identified the new entries to the top-30 between 2014 and 2018 to assess whether new entrants could "replace" some of the existing products with highest sales
- Evidence from 2014-2018 shows that a new entrant made it twice to the top-3 (note 2015 entry is Harvoni)
- From this analysis, it could be argued that:
  - A new entry per year to the top-10 is very likely, with an expected average gross sales value around €1.6bn
  - A second entry per year in the top-30 is also likely, with an expected average gross sales value around €933m
- As part of the analysis we artificially introduce in the top-30 two new entrants per year of the estimated average gross sales

Year	2018	2017	2016	2015	2014	Average
Highest Position	8	3	19	2	10	8.4
2nd highest position	27	12	24	20	*NE*	20.75
Highest gross sales	€ 1.597.593.586	€ 1.617.034.320	€ 920.056.776	€ 2.675.187.998	€ 1.222.534.039	€ 1.606.481.344
2nd highest gross sales	€ 743.594.976	€ 1.325.344.608	€ 794.405.954	€ 872.221.467	*NE*	€ 933.891.751

Notes: green cells show highest/best values and red cells lowest/worst values
Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: The results of the modelling - 2 per year, evolution of WTP of the two potential buyers with highest gross sales

OHE

Buyers WTP for a TEE over time – 2 TEE per year

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 799.676.431	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 802.075.891	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 782.743.804	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 609.167.556	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 561.629.743	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 519.348.560	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 455.176.405	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 497.763.254	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 473.385.710	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 471.971.805	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 494.214.321	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 469.592.056	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 499.322.934	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 557.750.544
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 520.981.967

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: The results of the modelling - 3 per year, evolution of WTP of the two potential buyers with highest gross sales

OHE

Buyers WTP for a TEE over time – 3 TEE per year

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 0	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 0	€ 0	€ 0	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 0	€ 0	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 0	€ 0	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 0	€ 0	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 0	€ 0	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 0	€ 0	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 0	€ 0	€ 0
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 0	€ 0	€ 0

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: The results of the modelling – estimated time evolution of the gross value of TEE and WTP with no replacement

OHE

Estimated time evolution of the gross value of TEE and WTP assuming no replacement of product (no new entrants)

		2018	2019	2020	2021	2022	2023	2024	2025	2026
2 TEEs per year	1st TEE gross Value	€ 2,248,421,237	€ 2,447,217,715	€ 2,454,560,688	€ 1,864,211,044	€ 1,589,341,573	€ 1,448,683,306	€ 1,512,424,270	€ 1,528,057,954	€ 1,706,861,624
	2nd TEE gross Value	€ 1,917,999,323	€ 2,297,344,952	€ 2,395,399,476	€ 1,718,732,983	€ 1,392,958,099	€ 1,444,356,388	€ 1,437,073,740	€ 1,523,284,927	€ 1,594,340,224
	Total gross value	**€ 4,166,422,578**	**€ 4,744,564,687**	**€ 4,849,962,175**	**€ 3,582,946,049**	**€ 2,982,301,695**	**€ 2,893,041,718**	**€ 2,949,500,034**	**€ 3,051,344,906**	**€ 3,301,203,874**
	1st TEE WTP	€ 734,715,778	€ 799,676,430	€ 802,075,891	€ 609,167,555	€ 519,348,560	€ 473,385,710	€ 494,214,321	€ 499,322,934	€ 557,750,544
	2nd TEE WTP	€ 626,743,931	€ 750,702,563	€ 782,743,803	€ 561,629,743	€ 455,176,404	€ 471,971,805	€ 469,592,056	€ 497,763,254	€ 520,981,967
	Total WTP	**€ 1,361,459,711**	**€ 1,550,378,994**	**€ 1,584,819,695**	**€ 1,170,797,299**	**€ 974,524,965**	**€ 945,357,515**	**€ 963,806,377**	**€ 997,086,189**	**€ 1,078,732,511**
3 TEEs per year	1st TEE gross Value	€ 2,248,421,237	€ 2,297,344,952	€ 1,551,129,306	€ 1,239,816,094	€ 1,158,294,073	€ 1,170,267,171			
	2nd TEE gross Value	€ 1,917,999,323	€ 1,980,250,088	€ 1,451,457,223	€ 1,109,477,890	€ 1,136,283,433	€ 1,143,973,880			
	3rd TEE gross Value	€ 1,787,076,048	€ 1,932,452,756	€ 1,180,219,866	€ 1,106,164,109	€ 1,100,586,673	€ 1,068,559,716			
	Total gross value	**€ 5,953,496,608**	**€ 6,210,047,797**	**€ 4,182,806,396**	**€ 3,455,458,094**	**€ 3,395,164,180**	**€ 3,382,800,768**			
	1st TEE WTP	€ 734,715,778	€ 750,702,563	€ 506,861,951	€ 405,134,248	€ 378,495,327	€ 382,407,772			
	2nd TEE WTP	€ 626,743,931	€ 647,085,591	€ 474,292,141	€ 362,543,681	€ 371,302,918	€ 373,815,923			
	3rd TEE WTP	€ 583,962,181	€ 631,466,875	€ 385,660,010	€ 361,460,838	€ 359,638,301	€ 349,172,864			
	Total WTP	**€ 1,945,421,892**	**€ 2,029,255,029**	**€ 1,366,814,104**	**€ 1,129,419,608**	**€ 1,109,138,768**	**€ 1,105,396,560**			

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: The results of the modelling - 2 per year, evolution of WTP of 2 potential buyers with highest gross sales, with replacement

OHE

Buyers WTP for a TEE over time – 2 TEE per year and replacement

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 799.676.431	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 802.075.891	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 782.743.804	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 609.167.556	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 561.629.743	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 519.348.560	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 455.176.405	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 497.763.254	€ 548.850.826
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 473.385.710	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 471.971.805	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 494.214.321	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 469.592.056	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 499.322.934	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 557.750.544
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 520.981.967
Entrant 1	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317
Entrant 2	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: The results of the modelling - 3 per year, evolution of WTP of 2 potential buyers with highest gross sales, with replacement

OHE

Buyers WTP for a TEE over time – 3 TEE per year and replacement

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 0	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 0	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 0	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 0	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 0	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 0	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 0	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 0	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 0
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 0
Entrant 1	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317
Entrant 2	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463

Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE Voucher: Summary of results (i)

OHE

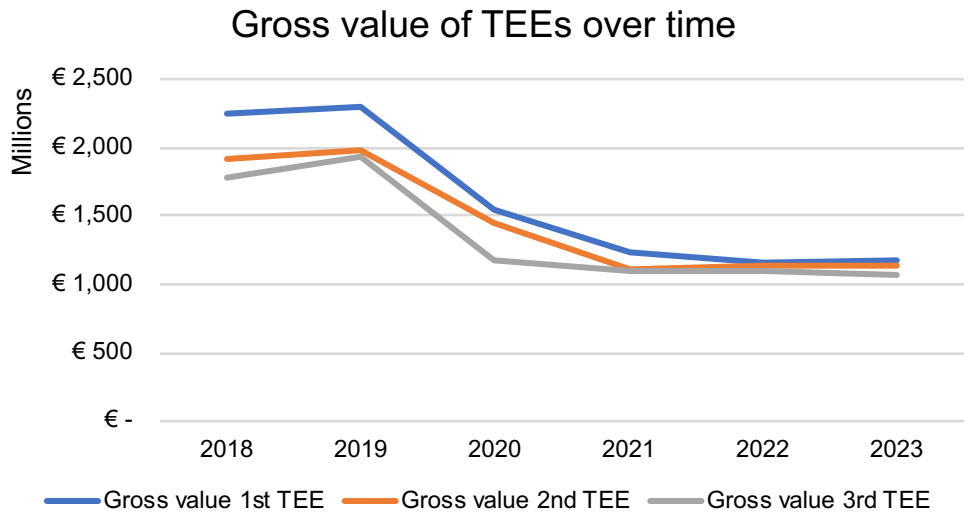
Based on our previous analyses we estimate the following maximum, minimum and average WTP of a TEE Voucher for the different scenarios: 2 or 3 TEE Vouchers per year, with and without replacement over the period 2018-2026

Scenario	Minimum WTP	Maximum WTP	Average WTP 2018-2026
Two TEE per year without replacement	€ 469,592,056	€ 802,075,891	**€ 590,386,848**
Three TEE per year without replacement [a]	€ 349,172,865	€ 802,075,891	**€ 482,525,717**
Two TEE per year with replacement	€ 473,385,710	€ 802,075,891	**€ 603,340,325**
Three TEE per year with replacement	€ 405,134,248	€ 802,075,891	**€ 519,454,071**

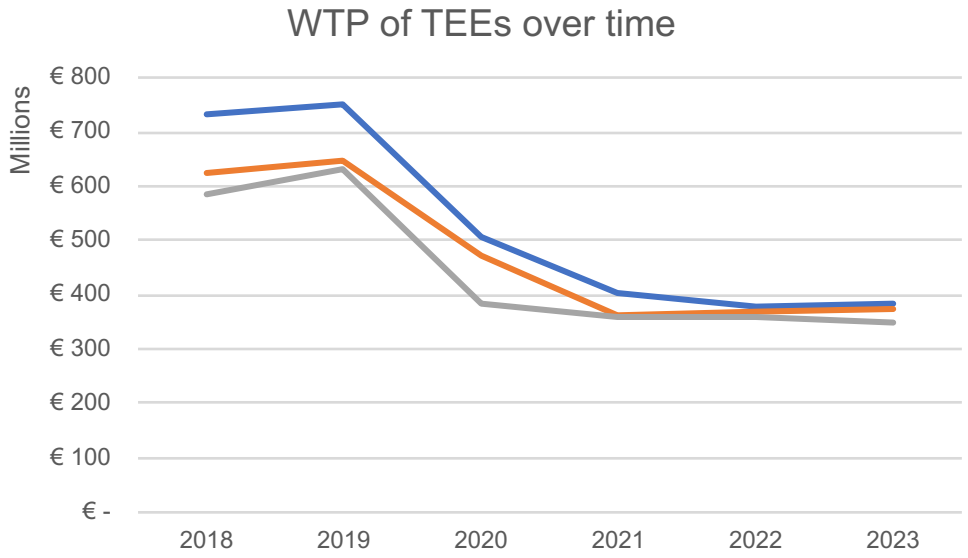
Notes: [a]average calculated only for the period 2018-2023
Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE: Summary of results (ii) Evolution of the estimated value of TEE and WTP when 3 TEE Vouchers per year are traded with no replacement

- The three highest gross values of TEEs and WTP go down as time progress as recipients with highest WTP acquire a TEE Voucher
- Assuming no new entrants, if three TEEs are traded per year the market for eligible top 50 products would be exhausted after 6 years
- Results must be taken with caution as for those products entering in the list in 2018 (mostly those towards the bottom of the rank) we have applied the average CAGR of the older products to predict future growth in sales



Sources: IQVIA and OHE Consulting Ltd.



