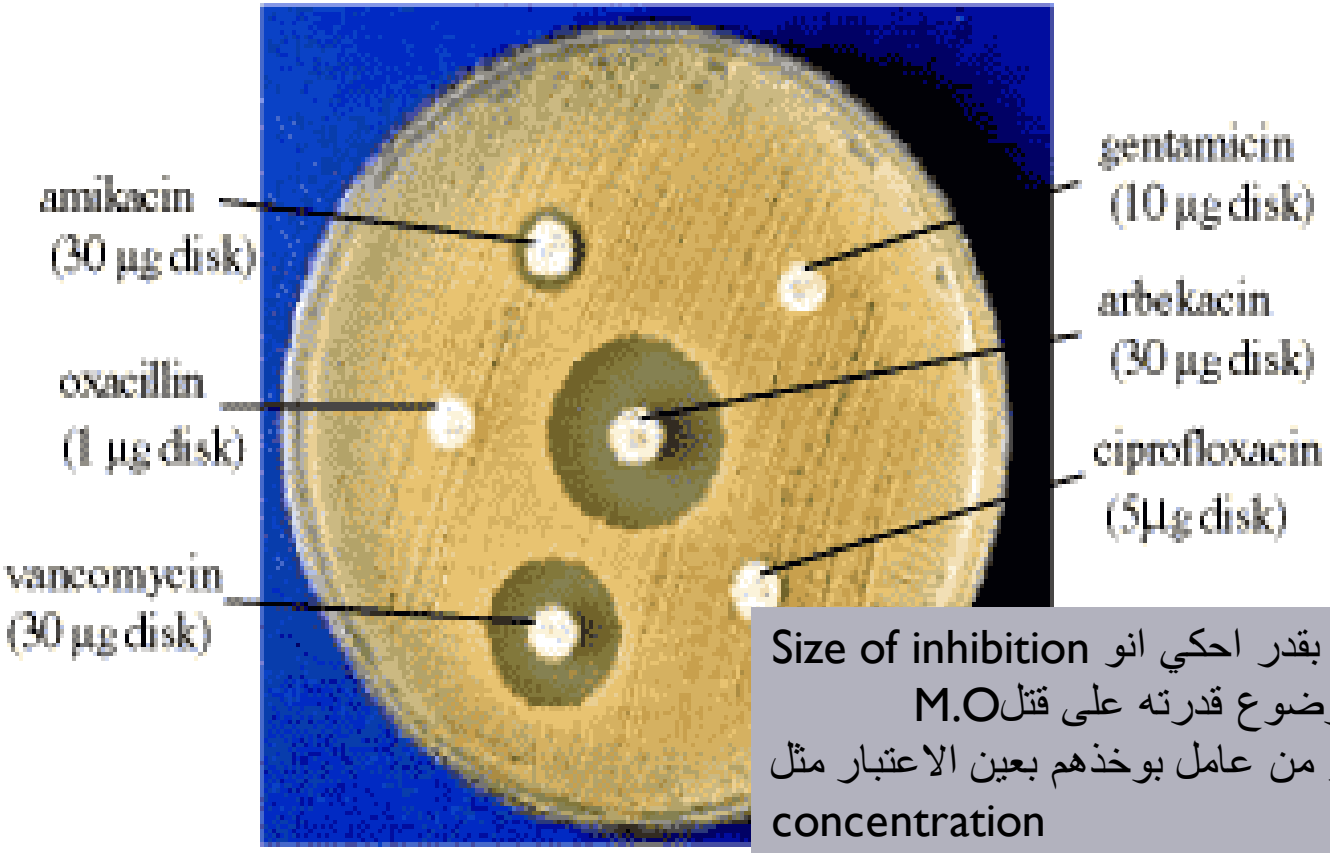
هون رح يكون افضل علاج
هوarbekacin..vancomycin
وناخذ بعين الاعتبار حاله المريض اذا عنده امراض كلى
واذا رح يصيرdrug drug interaction

Figure 2. ORSA isolate showing in vitro susceptibility only to arbekacin and vancomycin



حكينا ش دايما بقدر احكي انو Size of inhibition
بس لموضوع قدرته على قتلM.O relate
في اكثر من عامل بوخذهم بعين الاعتبار مثل
concentration
Solubility
Diffusion