Sources: IQVIA and OHE Consulting Ltd.

4. Value of a TEE: Summary of results (iii)

OIE

- We assume for ease of calculation that TEE Vouchers offer 1 year of TEE
- The results suggest that:
  - An **expected supply of 3 TEE Vouchers per year would generate net revenues after a few years of around €350m**
  - An **expected supply of 2 TEE Vouchers per year would generate net revenues after a few years of around €500m**
  - In both cases **some TEE Vouchers could sell for up to €800m**
- Note that there are a number of important assumptions underlying these estimates

5. Estimation of net revenues needed from a TEE Voucher

5. Estimation of net revenues needed from a TEE Voucher – the R&D cost of a new antibiotic

OHE

- To estimate the cost of developing a new antibiotic we followed the same methods of Mestre-Ferrandiz et al. 2012 (MF2012) which is in line with the established literature – a diagram showing a detailed description of methods is available next slide
- MF2012 estimate the R&D cost of a new drug based on four drivers of the cost:
  - Out-of-pocket cost of each development phase: how much is paid in cash
  - Development phases' success rates: the rate of projects that progress to the next phase
  - Cost of capital: the opportunity cost of investing in pharmaceutical R&D
  - Time of development: the time that takes to develop a new medicine from pre-clinical stage to market approval
- We updated the model to estimate the R&D cost of a new antibiotic by looking at Towse et al. 2017, Ferraro et al. 2017 and OHE Consulting Ltd. unpublished work, which provide:
  - Success rates specific for antibiotics and for both, same class and new class antibiotics
  - Out-of-pocket costs per development phase of new antibiotics
  - Development times for new antibiotics

5. Estimation of net revenues needed from a TEE Voucher – the method to estimate the R&D cost of a new antibiotic

OHE

The cost of R&D of a new successful drug (Mestre-Ferrandiz et al., 2012)

Development stage	Mean cost per stage	Stage duration (years)	Cost of capital	Capitalised Cost (CC) per stage	Probability of success	# of compounds per stage per 1 successful drug	Hypothetical capitalised cost per phase
Pre-clinical Research and development (PCRD)	MCPC: Mean Cost Pre-Clinical Phase	Time per development stage (years)	Cost of capital applied to estimate the capitalised cost per stage	CC of PCRD +	P1: probability of success pre-clinical R&D	#PCRD=1/PT	Hypothetical CC of PCRD=#PCRD* CC of PCRD +
Phase I (PI)	MCPI: Mean Cost of Phase I			CC of PI +	P2: probability of success phase I	#PI=#PCRD*P1	Hypothetical CC of PI=#PI*CC of PI +
Phase II (PII)	MCPII: Mean Cost of Phase II			CC of PII +	P3: probability of success phase II	#PII=#PI*P2	Hypothetical CC of PII=#PII*CC of PII +
Phase III (PIII)	MCPIII: Mean Cost of Phase III			CC of PIII +	P4: probability of success phase III	#PIII=#PII*P3	Hypothetical CC of PIII=#PIII*CC of PIII +
Regulatory review & MA (MA)	MCMA: Mean Cost of Marketing Authorisation			CC of MA = **Total CC**	P5: probability of success MA **Overall probability of success: PT=P1*P2*P3*P4*P5**	#MA=#PIII*P4 **Result=#MA*P5 = 1 successful drug**	Hypothetical CC of MA=#MA*CC of MA = **Total Hypothetical CC cost of a new successful medicine**

TIME LINE

Source: Mestre-Ferrandiz et al. 2012

5. Estimation of net revenues needed from a TEE Voucher – estimation of R&D cost for an "existing class"

OHE

The R&D cost of a new antibiotic (existing class in € 2018)

	PCRD	Phase I	Phase II	Phase III	Registration	Total
Success rate	0.35	0.67	0.46	0.7	0.87	0.066
Number of compounds needed per one successful	15.2	5.3	3.6	1.6	1.15	1
Cost per project and phase	€15.21m	€12.1m	€42.3m	€153.1m	€22.8m	€225.9m
Capitalised cost	€37.0m	€21.8m	€64.3m	€187.0m	€23.8m	€333.9m
Duration of each phase	5	1.33	2.2	2.4	0.9	11.83
Cost of capital	10%					
Expected capitalised cost adjusted by success rates	**€563.4m**	**€116.0m**	**€229.7m**	**€307.1m**	**€27.4m**	**€1243.5m**

Sources: Mestre Ferrandiz et al. 2012; Towse et al. 2017; OHE Consulting Ltd.

5. Estimation of net revenues needed from a TEE – estimation of R&D cost for a "new class"

OHE

The R&D cost of a new antibiotic (new class in € 2018)

	PCRD	Phase I	Phase II	Phase III	Registration	Total
Success rate	0.175	0.67	0.46	0.7	0.87	0.033
Number of compounds needed per one successful	30.4	5.3	3.6	1.6	1.15	1
Cost per project and phase	€15.21m	€12.1m	€42.3m	€153.1m	€22.8m	€225.9m
Capitalised cost	€37.0m	€21.8m	€64.3m	€187.0m	€23.8m	€333.9m
Duration of each phase	5	1.33	2.2	2.4	0.9	11.83
Cost of capital	10%					
Expected capitalised cost adjusted by success rates	**€1,126.8m**	**€116.0m**	**€229.7m**	**€307.1m**	**€27.4m**	**€1,806.9m**

Sources: Mestre Ferrandiz et al. 2012; Towse et al. 2017; OHE Consulting Ltd.

5. Estimation of net revenues needed from a TEE – share of R&D cost to be met by the EU

OHE

- Estimated R&D cost for both, existing class or new class antibiotics, represent the global cost
- In order to estimate the share of the global R&D cost to be met by the EU, we apportion the global cost by the EU market share over the Western pharmaceutical sales as per table below

Country	2017 $ (Bill)	2016 $ (Bill)	2015 $ (Bill)	2014 $ (Bill)	2013 $ (Bill)	Average
Western Market	784.6	769.5	733.4	717.2	670.3	733.0
EU	214.6	205.0	200.4	221.1	213.5	210.9
EU %	27.3%	26.6%	27.3%	30.8%	31.8%	**28.8%**

Source: IQVIA World Review Executive™ 2018.

- Applying the apportionment rate of **28.8%** to both estimated R&D costs we have that:
  - **The cost of R&D** of a new antibiotic (**existing class**) to be met by EU markets is **€358.13m**
  - **The cost of R&D** of a new antibiotic (**new class**) to be met by EU markets is **€520.39m**

5. Estimation of net revenues needed from a TEE Voucher

Based in the analysis presented in Section 5 of this report we have estimated:

- An overall probability of getting a new AMR product of 6.57% for an existing class, and 3.28% for a new class
- A duration of roughly 12 years to develop a new product
- Assuming that the European market represents a 25.2% of the total market we have:
  - An **expected cost of € 520.39 million of developing a new class of AMR product**, given by the capitalised cost over the probability of success (**taking into account only a share from Europe of total R&D costs**)
  - An **expected cost of € 358.13 million of developing an existing class of AMR product**, given by the capitalised cost over the probability of success (**taking into account only a share from Europe of total R&D costs**)

5. Impact of other pull revenues on required sums from an EU TEE Voucher

OHE

- Taking information from the top 5 grossing antibiotics in 2018, and applying the same set of assumptions used to estimate the WTP of buyers, we have that:

- Gross sales: €17.3 million
- Net profit under patent protection (π^M): € 9.71 million (assumption: 56% of gross sales)
- Net profit after patent protection (π^C): € 4.04 million (assumption: 41.6% of net profit under patent protection)
- Nine years of exclusivity $(t = 9)$

- The present value of the AMR product (at launch) is

$$PV^{AMR} = \pi^M \frac{(1-\delta^t)}{(1-\delta)} + \pi^C \frac{\delta^{t+1}}{(1-\delta)} = \mathbf{€\ 78.6\ m}$$

(δ is the discount factor of a cost of capital, CoC, of 10%)

- However, the total capitalised cost of the AMR product (at launch – Europe share) is of €358.13 million for an existing class, and € 520.39 million for a new class

This market needs an additional incentive of:

- **€279.5 million to make individual firms invest in an existing class of AMR product**
- **€441.8 million to make individual firms invest in a new class of AMR product**

6. The market for TEEs: demand and supply side incentives and equilibrium

6. The Market for TEE Vouchers : using a theoretical approach

OHE

The following slides set out the approach used in modelling the market for TEE Vouchers assuming:

- No intermediary, but with two types of market: (i) simultaneous sales and (ii) a sequential market
- An intermediary selling the TEE Vouchers under three different types of auction: (i) uniform price (price of the lowest winning bid, or the price of the second-highest bid); (ii) discriminatory price (price paid is the highest bid) (iii) Vickrey auction (winner pays the price of the (losing) second-highest bid).
- The assumption is that a TEE Voucher includes a 12 month TEE
- We assume simultaneous sales (i.e. one market per year for all TEE Vouchers granted in that year) and a uniform selling price each year based on the lowest winning bid based on their actual WTP)
- A summary of the results is set out on Slide 73
- Full details are set out in the Appendix.