اقدر اتوصل لمعلومات Inhibition of zone من خلال كثيره

لو بدي اعطي A مع B ما رح يعملو Additive ولكن رح يزيدو فعاليه بعض

لو بدي اعطي لمريض مضاد حيوي بحكي انهم additive انو effect الاثنين رح يعطو مفعول

A عنده القدره على قتل M.O وكذلك B ولما التقو مع بعض عملو More Kill

هون البكتيريا resistance to A وكذلك عند B بتكون resistance لذلك تظهر بينهم inhibiton of zone

هون صار عدم توافق A يخرب B والعكس

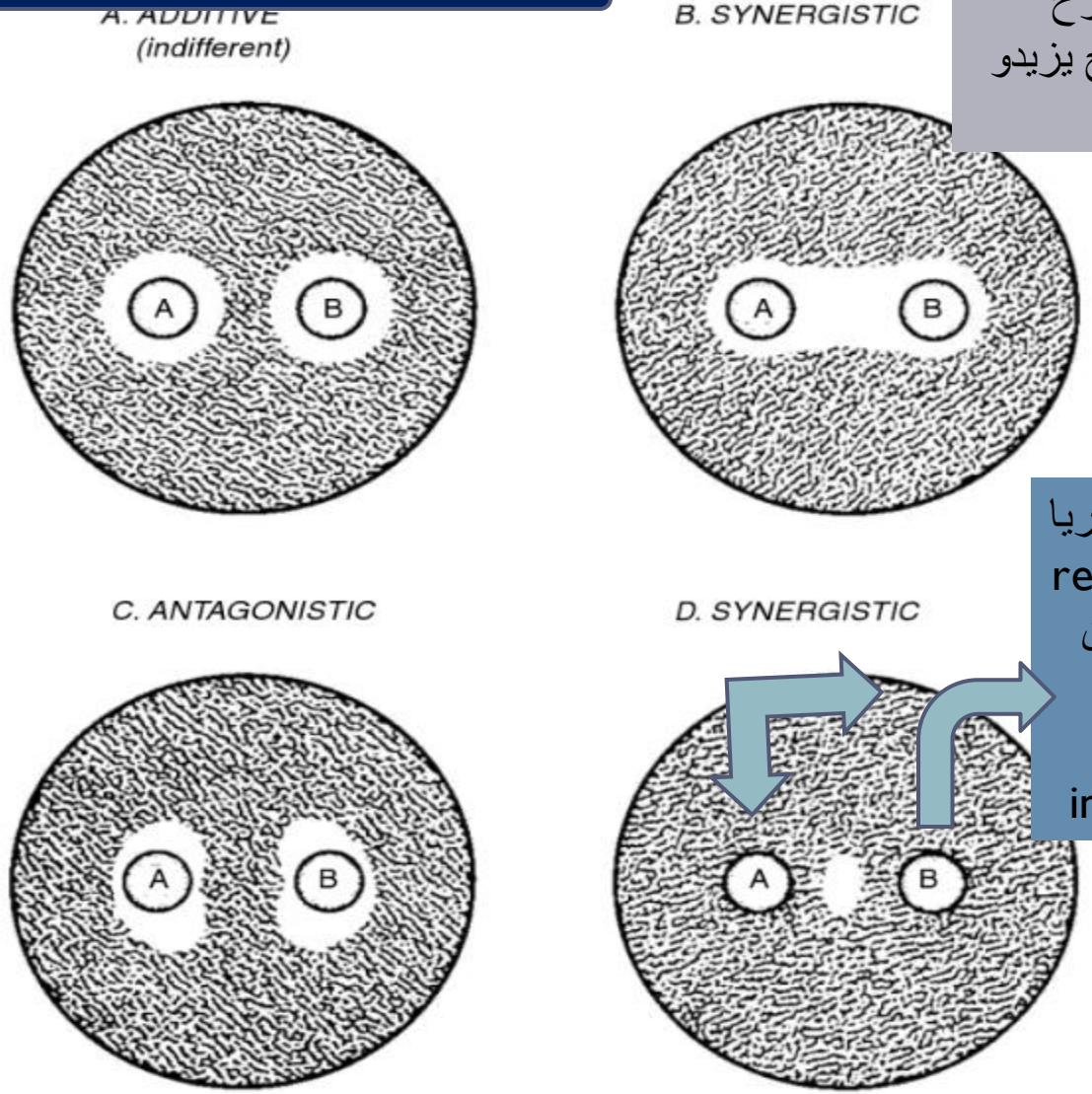


FIGURE 12.1 Assessing drug interactions using disk-diffusion. Shaded areas represent bacterial growth and clear areas represent zones of inhibition. (Adapted and reprinted with permission from Eliopoulos, G.M. and Moellering, R.C., Jr. *Antibiotics in Laboratory Medicine*, Lorain, V., Ed., Williams Wilkins, Baltimore, 1996, figure 9.10, p. 344.)

12.2.2.6 Interpretation

If the quality control is within limits, record the pattern of the zones of inhibition as follows (see Figure 12.1):

1. Indifference: Two independent circles
2. Synergism: Enhancement or bridging at or near the junction of the two zones of inhibition or inhibition of growth only due to the combined effects of both antibiotics A and B.
3. Antagonism: Truncation of zones is observed near the junction of the two zones.