6. The Market for TEEs: overview of the market

OHE

We explore how a market for TEEs will work by using a game theoretical approach:

- Players: the TEE Voucher generator, the TEE Voucher buyer and the Public Health Authority (the EMA)
- Actions:
  - TEE Voucher generator: “invest” / “don’t invest” in each phase for the development of a new AMR product, “sell” / “use” the TEE
  - TEE Voucher buyer: “buy” / “don’t buy” the TEE Voucher (if bought, we assume it is used)
- Payoffs:
  - TEE Voucher generator: expected benefit from (i) the new AMR product, (ii) the TEE Voucher (“sell” / “use”), (iii) other push/pull incentives and (iv) the R&D investment cost
  - TEE Voucher buyer: expected (net) profit from the use of a TEE Voucher (i.e., extending the exclusivity period of a blockbuster drug)
  - Public Health Authority: value generated by the new AMR product minus the cost of the TEE to health care systems

The market for TEEs will work if all payoffs are positive at equilibrium: the objective of this analysis is to assess how many new AMR products a market of TEEs would generate under different specifications

- 2/3 TEE Vouchers per year for only for “new class” antibiotics
- 2/3 TEE Vouchers per year for “existing class” antibiotics

We assume that Public Health Authority’s payoff is always positive

6. The Market for TEEs: Supply side - the TEE Voucher generator

OHE

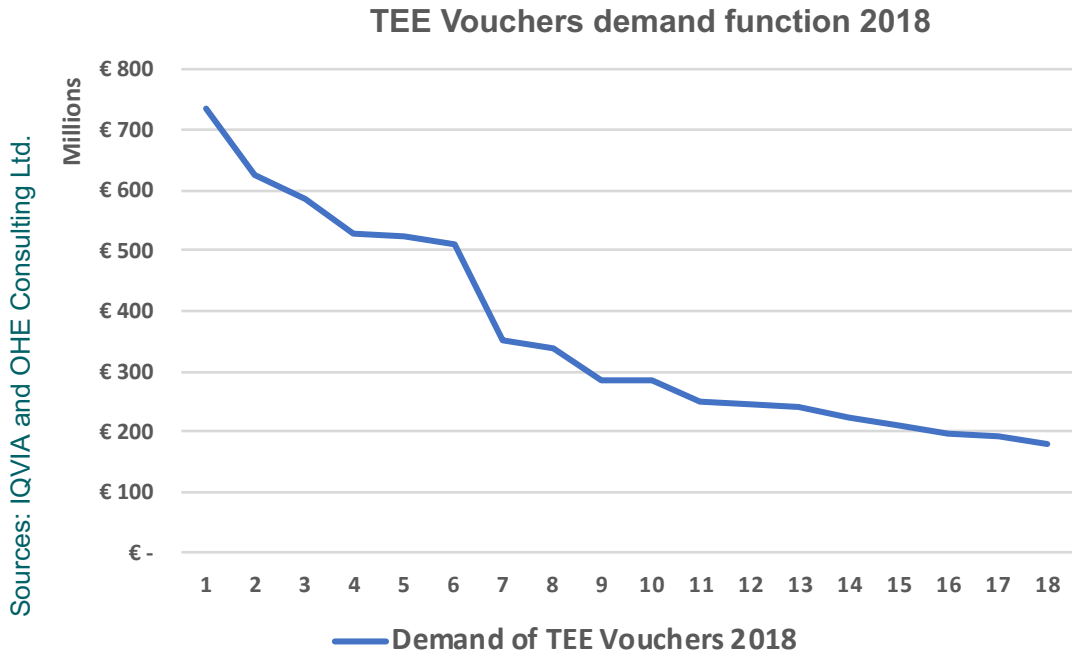
- We have estimated the capitalised R&D cost of a new successful “new-class” and an “existing class” antibiotic (estimates presented in section 5 of the report)
  - The R&D cost of a new **“existing class”** antibiotic (share of EU): **€358.13m**
  - The R&D cost of a new **“new class”** antibiotic (share of EU): **€520.39m**
- We have estimated the present value of an AMR product at launch based on sales data (IQVIA) of new antibiotics launched between 2009-2018 (estimate presented in section 5 of the report)
  - Present value at launch of a new antibiotic: **€78.6m**
- Based on the estimates presented in section 5 of the report, we estimate that the total incentive a supplier needs at PCRD stage to ‘start and keep’ investing in a new antibiotic until its market approval is:
  - **€279.5 million to make individual firms invest in an existing class of AMR product**
  - **€441.8 million to make individual firms invest in an new class of AMR product**

6. The Market for TEE Vouchers : Demand side - the TEE Voucher buyer

OHE

The demand of the TEE market will be determined by the WTP of potential buyers

- WTP of potential buyers will be determined by the profit a company may obtain using the exclusivity extension of the TEE Voucher net of profit it hypothetically would obtain after patent expiration
- Estimates of the WTP of potential buyers have been shown in Section 4 of this report
- The market for TEEs does not ensure a final price equal to the buyers WTP will be paid per each TEE Voucher: the final price will depend on competitive forces, mechanism of trade and buyers strategic behaviour.



Sources: IQVIA and OHE Consulting Ltd.

- Horizontal axis measures the number of TEE Voucher buyers (alternatively, the number of TEE Vouchers put in circulation)
- Vertical axis measure the WTP of the marginal buyer
- With 2/3 TEE Vouchers traded, the market price for each would be around €600m/€500m
- If the amount of funding needed by supply is €442m/€280m, then the market would function, although with limited capacity for “new class” AMR products
- Demand and prices will diminish over time, as buyers obtain their 1 TEE Voucher per product.

6. The Market for TEEs: results without an intermediary

OHE

- We first analyse a free market for TEE Vouchers without intermediary under two possible specifications: (i) simultaneous sales (one market per year), and (ii) sequential sales (each TEE Voucher sold individually at a time of choosing for the seller).
- With (i) simultaneous sales, and based on our data sample (top-50 products by sales in EU), the average price of a TEE Voucher results in €582.3m (with no strategic behaviour by sellers) or a higher €626.7m (if sellers behave strategically).
- Predicted market prices would be enough to incentivise the investment in the development of both, new class and existing class antibiotics.
- With (ii) sequential sales, predicted market prices are similar to (i). This is because:
  - If sellers can anticipate the price paid in the last future trade they will offer such price since the first sale of a TEE Voucher and therefore the price paid will result constant and equal to the price under simultaneous sales.
- In both cases the total value and number of TEE Vouchers traded and new AMR products incentivised will depend on how rapidly the WTP of potential buyers falls below the needed funding.

6. The Market for TEEs: results with intermediary (i)

OHE

- We now assume that there exists an intermediary who pays TEE Voucher generators the expected amount needed to "invest" in a new AMR product and then sells the TEE Vouchers at maximum price.
- We model using auction theory: uniform price, discriminatory price and Vickrey auction
- We see that gross results from the market with and without an intermediary **are closely equivalent** (under certain assumptions)
- We use two different approaches to model multi-TEE Vouchers auctions
  1. Simultaneous sales vs sequential sales: we explore differences of trading TEE Vouchers one by one versus trading all TEE Vouchers at once
  2. Uniform price vs discriminatory price vs Vickrey pricing: we explore how implemented mechanism (auction type) can affect strategies, outcomes and/or efficiency?
- We assume sealed-bid auctions or strategically equivalent clock auctions (i.e. no revelation of information during the auction)
- At first, each buyer wants only a single TEE Voucher – a condition called *singleton demand*
  - With singleton demand, bidders have only one allocation to evaluate
  - With a demand for more than one unit, a larger number of allocations can lead a bidder to reduce valuations, which can limit both efficiency and price competition.

6. The Market for TEEs: results with intermediary (ii)

OHE

- With an intermediary, results do not differ much from prices without an intermediary
  - With only one TEE Voucher sold to each buyer expected prices are €526.5m (€522.0m) when 2 (3) TEE Vouchers are sold
  - Prices are expected to be the same under simultaneous sales and sequential sales
- With multi-units and different pricing rules, uniform pricing, discriminatory pricing and Vickrey auctions, prices are expected in the range €526.6m to €583.9m
- These sums would be more than enough to incentivise sellers to invest in new AMR products
- However, the intermediary could transfer to developers only the minimum required funding (€441.8m/€279.5m) to incentivise investment to minimise the impact of TEE Vouchers on health systems
- An intermediary could make differential rewards to “new class” and “existing class” antibiotics.
- An alternative would be for “new class” and “existing class” antibiotics to have differential TEE periods, i.e. the length of exclusivity attached to the TEE Voucher would differ. We have not modelled this. However, it could be quite disruptive without an intermediary as buyers would have to choose whether to wait for a TEE Voucher with a longer TEE to become available.

6. The Market for TEEs: Summary of model results

- **Without replacement** of buyers**, 2 TEE Vouchers per year** would be enough for developing 18 “new class” products in 9 years (and possibly more in subsequent years)
- **The average price paid per TEE Voucher considering the whole period is €518.4m**
- Without replacement of buyers, **3 TEE Vouchers per year** would be enough to develop 18 “existing class” products in 6 years
- Using data available, **the average price paid for a TEE Voucher considering the six year period is €445.2m**
- Difference between WTP (~€350m) and required incentive (€259.5m) shows that there is a strong potential to develop more in years after 2023
- **With replacem**ent of buyers, **2 TEE Vouchers per year** would be enough to develop 18 “new class” products in 9 years
- The **average price paid per TEE Voucher considering the whole period of 9 years is €584.1m**
- Difference between WTP (~€520m) and required incentive (€441.8m) shows that there is a strong potential to develop more in years after 2026
- **With replacement** of buyers**, 3 TEEs per year** would be enough to develop 25 “existing class” products in 9 years
- The **average price paid per TEE Voucher considering the whole period of 9 years is €457.4m**
- Difference between WTP (~€400m) and required incentive (€279.5m) shows that there is a strong potential to develop more in years after 2026

6. Market for TEEs: Estimated Duration of a TEE Voucher

OHE

We revised our previous analyses to use the results of the modelling to generate the minimum and average WTP of a TEE for the different scenarios: 2/3 TEE per year, with/without replacement and period 2018-2026.

In this slide, we add in the required incentives required based on a share of global R&D cost and existing revenues

We translate this into **required lengths of a TEE Voucher using the minimum and average TEE Vouchers expected**. **These are indicative and highly sensitive to all of the assumptions used**

Scenario	Minimum WTP for a TEE 2018-2026	Average WTP for a TEE 2018-2026[a]	Contribution to R&D cost required from a TEE Voucher	Duration of TEE required Years (in relation to minimum WTP)	Duration of TEE required Years (in relation to average WTP)
Two TEE per year without replacement (new class)	€469.6m	€518.4m	€441.8m	0.94	0.85
Two TEE per year with replacement (new class)	€473.4m	€584.1m	€441.8m	0.93	0.76
Three TEE per year without replacement (existing class)	€349.2m	€445.2m	€279.5m	0.80	0.63
Three TEE per year with replacement (existing class)	€405.1m	€457.4m	€279.5m	0.69	0.61

Sources: IQVIA and OHE Consulting Ltd.
Notes: [a]Averages reported in the table match those reported in the analysis of the appendix as they are based on the lowest winning WTP.

6. Market for TEEs: Estimated Duration of a TEE Voucher

OHE

- These results suggest that:
  - **A TEE period of 9-12 months** would be needed for new classes of antibiotics
  - **A TEE period of 7-10 months** would be needed for existing classes of antibiotics

Use of an Intermediary

- Selling prices for the TEE Vouchers are similar, but an intermediary has policy attractions:
- It could transfer to developers the agreed required funding, guaranteeing the amount to developers and minimising the impact of TEE Vouchers on health systems
- It could make differential rewards to “new class” and “existing class” antibiotics.
- An alternative would be for “new class” and “existing class” antibiotics to have differential TEE periods, i.e. the length of exclusivity attached to the TEE Voucher would differ. However, this could be quite disruptive without an intermediary, as buyers would have to choose whether to wait for a TEE Voucher with a longer TEE to become available. We have not modelled this.

7. The use of guardrails

7. The use of guardrails (i)

OHE

1. Reducing the impact on the generic industry

- Any product with an EMA license to be eligible to receive one TEE. The EFPIA AMR Incentives TTF view was for at least two years of exclusivity to be remaining on the recipient product, as in the paediatric extension legislation. Note that there will be some initial impact on the generic industry as fewer products will be coming off patent than previously expected.

2. Limiting the numbers of new products that are given a TEE

- Use of an eligibility criteria to limit the number of designations. EMA recommends additions and removals from the priority pathogen list.
- Once a designation is received the drug candidate remains eligible for a TEE even if the category of pathogen is subsequently removed from the eligible criteria.
- Alternative proposal (BIO) is that a “predetermined number of rewards for each area of prioritised medical need will be conferred for those that achieve regulatory approval.” i.e. a fixed number of TEEs per pathogen area. If this route was adopted the EMA could set the number of TEEs as well as of pathogens. This could not be reduced in relation to products already designated.

7. The use of guardrails (ii)

OHE

3. Ensuring appropriate stewardship:

- Proposing an Antibiotic Management Plan (AMP) to maximise the utility of the new antibiotic, as an integral part of the Risk Management Plan (RMP)
- Establish a corporate Antibiotic Life Management Officer to oversee implementation of company-wide Antibiotic Management and AMR activities.
- Develop a plan describing activities to minimize development of resistance.
- Support HCP and patient education programs, if applicable (but see final bullet).
- Collaborate to support development of an automated susceptibility test.
- In line with the AMR Industry Roadmap, align promotional activities and sales incentives with the goal of advancing infection control.
- Implement and share data from surveillance programs as part of an RMP.

Note that health systems have most control over antibiotic usage.

7. The use of guardrails (iii)

OHE

4. Avoiding overpayment for new antibiotics (i)

- One TEE Voucher per qualifying molecule and one TEE per recipient product.
- TEE Vouchers are freely tradable. A developer can sell a TEE Voucher or use within its business.
- Although the transfer of the TEE to the recipient product to be unconditional, i.e. irrevocable, there might be circumstances in which the owner of the qualifying molecule selling the TEE Voucher may have to return revenue received (e.g. product withdrawal for safety reasons). This could be time limited. Consideration of this is out of project scope but will likely be part of any EU legislation.
- Obligations on the developer of the qualifying antibiotic to commercialise or license the product once it has received a TEE (which might include supply availability and pricing) are also outside of the project scope. However, industry should expect that EU legislation would include these, to avoid a situation in which the innovator obtained a TEE Voucher, sold the TEE Voucher, and then did not make the product available in the EU.

7. The use of guardrails (iv)

OHE

4. Avoiding overpayment for new antibiotics (ii)

- Initial TEE Vouchers could sell for up to €800m depending on the period of exclusivity. These are likely to be products already in development, i.e. not from R&D stimulated by the introduction of the TEE Voucher. Some options to avoid excess payment (i.e., substantially above that needed to stimulate R&D) are set out below.
- **Use of an intermediary in the TEE market**: (i) offering a guaranteed amount of money (reflecting other incentives and the R&D needed) and (ii) also then auctioning the TEE to buyers in order to maximise revenue
- **Adjusting the period of exclusivity**:
  - estimating the period needed to deliver (say) €1billion of net revenues in advance (an example from the OHE 2017 publication is set out in the next slide),
- **Setting a cap**, i.e. the TEE continued until (say) €500m of net revenues was hit. This could produce some uncertainty in the generic market and so would be less desirable.

7. The use of guardrails (v)

OHE

Extract from Ferraro et al 2017 Incentives for New Drugs to Tackle Anti-Microbial Resistance, OHE Research Paper.

	Composite Case A	Composite Case B	Composite Case C
Estimated cost of R&D	US$2 bn	US$2 bn	US$2 bn
EU participation in R&D (33%)	US$0.67 bn	US$0.67 bn	US$0.67 bn
Estimate of gross margin	65%	65%	65%
Money needed to raise	US$1.03 bn	US$1.03 bn	US$1.03 bn
Range of Sales in Europe	≥$3 bn	$2 bn- $3 bn	$1 bn- $2 bn
Years of TIPR required (using the base point of the range)	**0.34**	**0.52**	**1.03**

Source: own elaboration

8. The Impact on EU Member State Health Budgets

8. Cost to EU Member State healthcare systems (i)

OHE

- For the two cases, 2 and 3 TEE Vouchers per year we also estimate the total value of all traded TEE Vouchers, which can be used as a proxy of the **gross cost** of the TEE Vouchers to health systems
- To estimate the **net cost**, we subtract from this the cost of buying **generic versions** of the products with a patent extended by means of the TEE Voucher – since these purchases will no longer be necessary during the TEE period
  - If 2 TEE Vouchers are traded per year, we estimate that the net cost for health systems is within the range of **€0.57bn to €1.21bn per annum, depending on TEE duration and potential 'new buyer' entries**
  - If 3 TEE Vouchers are traded per year, we estimate that the net cost for health systems is within the range of **€0.71bn to €1.51bn per annum depending on TEE duration and potential 'new buyer' entries**
- **Pharmaceutical expenditure caps** present in some health systems will also affect the net cost, because higher spend on drugs with TEEs is (partially) recovered; on slide 88 we present the re-modelled net cost adjusted for these caps

8. Cost to EU Member State healthcare systems (ii)

OHE

TEE impact to Member States: two TEE Vouchers per year of 6/12 months duration in millions of euro

Country	Market Share	Replace-ment	2018		2019		2020		2021		2022		2023		2024		2025		2026		Total		AVG per annum	
	Duration of TEE Voucher:		6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m
France	16.16%	Yes	110	220	125	251	128	256	95	189	84	169	81	161	82	165	83	166	89	179	877	1755	98	195
		No	110	220	125	251	95	189	95	189	79	158	76	153	78	156	81	161	89	179	827	1655	92	184
Germany	21.78%	Yes	148	356	169	317	173	328	128	300	114	295	109	298	111	308	112	320	121	247	1183	2768	131	308
		No	148	297	169	338	128	255	128	255	106	212	103	206	105	210	109	217	121	241	1115	2231	124	248
Italy	12.49%	Yes	85	170	97	194	99	198	73	146	65	130	62	125	64	127	64	128	69	138	678	1356	75	151
		No	85	170	97	194	73	146	73	146	61	122	59	118	60	120	62	125	69	138	639	1279	71	142
Spain	7.12%	Yes	85	97	97	110	99	113	73	83	65	74	62	71	64	73	64	73	69	79	678	773	75	86
		No	49	97	55	110	42	83	42	83	35	69	34	67	34	69	36	71	39	79	365	729	41	81
UK	12.59%	Yes	148	172	169	195	173	200	128	147	114	132	109	126	111	128	112	129	121	139	1183	1368	131	152
		No	86	172	98	195	74	147	74	147	61	123	60	119	61	121	63	126	70	139	645	1290	72	143
Rest of EEA	29.86%	Yes	110	407	125	463	128	473	95	350	84	312	81	298	82	304	83	306	89	330	877	3243	98	360
		No	203	407	232	463	175	350	175	350	146	291	141	282	144	288	149	298	165	330	1529	3058	170	340
Total	100%	Yes	681	1,362	775	1,550	792	1,585	585	1,171	522	1,044	499	998	510	1,019	512	1,024	553	1,107	5,430	10,860	603	1,207
		No	681	1,362	775	1,550	585	1171	585	1171	487	975	473	945	482	964	499	997	553	1,107	5,120	10,241	569	1,139

Note: These costs are estimated as the total value of all TEE Vouchers, less the spend on generics of the products with a patent extended through the Vouchers

8. Cost to EU Member State healthcare systems (iii)

OHE

TEE impact to Member States: three TEE Vouchers per year of 6/12 months duration in millions of euro

Country	Market Share	Replace-ment	2018		2019		2020		2021		2022		2023		2024		2025		2026		Total		AVG per annum	
	Duration of TEE Voucher:		6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m	6m	12m
France	16.16%	Yes	1312	314	117	328	122	243	111	223	109	219	111	221	114	228	119	237	92	183	1027	2,197	114	244
		No	157	314	164	328	110	221	91	182	90	179	89	179	NA	NA	NA	NA	NA	NA	702	1,403	117	234
Germany	21.78%	Yes	178	424	158	442	164	328	150	300	147	295	149	298	154	308	160	320	124	247	1384	2,962	154	329
		No	212	424	221	442	149	298	123	246	121	242	120	241	NA	NA	NA	NA	NA	NA	946	1,892	158	315
Italy	12.49%	Yes	102	243	91	253	94	188	86	172	84	169	85	171	88	177	92	183	71	142	793	1,698	88	189
		No	122	243	127	253	85	171	71	141	69	139	69	138	NA	NA	NA	NA	NA	NA	542	1,085	90	181
Spain	7.12%	Yes	58	139	52	145	54	107	49	98	48	96	49	97	50	101	52	105	40	81	453	968	50	108
		No	69	139	72	145	48	97	40	80	40	79	39	79	NA	NA	NA	NA	NA	NA	309	619	52	103
UK	12.59%	Yes	103	245	92	256	95	190	87	174	85	170	86	172	89	178	93	185	72	143	800	1,712	89	190
		No	123	245	128	256	86	172	71	142	70	140	70	139	NA	NA	NA	NA	NA	NA	547	1,094	91	182
Rest of EEA	29.86%	Yes	244	581	217	606	225	450	206	411	202	404	204	409	211	422	219	439	170	339	1897	4,060	211	451
		No	290	581	303	606	204	408	168	337	166	331	165	330	NA	NA	NA	NA	NA	NA	1297	2,593	216	432
Total	**100%**	**Yes**	**816**	**1,945**	**727**	**2,029**	**753**	**1,506**	**688**	**1,378**	**676**	**1,352**	**684**	**1,368**	**707**	**1,413**	**735**	**1,469**	**568**	**1,135**	**6,354**	**13,597**	**706**	**1,511**
		No	**973**	**1,945**	**1,015**	**2,029**	**683**	**1,367**	**565**	**1,129**	**555**	**1,109**	**553**	**1,105**	**NA**	**0**	**NA**	**0**	**NA**	**0.0**	**4,343**	**8,686**	**724**	**1,447**