شرح السلايد الي قبل

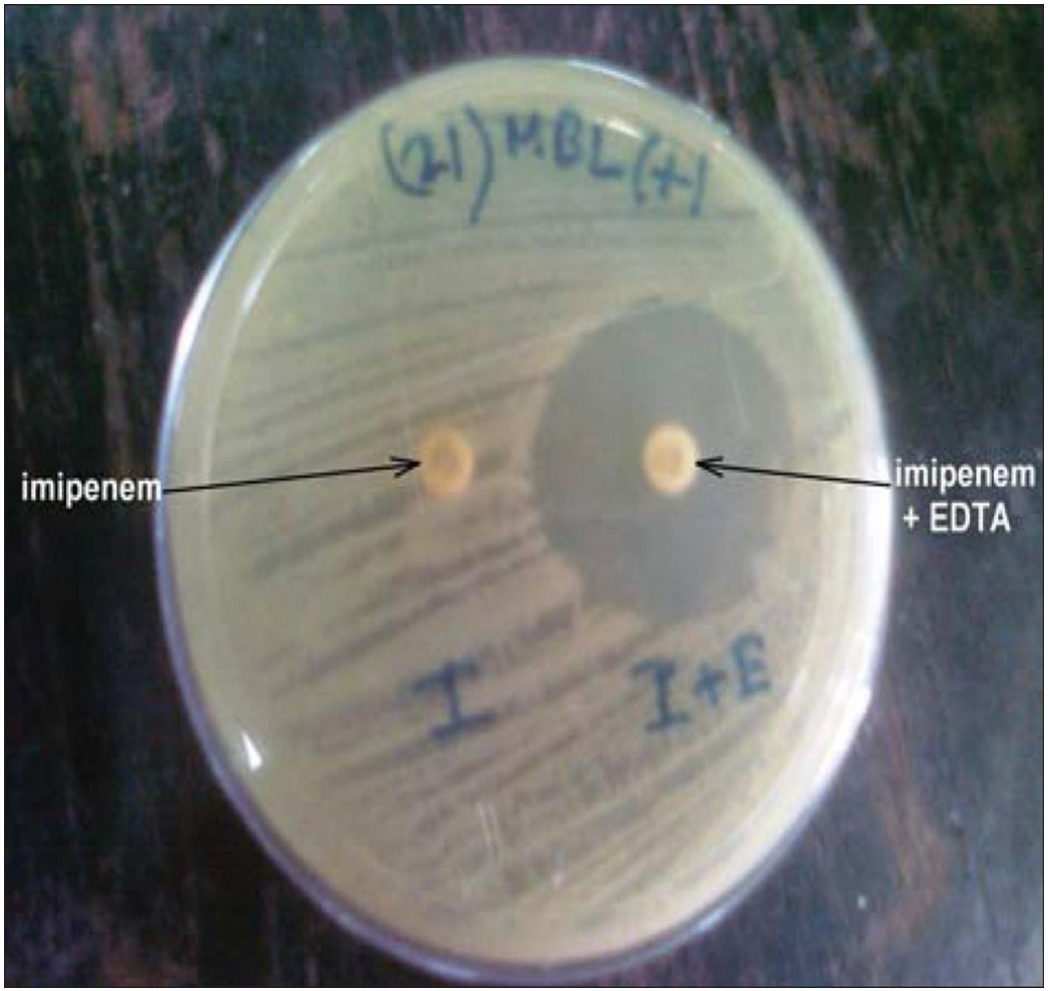
12.2.2.7 Limitations

This methodology yields only qualitative information about the antimicrobial agent combination. Using this technique, it may be difficult to distinguish indifferent