Note: These costs are estimated as the total value of all TEE Vouchers, less the spend on generics of the products with a patent extended through the Vouchers

8. Cost to EU Member State healthcare systems (iv)

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- We re-model the cost for health systems, adjusting for the pharmaceutical expenditure caps in place in the 5 largest EU markets (with the exception of Germany, where there is no such cap)
  - We assume that, since the cost of introducing a TEE is additional to planned spending in existing healthcare budgets, all of this cost is subject to the rebates defined by the pharmaceutical expenditure cap[1]
  - Since these rebates have not yet been defined for Spain, we conservatively make no adjustment
  - We also conservatively make no adjustment for the rest of the EEA
  - (These estimates are also net from the expenditure on generic versions of the products benefitting from the TEE Voucher)

1 For the UK the overall growth rate for branded medicines is currently capped at 2%. For France the growth rate for innovative hospital medicines is currently capped at 2% (all other medicines are capped at 0%, but we use the 2% rate for our adjustments). In Italy, companies are expected to pay back 50% of overspend on non-retail products in the National Health Budget). Source: EFPIA (2019) Overview of clawbacks, rebates & discounts, taxes and price freezes and cuts in Europe

8. Cost to EU Member State healthcare systems (v)

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- For the two cases, 2 and 3 TEEs per year we estimate the total adjusted value of all traded TEE Vouchers as follows:
  - If 2 TEE Vouchers are traded per year, we estimate that the cost for health systems is within the range of **€0.35bn to €0.84bn per annum, depending on TEE duration** *(compared to €0.57bn to €1.21bn per annum without adjusting for caps)*
  - If 3 TEE Vouchers are traded per year, we estimate that the cost for health systems is within the range of **€0.46bn to €0.99bn per annum depending on TEE duration** *(compared to €0.71bn to €1.51bn per annum without adjusting for caps)*

9. Issues for discussion with the EFPIA AMR Task Force

9. Issues for the EFPIA AMR TTF

OHE

- Results are highly sensitive to assumptions.
- The TF has indicated preference for a narrow qualifying list of molecules for a TEE Voucher.
  - Depending on the pathogen list used the numbers of qualifying new drugs could range from less than one per annum to around 3 per annum over time.
  - The option of a differential reward for a first in class versus follower will be difficult to implement without use of an intermediary, which was not supported by the TF
- **The variation in, and potential upper size of, the value of TEE Vouchers may present concerns for Member State health systems (too high) and for antibiotic developers (too low).** Options to address this could include: (i) a cap on the net revenue earned by the recipient of a TEE Voucher; (ii) a variable length of the TEE depending on expected revenues; (iii) use of an intermediary
- We take account of potential sales in our estimate of the size of TEE Voucher needed by developers but of **neither (i) improvements in reimbursement arrangements nor (ii) any push monies received**

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APPENDIX TO MAIN REPORT – DECEMBER 2019

APPENDIX: Options for Structuring the Market for TEE Vouchers

DECEMBER 2019

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- The modelling in this Appendix is intended only to inform discussions in relation to public policy making.
- It is not intended to provide advice to any company, named or not named, about the bidding strategies they should utilise in a particular form of market organisation.
- No company names are used. Products and companies are referred to as P-1, P-2, etc. and C-1, C-2, etc. The examples are for illustrative purposes only and are based on the current "best selling" products in the EU. The purpose of using these examples is to show possible public policy consequences of adopting different forms of market organisation for the sale of TEE Vouchers.

Options for structuring the market for TEE Vouchers

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1. Overview of the model
2. Baseline assumptions & notation
3. Timing
4. Supply side and backward induction
5. Market for TEE Vouchers without an intermediary
6. Market for TEE Vouchers with an intermediary
7. Results and expected market performance
8. Summary and Implications

1. Overview of the Model

1. Overview of the model (i)

OHE

- The value of a TEE (its final price from now on) is set in the market, and it depends on supply and demand factors beyond the incentives of sellers/buyers
- Supply-side factors include:
  - The total number of TEEs granted to innovators: the higher the number of TEEs in the market the lower the price per TEE paid
  - The length of a TEE: the longer the length of the extension the higher the price of the TEE
- Demand-side factors include:
  - The number of buyers: under regular assumptions, more buyers means more competition in the market, which increases the willingness to pay (WTP) of the marginal buyer (the last one purchasing) and determines the price of the TEE
- Market structure:
  - Timing for trading: whether (i) each seller can freely sell its TEE at the time its antibiotic is approved by the EMA or (ii) TEEs from a given period must be traded at once in an organised auction will affect final prices.
  - Qualifying criteria applied to sellers/buyers participating in the market will affect the TEE price
  - Information available to buyers/sellers: about the number of TEEs to be traded, the auction calendar, incentives of sellers/buyers is available to all parties will affect the final TEE price.

1. Overview of the model (ii)

OHE

We explore how a market for TEEs will work by using a game theoretical approach:

- Players: the TEE holder, the TEE buyer and the Public Health Authority (the EMA)
- Actions:
  - TEE generator: “invest” / “don’t invest” in each phase for the development of a new AMR product, “sell” / “use” the TEE
  - TEE buyer: “buy” / “don’t buy” the TEE (if bought, we assume it is used)
- Payoffs:
  - TEE generator: expected benefit from (i) the new AMR product, (ii) the TEE (“sell” / “use”), (iii) other push/pull incentives and (iv) the R&D investment cost
  - TEE buyer: expected (net) profit from the use of a TEE (i.e., extending the exclusivity period of a blockbuster drug)
  - Public Health Authority: value generated by the new AMR product minus the cost of the TEE to health care systems

2. Baseline Assumptions and Notation

2. Baseline assumptions & notation (i)

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We start modelling the TEE market by using the following set of baseline assumptions:

1. The market is made of a single TEE with a fixed length of one year
2. The fixed cost of R&D investments are made in stages, and they are the same for all innovators
3. There is perfect information about the level of profit of all blockbuster drugs owned by potential buyers of TEEs – common knowledge of the willingness to pay of all buyers
4. Generic competition after patent expiration affects equally to all potential buyers of TEEs (and it is constant along years)
5. In the case of investing in R&D, the probability of success of each phase is constant and the same for all firms
6. All firms have the same discount factor
7. If a TEE holder decides to sell it, it could be with or without an intermediary
8. The Public Health Authority is always incentive compatible to incentivise new antibiotics to tackle AMR

2. Baseline assumptions & notation (ii)

OHE

- ρ_{phase}: probability of success of phase of development
- π_H^v: expected profit or payoff of the TEE generator when it uses the TEE in one of its own products
- π_{PH}^v: expected net benefit coming from the new antibiotic for the Public Health Authority when the TEE generator uses it in one of its products
- π_H^P: expected profit or payoff of the TEE generator when it sells the TEE to another firm owning a blockbuster drug
- $\pi_B^P = \pi^M - \pi^C - p^{TEE}$: Expected profit of the buyer of the TEE which is the result of the profit obtained by selling the blockbuster drug at monopoly price during the TEE extended term (π^M), less the price paid for the TEE (p^{TEE}), less the profit it would have obtained by selling the drug under generic competition (π^C)
- π_{PH}^P: expected net benefit coming from the new antibiotic for the Public Health Authority when the TEE generator sells it to another firm owning a blockbuster drug
- π_i^{NI}: expected gain for the developer of "don't invest" at phase of development $i = \{PCDR, PI, PII, PIII, R\}$ where $PCDR$ is Pre-Clinical Research and Development, PI is Phase I, PII is Phase II, $PIII$ Phase III, and R is registration
- π_i^I: expected gain for the developer of "invest" at phase $i = \{PCDR, PI, PII, PIII, R\}$

3. Timing

3. Timing (i)

OHE

Stage 1: the TEE generator decides whether to “invest” or “don’t invest” in R&D. This stage is sub-divided by other five stages each one representing a phase in the product development: Pre Clinical Research and Development (PCRD), Phase I, Phase II, Phase III, and Registration phase.

- If the company “invest”, it faces the cost of the phase and moves to the next stage
- If the company “don’t invest”, the game is over and company gets losses from investments carried out

Stage 2: this stage is a lottery. Nature decides the “success” or “failure” of the investment in each phase of Stage 2 - “success” occurs with probability ρ_{phase}

- If “success”, then the firm goes back to Stage 1 to decide to “invest” or “don’t invest” in the next sub-stage. If the game already reached the registration phase, the firm gets the TEE, and the game goes to Stage 3
- If “failure”, the game is over and company gets losses from investments carried out

Stage 3: the TEE generator can either decide to “offer for sale” or “use”

- If “offer for sale”, the TEE goes to the market for TEEs, and the game goes to stage 4
- If “use”, the firm gets a patent extension in her blockbuster drug, the game ends and payoffs are realised:

- For the TEE generator, the present value of the blockbuster drug during the length of the TEE (once the patent expires), plus profits from selling the new antibiotic, minus the capitalised R&D cost (called π_H^v)
- For the Public Health Authority, the expected present value of the new AB product minus the expected present value of the efficiency loss of extending the patent of the TEE generator blockbuster drug (called π_{PH}^v)

3. Timing (ii)

OHE

Stage 4: the TEE is offered the market for TEEs:

- the buyer decide whether to “buy” or “don’t buy”
- the seller decides whether to “sell” or “don’t sell” at a given price
- Either way, the game ends and payoffs are realised:
- <u>If Seller sells the TEE:</u>

- The TEE generator gets p^{TEE} minus the capitalised R&D cost, (called π_H^P)
- The buyer of the TEE receives the present value of $\pi^M - \pi^C$ on her blockbuster drug during the length of the TEE (once the patent expires) minus p^{TEE} (called π_B^P)
- The Public Health Authority gets the expected present value of the new AB product minus the expected present value of the efficiency loss of extending the patent of the buyer blockbuster drug (called π_{PH}^P)

- <u>If seller does not sell the TEE:</u>

- both the TEE generator and the Public Health Authority get the same payoffs as if the firm had decided to use it in the previous stage, π_H^v and π_{PH}^v, respectively

To keep things simple, we do not model the decision of the Public Health Authority to “grant” or “deny” assuming that PHA always “grant” the TEE when the investment is successful (assumption 8)

4. Supply side and Backward Induction

4. Supply side and backward induction (i)

OHE

- We now determine the value of the TEE that incentivises the investment in antibiotic R&D
- The incentives are calculated by an individual firm, which means that we are going to figure the final prize that the firm should get to incentivise her to invest through all the stages up to the last one, conditional on the individual probability of success/fail of each stage
- We solve the game backwards, and we analyse the present value of the prize at the moment the firm has to decide to “invest” or to “don’t invest” in the new phase (conditional on previous successes)
- A necessary, but not sufficient, condition to get an AMR product is to make firms invest in R&D in each phase of the product development, and that depends on the size of the pot at the end of the road
- The size of the pot is made of:

  i. The present value of the profits the firm gets by producing the new AMR product

  ii. The value of the TEE, which depends on the value of one of its own products or the estimated market price

  iii. Other push and pull incentives. We have not estimated these other than the expected value of sales.

4. Supply side and backward induction (ii)

OHE

- We have estimated the capitalised R&D cost of a new successful "new-class" and an "existing class" antibiotic (estimates presented in section 5 of the report)
  - The R&D cost of a new **"existing class"** antibiotic (share of EU): **€358.1m**
  - The R&D cost of a new **"new class"** antibiotic (share of EU): **€520.4m**
- We have estimated the present value of an AMR product at launch based on sales data (IQVIA) of new antibiotics launched between 2009-2018 (estimate presented in section 5 of the report)
  - Present value at launch of a new antibiotic: **€786m**
- Based on the estimates presented in section 5 of the report, we estimate that the total incentive a supplier needs at PCRD stage to 'start and keep' investing in a new antibiotic until its market approval is:
  - **€279.5 million to make individual firms invest in an existing class of AMR product**
  - **€441.8 million to make individual firms invest in an new class of AMR product**

4. Supply side and backward induction (iii)

OHE

- To keep investing in the development of a new antibiotic, the expected value of the pot at each “invest” decision point (one per phase) should be higher than expected gains of “don’t invest”
- In the last phase “registration” the firm has two alternatives: “invest” or “don’t invest”
  - If “don’t invest”, the firm gets π_R^{NI} which is a benefit (negative) equal to the sum of all capitalised investments carried out until then and the game ends
  - If “invest”, the firm gets π_R^{I} which is a benefit equal to the pot with probability less the total capitalised hypothetical cost of development, and the game ends so
  - The firm invests at registration phase if and only if $\pi_R^{I} \geq \pi_R^{NI}$
- In Phase III the firm has also to take the decision to “invest” or not
  - If “don’t invest”, the firm gets π_{PIII}^{NI}, a profit (negative) equal to the sum of all capitalised investments carried out until then and the game ends
  - If “invest”, the firm succeed phase III and goes to the registration phase with probability 0.7, where it will have to incur in a new investment to win the pot with probability 0.87, so therefore it faces and expected profit of π_{PIII}^{I} which is the expected value of the pot at this stage less the investment carried out less the expected investment needed to succeed
  - The firm invests at phase III if and only if $\pi_{PIII}^{I} \geq \pi_{PIII}^{NI}$
- Solving backwards the firm’s decision problem iteratively phase by phase, we obtain that the firm will invest at the beginning of the phase PCRD if and only if $\pi_{PCRD}^{I} \geq \pi_{PCRD}^{NI}$ which means that the expected value of the pot (capitalised) less the expected R&D cost (capitalised and adjusted by success rates to produce at least one new medicine) is positive
- From previous slide we know that, to meet the investment condition for the developer, the (expected) value of the pot needs to be at least €279.5m for a existing class antibiotic (€441.8m for a new class antibiotic)

5. The Market for TEEs Without an Intermediary

5. The market for TEEs without an intermediary (i)

OHE

- We now introduce the demand-side in our market
- In any market, with and without an intermediary, we say that there are “gains from trade” when the value for the seller is lower than the potential value for the buyer
  - Then, it is efficient to trade as mutual gains are materialised for suppliers (sellers) and consumers (buyers)
- Nevertheless, it’s important to remark that when information is not symmetric, buyers and sellers know their own valuations but not others’ valuations (not the case of our model), trade might not always occur even though it is efficient to happen
  - A seller having a valuation for the TEE lower than a potential buyer’s valuation does not mean trade will occur
  - Even if the good is traded, individual negotiations could end up in any market price in between the seller’s and the buyer’s valuations, <u>which is difficult to estimate</u> and depends on players’ individual bargaining power

5. The market for TEEs without an intermediary (ii)

OHE

The table below shows estimates of the WTP for a TEE based on the calculations presented in section 4 of this report (only eligible products in the top-30)

Product #	Company #	Year of patent expiry	Estimated WTP (in million)
P-1	C-1	2028	€ 734.72
P-2	C-2	2026	€ 626.74
P-3	C-2	2026	€ 583.96
P-4	C-3	2028	€ 526.56
P-5	C-4	2031	€ 522.04
P-6	C-5	2025	€ 509.42
P-7	C-6	2026	€ 350.90
P-8	C-7	2026	€ 338.24
P-9	C-8	2024	€ 286.38
P-10	C-9	2028	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

C-1 is the firm with the highest estimated willingness to pay for a TEE, followed by C-2 (owns two products), and C-3

5. The market for TEEs without an intermediary (iii)

OHE

Company #	Estimated WTP (in million)	Estimated selling price to C-1
C-1	€ 734.72	-
C-2	€ 626.74	€ 680.73
C-3	€ 526.56	€ 630.64
C-4	€ 522.04	€ 628.38
C-5	€ 509.42	€ 622.07
C-6	€ 350.90	€ 542.81
C-7	€ 338.24	€ 536.48
C-8	€ 286.38	€ 510.55
C-9	€ 285.66	€ 510.19
Expected market price (average in million)		**€ 582.73**

Sources: IQVIA and OHE Consulting Ltd.

- However, the seller does not behave strategically in the example by disregarding all possible competitive pressures coming from other potential buyers operating in the market
- The seller can optimise the result by:
  - For example, if C-5 is the TEE Voucher holder and negotiates with C-1, C-1 could offer the expected price of €622.07 million, but C-5 could always get a better deal with C-2 whose WTP is higher than €622.07 million
  - This threat pushes C-1 to make a better offer up to the price where C-2 is indifferent about buying or not, which is **€ 626.74 million**
- **Thus, the market price would be determined by the WTP of the first buyer who does not buy the TEE Voucher – C-2 in the example above when only one TEE Voucher is traded. This is the offer the buyer needs to equate in order to be the buyer and limits the surplus it can obtain.**

5. The market for TEEs without an intermediary (iv)

OHE

- As seen previously, the total capitalised cost of the AMR product (at launch) is €358.1 million for an existing class, and €520.4 million for a new class
- The market for the new AMR product is expected to give the company a profit of € 78.6 million
- An expected price for a TEE Voucher of € 582.3 million (no strategic behaviour) would be **enough to incentivise both an existing class and a new class**
- In terms of social welfare, it is efficient to use TEEs if they incentivise the investment in R&D when the value for the society of the AMR product is higher than the cost of developing it
  - For an existing class, there is a "surplus" for the industry of € 248.8 million (TEE Voucher price + Profit – R&D cost)
  - For a new class, there is a "surplus" for the industry of € 86.5 million (TEE Voucher price + Profit – R&D cost)
- This "surplus" is a transfer from consumers to the industry, and it could be seen as an overpayment for inducing investment, although t should be viewed in the context of the therapeutic value that the new antibiotic for AMR generates
- The overpayment (inefficiencies) could be reduced by restricting the length of the extension attached to the TEE Voucher
- **If we used the expected price of the more sophisticated version, € 626.74 million, the "overpayment" is higher and is unlikely to be compensated by the therapeutic value of the new antibiotic and society's/system's willingness to pay for it**

5. The market for TEEs without an intermediary (v)

- With **more than one TEE Voucher to be sequentially traded in the market**, a firm that wants to buy one has to answer the following question: should I buy or should I wait?
- If the decision is to wait, it the firm expects lower prices in the future due to lower competition resulting from the fact that one buyer has already bought the first TEE Voucher and retired from the market
  - For example, if there are 2 TEE Vouchers in the market to be sold sequentially, at first sight, we would expect:
    - C-1 buying the first TEE Voucher at a price equal to €626.74 million
    - C-2 buying the second TEE Voucher at a price equal to €526.56 million
  - However, C-1 knows that not buying the first and waiting for the second TEE Voucher, would be better given that the expected market price for the second TEE Voucher is lower. Therefore, the dominant strategy is to offer the price of the second TEE Voucher in both periods

At equilibrium, we will expect similar prices for the TEE Vouchers at each trade regardless the number of TEE Vouchers sold

5. The market for TEEs without an intermediary (vi)

OIE

- With **more than one TEE Voucher in the market to be sold simultaneously**, the price at which it will buy the TEE Voucher becomes the key decision
  - For example, if there are 2 TEE Vouchers in the market sold simultaneously, at first sight, we would expect:
    - C-1 buying one TEE Voucher at a price equal to € 626.74 million
    - C-2 buying another TEE Voucher at a price equal to € 526.56 million
  - However, C-1 knows that the second TEE would be sold at a lower price, which gives it an incentive to put its offer down to € 526.56 million

In equilibrium, we should expect same prices for both TEE Vouchers, equal to the third highest WTP (C-3) – the first one not buying the voucher

6. Market for TEEs with an Intermediary

6. Market for TEEs with an intermediary (i)

OHE

- We now assume that there exists an intermediary in charge of selling the TEE Vouchers who pays to TEE Voucher generators the exact amount they need to “invest” in a new AMR product and then tries to sell the TEE Vouchers in the market at the maximum price (we only model the selling market)
- We model the market using action theory: uniform price, discriminatory price and Vickrey auction
- We then see that gross results from the market with and without an intermediary **are closely equivalent** (under certain assumptions)
- We use two different approaches to model multi-TEE Vouchers auctions
    1. Simultaneous sales vs sequential sales: we explore differences of trading TEE Vouchers one by one versus trading all TEE Vouchers at once
    2. Uniform price vs discriminatory price vs Vickrey pricing: we explore how implemented mechanism (auction type) can affect strategies, outcomes and/or efficiency?
- We assume sealed-bid auctions or strategically equivalent clock auctions (no revelation of information during the auction)
- At first, each buyer wants only a single TEE Voucher – a condition called *singleton demand*
    - With singleton demand, bidders have only one allocation to evaluate
    - With a demand for more than one unit, a larger number of allocations can force a bidder to reduce its valuation activities, which can limit both efficiency and price competition.