from synergistic interaction [1,2,5].

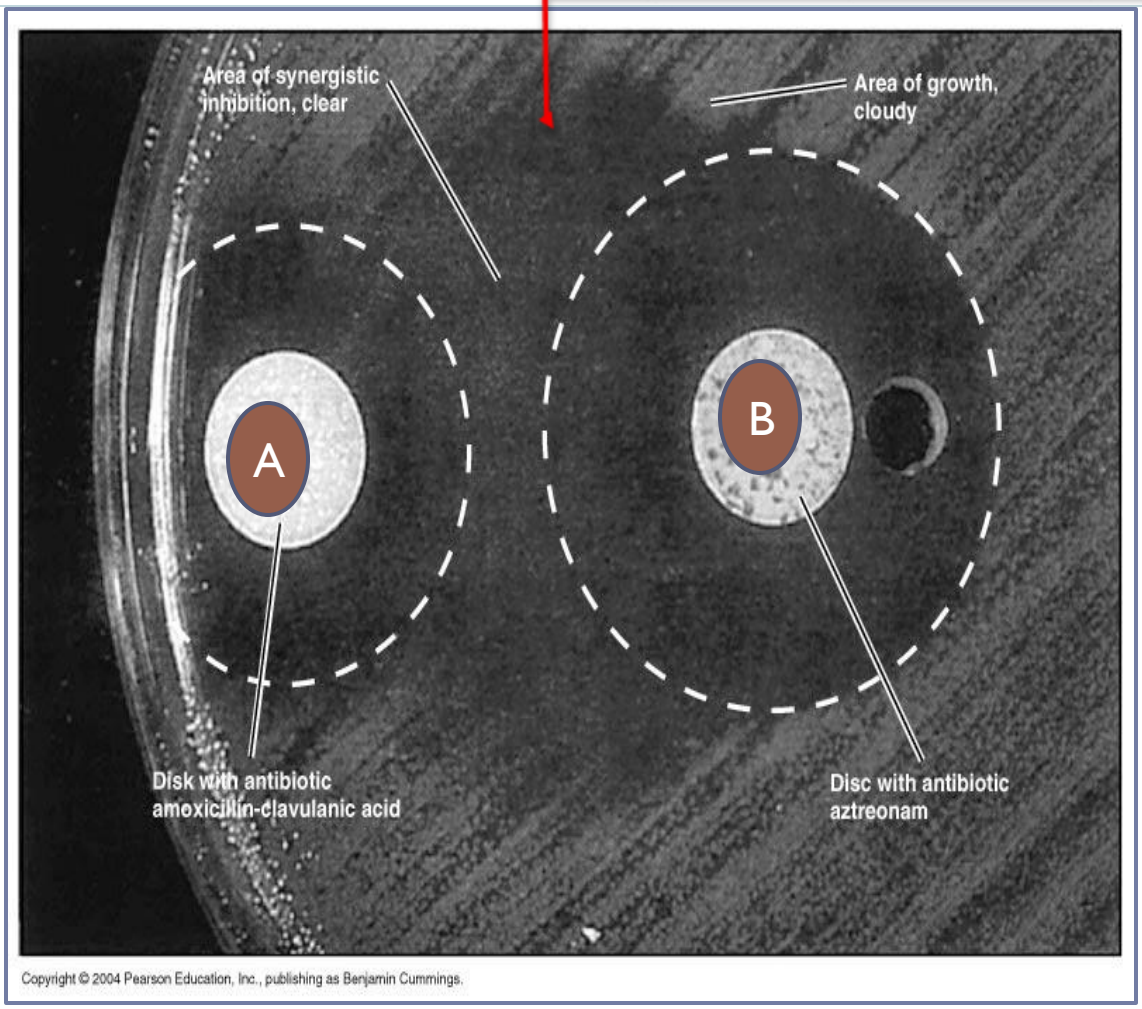
- **Synergistic effect**:The effect when chemical substances interact resulting in an overall effect that is greater than the sum of individual effects of any of them

استخدامهاETDA
chelating agent
لموضوع of stabilizing
formula
وحطيناهل ضمن
chemical biocideلانها
potentiation تعمل
chemical تزيد فعاليه
biocide

من اقوى المضادات
الحيويه ولكن لحاله غير
قادر على قتل
bacteriaالمزروعه
على agar plat ولكن
لما حطينا ETDA صار
zone of inhibition



A…B بين zoon of inhibition سبب تشكل
synergistic لانهم



سبب تشكل zoon of inhibition بين A…B لانهم synergistic

هون يجي
the سؤال
bacteria grow on this agar plate is sensitive to antibiotic

4 ..no
2 no
3 and5 ..yes because its resistance to each other

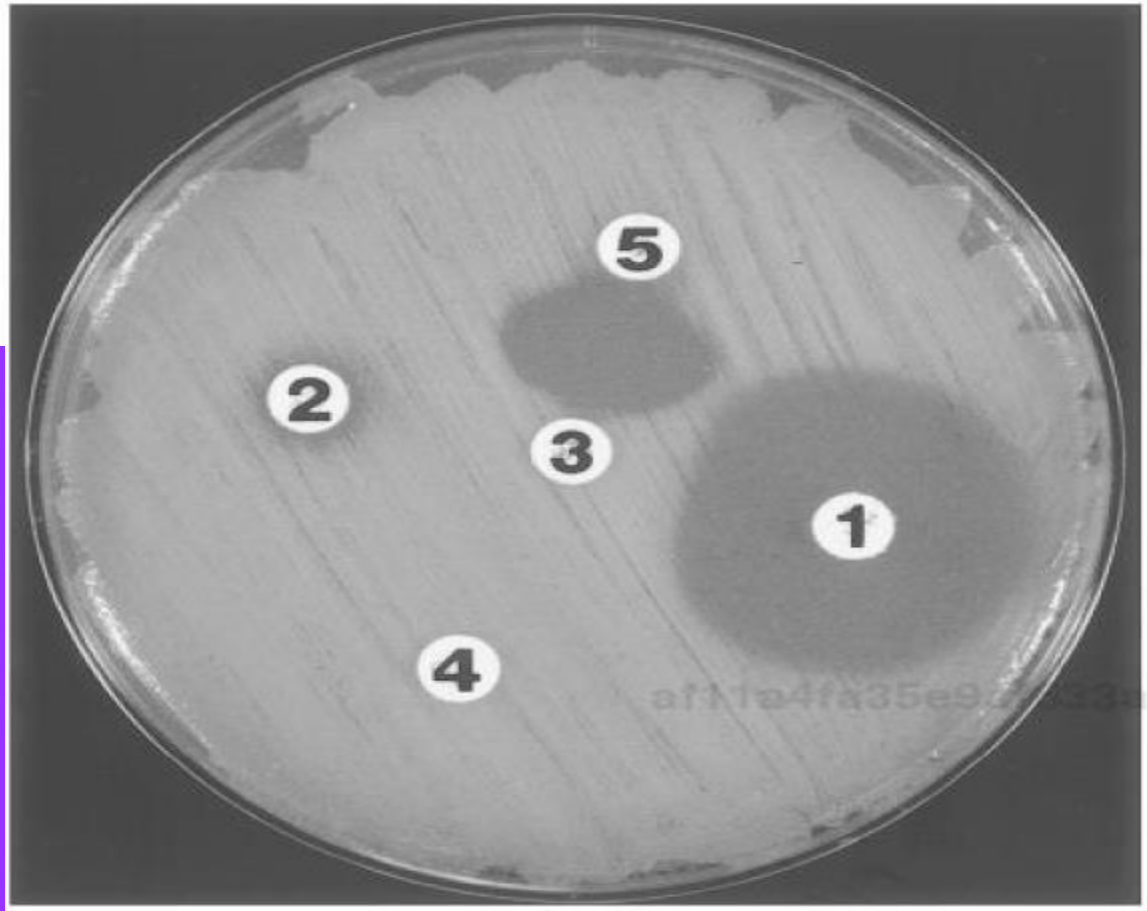
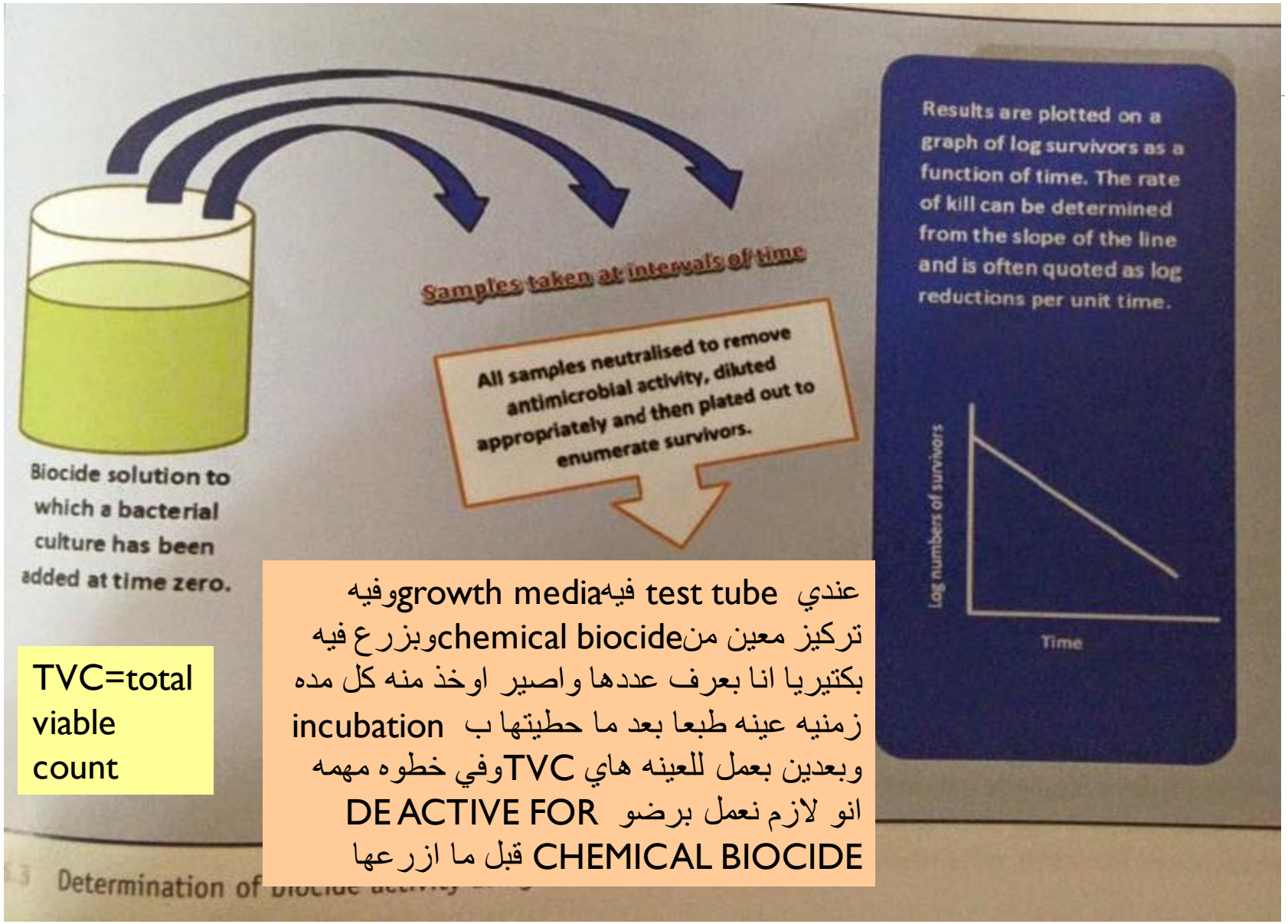


Figure 18.4 Disc test with inhibition zones around two (1, 2) of five discs. The zone around disc 1 is clear and easy to measure, whereas that around disc 2 is indistinct. Although none of the antimicrobials in discs 3, 4 or 5 appear to inhibit the bacterium, synergy (as evidenced by inhibition of growth between the discs) is evident with the antimicrobials in discs 3 and 5. Slight antagonism of the drug in disc 1 by that in disc 3 is evident.