6. Market for TEEs with an intermediary (ii) – sequential sales / one unit

OHE

- Similar to the case of a market with no intermediary, if firms bid their WTP in each round, then we would observe prices declining over time

Company #	Estimated WTP (in million)
C-1	€ 734.72
C-2	€ 626.74
C-3	€ 526.56
C-4	€ 522.04
C-5	€ 509.42
C-6	€ 350.90
C-7	€ 338.24
C-8	€ 286.38
C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- In the first auction, C-1 buys the TEE Voucher at a price equal to € 626.74 million and abandons the market
- In the second auction, C-2 buys the TEE Voucher at a price equal to € 526.56 million and abandons the market – auctions continue with the third TEE Voucher, fourth TEE Voucher and so forth
- If there would be 3 TEE Vouchers on sale, prices in each round would be € 626.74, € 526.56, and € 522.04 million, respectively – always the WTP of the highest bidder that does not buy

6. Market for TEEs with an intermediary(iii) – sequential sales / one unit

OHE

- However, this result implies no-strategic behaviour of bidders as:
  - C-1 has an incentive to wait until second, third or any other later period to buy a TEE Voucher at a lower price.
  - C-2 also has an incentive to wait until third or any other later period
- Following this logic, arbitrage prevails if prices are announced after each sale and then:

Prices are **a martingale** (Weber's Theorem, 1983): the expected future price equals its current value, when conditioned on its history,

$$\mathbb{E}[P_{t+1}|P_1, P_2, \dots, P_t] = P_t$$

- The "theory" suggests that if the intermediary sells the TEE Vouchers sequentially, on the basis of one TEE Voucher at a time, then all are sold at the same constant equilibrium price
  - Bidders in earlier periods will offer the predicted transaction price of the latest auction
- Nevertheless, in "reality" we observe declining price in many markets where several identical objects are sold in this way

6. Market for TEEs with an intermediary (iv) – simultaneous sales / multi-units

OHE

- If the intermediary decides to auction multiple units simultaneously, then the situation changes significantly
- Most important, bidders have different bidding strategies depending on the type of the auction and its pricing rule
- Different types of auctions are listed below:

1. **Uniform price auction:** all bidders pay a price for each unit bought equal to the highest losing winning bid price (or alternatively the lowest winning bid) regardless their actual bid
2. **Discriminatory price auction:** the price paid for each unit is the winning (or the highest) bid for that unit
3. **Vickrey auction:** the highest bidder win but pays the price of the second-highest bid – in a multiple units auction, a bidder who wins *k* objects pays the sum of the *k* highest rejected bids submitted by the other bidders

6. Market for TEEs with an intermediary (v) – simultaneous sales / uniform price

OHE

- A uniform price auction is one where *k* identical objects are auctioned and sold at identical prices
- A uniform price auction avoids the *declining price anomaly* observed empirically in sequential auctions where bidders always have to guess about future prices, which inevitably causes some price variation
- Uniform price auction has some desire features:
  - It avoids price variation in sales of homogeneous items, something that bidders dislike
  - It reduces the transaction costs of repeatedly bidding for identical goods

6. Market for TEEs with an intermediary (vi) – simultaneous sales / Vickrey price

OHE

- When bidders have singleton demand, **Vickrey** auctions and **Uniform price** auction produce equal results – Uniform price auction is a particular case of Vickrey auctions in such a case
- Let's assume there are 2 TEE Vouchers ($k = 2$), and firms bid their willingness to pay

Company #	Estimated WTP (in million)
C-1	€ 734.72
C-2	€ 626.74
C-3	€ 526.56
C-4	€ 522.04
C-5	€ 509.42
C-6	€ 350.90
C-7	€ 338.24
C-8	€ 286.38
C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- In a Vickrey auction C-1 and C-2 win one TEE Voucher each and they pay a price equal to the highest rejected bid submitted by other bidders, which is $P_1 = P_2 =$ € 526.56 million
- As in uniform price auctions, for a bidder with singleton demand:
  - Its best strategy is to bid one's value – "truthful" bidding or information revelation principle
  - The price the winner pays is equal to the $k + 1$ bid or the highest losing bid

6. Market for TEEs with an intermediary (vii) – demand for multiple units

OIE

- So far, we showed how TEE Vouchers could be sold in simultaneous or sequential auctions when each bidder can buy at most one single item
- When bidders demand multiple units, market power becomes important
  - Bidders can often reduce prices they pay by buying fewer units than they would want to at their final prices
  - When there are several large bidders, each aiming to buy multiple units, it is also possible that larger bidders will coordinate strategies – for example by agreeing to reduce demand in concert
- We continue our analysis using a framework of simultaneous sales of TEE Vouchers with different pricing rules
- From now on, we assume that bidders are allowed to bid for more than one TEE Voucher at a time.

6. Market for TEEs with an intermediary (viii) – demand for multiple units

OHE

Assumptions:

- We assume the bidders have declining marginal WTP for the goods they acquire
  - That is, bidder's WTP for the first unit is the highest and then decreases (or remain the same) with each successive unit
- TEE Vouchers are homogeneous goods or perfect substitutes for all firms: conditional on paying the same price, they only care about buying 1 TEE Voucher
- No complementarities between the number of TEE Vouchers demanded: there is no added value from buying 2 or more TEE Vouchers as a package as compared to the sum of the individual value of all individual TEE Vouchers

6. Market for TEEs with an intermediary (ix) – Multi-units demand auction / uniform price

OHE

- We now have to take into account that C-2 can buy more than one TEE Voucher (one for each, P-2 and P-3), and that there are 2 TEE Vouchers ($k = 2$),

Product #	Company #	Estimated WTP (in million)
P-1	C-1	€ 734.72
P-2	C-2	€ 626.74
P-3	C-2	€ 583.96
P-4	C-3	€ 526.56
P-5	C-4	€ 522.04
P-6	C-5	€ 509.42
P-7	C-6	€ 350.90
P-8	C-7	€ 338.24
P-9	C-8	€ 286.38
P-10	C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- If firms bid 'truthfully' and reveal willingness to pay, then:
  - Bids are equal to their actual maximum WTP
  - C-1 and C-2 win a TEE Voucher each
  - The price paid by both, C-1 and C-2, is €583.96 million which is equal to the first rejected bid

6. Market for TEEs with an intermediary (x) – Multi-units demand auction / uniform price

OHE

- However, if C-2 bids strategically, it would maximise its surplus as compared to bidding truthfully

Product #	Company #	Estimated WTP (in million)
P-1	C-1	€ 734.72
P-2	C-2	€ 626.74
P-3	C-2	€ 583.96
P-4	C-3	€ 526.56
P-5	C-4	€ 522.04
P-6	C-5	€ 509.42
P-7	C-6	€ 350.90
P-8	C-7	€ 338.24
P-9	C-8	€ 286.38
P-10	C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- If C-2 bid its true WTP, then it would win one TEE Voucher at a price of € 583.96 million
- But alternatively, if it bids € 626.74 and € 526.56 million, then:
  - C-1 and C-2 are the winners of one TEE Voucher each
  - The final price paid by C-1 and C-2 would be € 526.56 million – equal to the highest losing bid

6. Market for TEEs with an intermediary (xi) – Multi-units demand auction / uniform price

OHE

- Uniform price auctions have desirable properties
  - Fairness: identical goods sell for identical prices
  - Simplicity: auction price equates demand and supply

- "Demand reduction" would be the primary concern in this market
  - If companies want more than one unit, which is a likely scenario given the example above where BMS would want to buy two TEE Vouchers, they have an **incentive to bid less than their true WTP** to push the equilibrium price down

6. Market for TEEs with an intermediary (xii) – Multi-units demand auction / discriminatory price

OHE

- C-2 now is allowed to buy one TEE Voucher per product (P-2 and P-3) and there are 2 TEE Vouchers ($k = 2$)

Product #	Company #	Estimated WTP (in million)
P-1	C-1	€ 734.72
P-2	C-2	€ 626.74
P-3	C-2	€ 583.96
P-4	C-3	€ 526.56
P-5	C-4	€ 522.04
P-6	C-5	€ 509.42
P-7	C-6	€ 350.90
P-8	C-7	€ 338.24
P-9	C-8	€ 286.38
P-10	C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- If firms bid "truthfully and reveal their actual WTP, then:
  - Bids will be equal to their actual WTP
  - C-1 and C-2 get one TEE Voucher each
  - Prices paid by C-1 and C-2 are equal to their bids (their actual WTP) which give them zero surplus
  - As a consequence, **both wining bidders would have incentives to hide their bids** (or WTP)

6. Market for TEEs with an intermediary (xiii) – Multi-units demand auction / discriminatory price

OHE

- If C-1 behaves strategically, then it would bid just above of € 626.74 million
- C-2 also can also behave strategically, therefore it would bid just above €583.96 million (the WTP of the following bidder)
- If C-1 anticipates C-2's bid, then it could also win the TEE Voucher by bidding just above C-2's bid, say €583.96 million
- Then, at equilibrium, we expect that both TEE Vouchers are sold at the same price equal to €583.96 million.

In our example, if the WTP are public information, the expected price in the discriminatory auction is the same than in the uniform price auction

Put in other words, if values are common knowledge, price discrimination is not implementable

6. Market for TEEs with an intermediary (xiv) – Multi-units demand auction / discriminatory price

OHE

- Discriminatory auctions raise the issue of “demand reduction” anticipating the clearing price
- Comparison with uniform price auction with multi-unit demand is difficult
  - Both auctions can be inefficient and encourage demand reduction: no clear efficiency or price ranking
  - Uniform price has been sometimes defended as better pricing rule for small bidders: easier to participate and get the “market price”

6. Market for TEEs with an intermediary (xv) – Multi-units demand auction / Vickrey price

OHE

- We now present the results for a Vickrey auction, assuming that there are 2 TEE Vouchers ($k = 2$)

Product #	Company #	Estimated WTP (in million)
P-1	C-1	€ 734.72
P-2	C-2	€ 626.74
P-3	C-2	€ 583.96
P-4	C-3	€ 526.56
P-5	C-4	€ 522.04
P-6	C-5	€ 509.42
P-7	C-6	€ 350.90
P-8	C-7	€ 338.24
P-9	C-8	€ 286.38
P-10	C-9	€ 285.66

Sources: IQVIA and OHE Consulting Ltd.