TVC=total viable count

عندي test tube فيهgrowth mediaوفيه تركيز معين منchemical biocideوبزرع فيه بكتيريا انا بعرف عددها واصير اوخذ منه كل مده زمنيه عينه طبعا بعد ما حطيتها ب incubation وبعدين بعمل للعينه هاي TVCوفي خطوه مهمه انو لازم نعمل برضو DE ACTIVE FOR CHEMICAL BIOCIDE قبل ما ازرعها

Measurement of antibacterial activity: 3. kill curves

تعطينا هاي الطريقه Qualitative And Quantitative

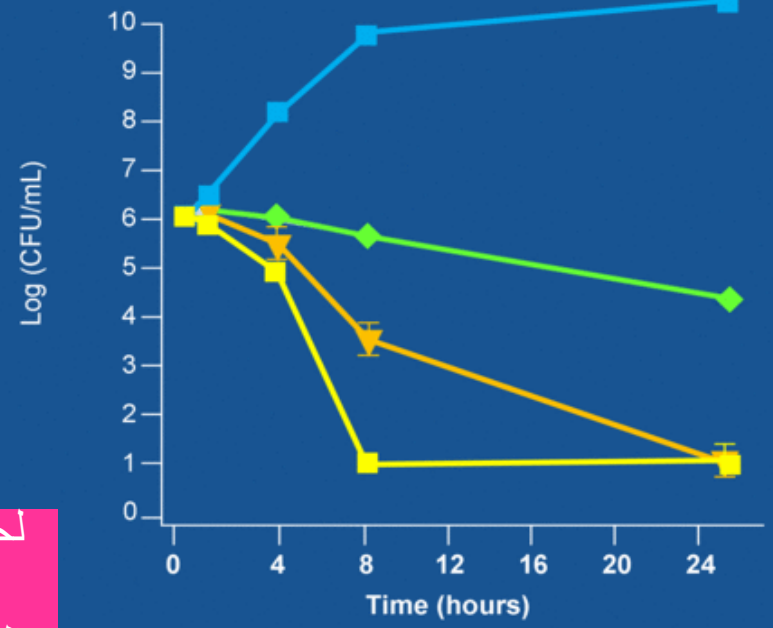
- MIC and agar diffusion methods give qualitative information about antimicrobial activity
- They do not give any quantitative details on the rate at which the agent kills cells and how it might be influenced by environmental factors
- Kill curves: inoculate a biocide solution with a known concentration of viable cells and then take samples at intervals of time to determine the number of surviving cells at each time point
- When the sample is taken the antimicrobial agents must be neutralized:

- Dilution
- Specific neutralizer
- General neutralizer (a combination of Tween 80 and lecithin)

شرحه بالسلايد الي تحته

Bactericidal Activity against MRSA

In Vitro Time-Kill Curves



All agents tested at 8x MIC[1] for MRSA ATCC 33591 using earlier methodology[2]

Pace, AAC, 2003;47(11):3602-3604; CLSI M7 A9

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الهدف من انو لتاكد انو control وانو inhibitionصار القتل صار من منش antibacterial من اشي ثاني

Same effect but the rate of kill different

هون صار quantitative

لحد هون ماده الفيرست

Preservative efficacy testing

(Antimicrobial test)

- The activity of the preservative influenced by:

- pH

بعض منهم يكون بدو وسط حمضي او قاعدي

- Multiphase systems

في منهم يحب طبقتين water and oil
وفي اشي يحب water
واشيoilوفي اشي يخرب ائا راح على oilوكذلك نفس الاشي
للwater

- Suspended solid

اذا في polymerفي بعض
to get يصير رحpreservative
polymer علىadsorp

- Adsorption on packaging

ضروري اعمله لاي مستحضر صيدلاني ينزل على السوق فيه preservative
ليه اعمله ⟸ لان تاثير الpreservative فيكثير عوامل تلعب فيه

- Final product should be tested when the product is first manufactured and also during storage, why?