- If firms bid "truthfully" and reveal their actual WTP, then:
  - Bids will be equal to their true WTP
  - C-1 and C-2 win one TEE Voucher each
  - Prices paid by C-1 and C-2 are equal to the value of the losing bids that each bidder displaces

6. Market for TEEs with an intermediary (xvi) – Multi-units demand auction / Vickrey price

OIE

A property of Vickrey auction is that it is strategy proof and therefore revealing the true WTP is a dominant strategy for bidders

Under Vickrey auction then, C-1 and C-2 will bid their maximum WTP and resulting prices will be:

- C-1 pays **€ 583.96 million:** the value of the bid that it displaces (C-2 bid)
- C-2 pays **€ 526.56 million**: the value of the bid it displaces (C-3 bid)

Being strategy proof, Vickrey pricing addresses the issue of demand reduction

Vickrey auctions are efficient although the resulting prices are not uniform prices – they do not meet the concept of fairness

7. Results and Expected Market Performance

7. Results and expected market performance (i)

OHE

- We now focus on analysing the market for multiple TEE Vouchers along multiple years
- For simplicity we assume that buyers do not behave strategically
  - Buyers' strategic behaviour is difficult to predict in a market with multiple units and multiple periods
  - We assume prices are determined competitively (the lowest WTP of winning bids)
- We assume that incentives to innovate exist whenever the lowest WTP of winning bids (the competitive price) for a TEE Voucher is higher than the expected capitalised cost of investing in a new AMR product **net of profits** ("new class" or "existing class")
- This analysis gives us an "upper bound" of TEE Vouchers per years that might be traded in the market I the long run
- We use the information of the TOP 50 eligible blockbuster drugs
- We also assume that buyers with the highest WTP are the first ones to buy a TEE Voucher
- Results are presented in the following way:
  1. Two TEE Vouchers per year, for "new class" AMR products
  2. Three TE Vouchers per year, for "existing class" AMR products
- We analyse both cases, 1. and 2., under:
  - No entry of new competitors, or "no replacement" (i.e. the number of potential buyers decreases as the number of TEEs traded increases)
  - "Replacement" of withdrawn products by hypothetical new entrants

7. Results and expected market performance (ii)

OHE

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 799.676.431	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 802.075.891	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 782.743.804	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 609.167.556	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 561.629.743	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 519.348.560	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 455.176.405	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 497.763.254	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 473.385.710	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 471.971.805	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 494.214.321	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 469.592.056	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 499.322.934	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 557.750.544
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 520.981.967
Expected R&D cost less expected profit	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**

Sources: IQVIA and OHE Consulting Ltd.

- **Without replacement of buyers, 2 TEE Vouchers per year would be enough for developing 18 “new class” products in 9 years (and possibly more in subsequent years)**
- **The average price paid per TEE Voucher considering the whole period is €518.4m**

7. Results and expected market performance (iii)

OHE

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 0	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 0	€ 0	€ 0	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 0	€ 0	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 0	€ 0	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 0	€ 0	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 0	€ 0	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 0	€ 0	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 0	€ 0	€ 0
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 0	€ 0	€ 0
Expected R&D cost less expected profit	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**	**€ 165.570.794**

Sources: IQVIA and OHE Consulting Ltd.

- **Without replacement of buyers, 3 TEE Vouchers per year would be enough to develop 18 "existing class" products in 6 years**
- **Using data available, the average price paid for a TEE Voucher considering the six year period is €445.2m**
- **Difference between WTP (~€350m) and required incentive (€279.5m) shows that there is a strong potential to develop more in years after 2023 (the scope of our data)**

7. Results and expected market performance (iv)

OHE

- Finally, we analyse the market with replacement, **assuming** that there are **two new entrants per year**, which are included in the ranking
- We use the average gross sales of the first and second highest entrant in the last five years, and we calculate their WTP
- We do not adjust their WTP across years (because we are using a simple average of gross sales of new entrants in the last five years)

7. Results and expected market performance (v)

OHE

Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 799.676.431	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 802.075.891	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 782.743.804	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 609.167.556	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 561.629.743	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 519.348.560	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 455.176.405	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 497.763.254	€ 548.850.826
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 473.385.710	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 471.971.805	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 494.214.321	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 469.592.056	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 499.322.934	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 557.750.544
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 520.981.967
Entrant 1	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317
Entrant 2	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463
Expected R&D cost less expected profit	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**	**€ 307.543.721**

Sources: IQVIA and OHE Consulting Ltd.

- **With replacement of buyers, 2 TEE Vouchers per year would be enough to develop 18 “new class” products in 9 years**
- **The average price paid per TEE Voucher considering the whole period of 9 years is €584.1m**
- **Difference between WTP (~€520m) and required incentive (€441.8m) shows that there is a strong potential to develop more in years after 2026 (the scope of our data)**

7. Results and expected market performance (vi)

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Product # / WTP	2018	2019	2020	2021	2022	2023	2024	2025	2026
P-1	€ 734.715.779	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-2	€ 626.743.932	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-3	€ 583.962.181	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-4	€ 526.563.748	€ 750.702.563	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-5	€ 522.045.067	€ 647.085.591	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-6	€ 509.426.472	€ 631.466.875	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-7	€ 350.909.839	€ 421.737.888	€ 506.861.952	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-8	€ 338.249.831	€ 400.536.187	€ 474.292.142	€ 0	€ 0	€ 0	€ 0	€ 0	€ 0
P-9	€ 286.385.012	€ 332.336.045	€ 385.660.011	€ 447.539.910	€ 0	€ 0	€ 0	€ 0	€ 0
P-10	€ 285.664.721	€ 320.950.009	€ 360.593.733	€ 405.134.248	€ 0	€ 0	€ 0	€ 0	€ 0
P-11	€ 251.190.033	€ 276.970.741	€ 305.397.433	€ 336.741.679	€ 371.302.918	€ 409.411.326	€ 451.430.963	€ 0	€ 0
P-12	€ 242.984.256	€ 277.655.024	€ 317.272.871	€ 362.543.681	€ 414.274.062	€ 0	€ 0	€ 0	€ 0
P-13	€ 242.258.512	€ 276.825.726	€ 316.325.242	€ 361.460.838	€ 413.036.710	€ 0	€ 0	€ 0	€ 0
P-14	€ 221.998.947	€ 253.675.379	€ 289.871.634	€ 331.232.636	€ 378.495.327	€ 432.501.805	€ 0	€ 0	€ 0
P-15	€ 210.938.732	€ 241.037.011	€ 275.429.932	€ 314.730.286	€ 359.638.302	€ 410.954.121	€ 0	€ 0	€ 0
P-16	€ 196.286.170	€ 224.293.715	€ 256.297.580	€ 292.867.990	€ 334.656.534	€ 382.407.772	€ 436.972.506	€ 0	€ 0
P-17	€ 191.876.058	€ 219.254.335	€ 250.539.145	€ 286.287.900	€ 327.137.549	€ 373.815.923	€ 427.154.709	€ 488.104.263	€ 0
P-18	€ 179.227.017	€ 204.800.437	€ 234.022.859	€ 267.414.950	€ 305.571.668	€ 349.172.865	€ 398.995.399	€ 455.926.977	€ 0
Entrant 1	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317	€ 524.949.317
Entrant 2	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463	€ 305.167.463
Expected R&D cost less expected profit	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794	€ 165.570.794

Sources: IQVIA and OHE Consulting Ltd.

- **With replacement of buyers, 3 TEEs per year would be enough to develop 25 "existing class" products in 9 years**
- **The average price paid per TEE Voucher considering the whole period of 9 years is €457.4m**
- **Difference between WTP (~€400m) and required incentive (€279.5m) shows that there is a strong potential to develop more in years after 2026 (the scope of our data)**

8. Summary and Implications

8. Summary and Implications (i)

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- **Without replacement** of buyers**, 2 TEE Vouchers per year** would be enough for developing 18 “new class” products in 9 years (and possibly more in subsequent years)
- **The average price paid per TEE Voucher considering the whole period is €518.4m**
- Without replacement of buyers, **3 TEE Vouchers per year** would be enough to develop 18 “existing class” products in 6 years
- Using data available, **the average price paid for a TEE Voucher considering the six year period is €445.2m**
- Difference between WTP (~€350m) and required incentive (€279.5m) shows that there is a strong potential to develop more in years after 2023
- **With replacem**ent of buyers, **2 TEE Vouchers per year** would be enough to develop 18 “new class” products in 9 years
- The **average price paid per TEE Voucher considering the whole period of 9 years is €584.1m**
- Difference between WTP (~€520m) and required incentive (€441.8m) shows that there is a strong potential to develop more in years after 2026
- **With replacement** of buyers**, 3 TEEs per year** would be enough to develop 25 “existing class” products in 9 years
- The **average price paid per TEE Voucher considering the whole period of 9 years is €457.4m**
- Difference between WTP (~€400m) and required incentive (€279.5m) shows that there is a strong potential to develop more in years after 2026

8. Summary and Implications (ii)

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We revised our previous analyses to use the results of the modelling to generate the minimum and average WTP of a TEE for the different scenarios: 2/3 TEE per year, with/without replacement and period 2018-2026.

In this slide, we add in the required incentives required based on a share of global R&D cost and existing revenues

We translate this into **required lengths of a TEE Voucher using the minimum and average TEE Vouchers expected. These are indicative and highly sensitive to all of the assumptions used**

Scenario	Minimum WTP for a TEE 2018-2026	Average WTP for a TEE 2018-2026[a]	Contribution to R&D cost required from a TEE Voucher	Duration of TEE required Years (in relation to minimum WTP)	Duration of TEE required Years (in relation to average WTP)
Two TEE per year without replacement (new class)	€469.6m	€518.4m	€441.8m	0.94	0.85
Two TEE per year with replacement (new class)	€473.4m	€584.1m	€441.8m	0.93	0.76
Three TEE per year without replacement (existing class)	€349.2m	€445.2m	€279.5m	0.80	0.63
Three TEE per year with replacement (existing class)	€405.1m	€457.4m	€279.5m	0.69	0.61

Sources: IQVIA and OHE Consulting Ltd.
Notes: [a]Averages reported in the table are based on simultaneous markets and a uniform price set at the lowest winning WTP.

8. Summary and Implications (iii)

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- These results suggest that:
  - **A TEE period of 9-12 months** would be needed for new classes of antibiotics
  - **A TEE period of 7-10 months** would be needed for existing classes of antibiotics
- **Use of an Intermediary**
- Selling prices for the TEE Vouchers are similar, but an intermediary has policy attractions:
- It could transfer to developers the agreed required funding, guaranteeing the amount to developers and minimising the impact of TEE Vouchers on health systems
- It could make differential rewards to “new class” and “existing class” antibiotics.
- An alternative would be for “new class” and “existing class” antibiotics to have differential TEE periods, i.e. the length of exclusivity attached to the TEE Voucher would differ. However, this could be quite disruptive without an intermediary, as buyers would have to choose whether to wait for a TEE Voucher with a longer TEE to become available. We have not modelled this.

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