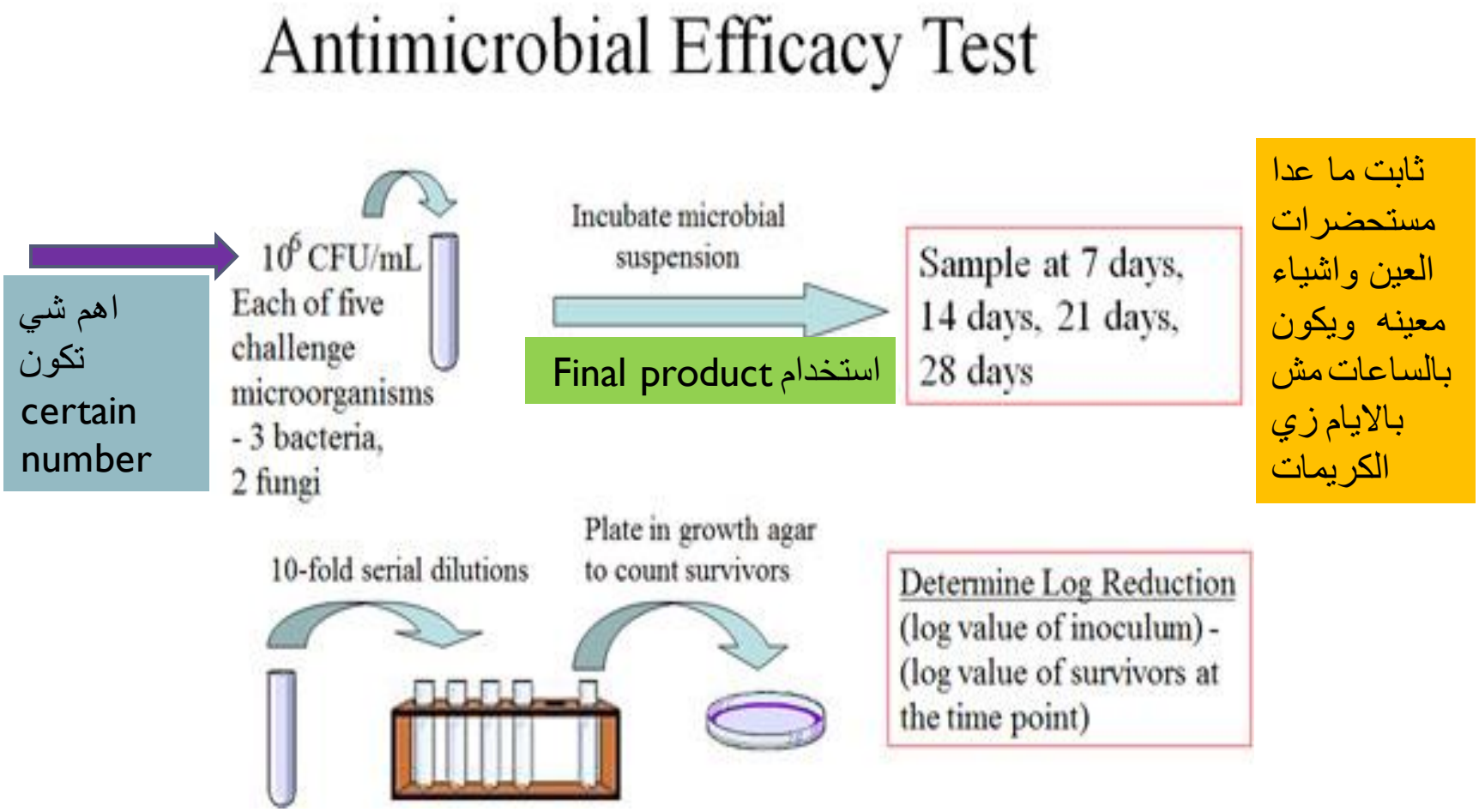
to show there is no deterioration of preservative action over time

Preservative efficacy testing

- Pharmacopeia testing procedure for the final product (pharmaceutical and cosmetic products)
- The product is tested in its final container and different samples are inoculated with a range of different cultures (described in details in various pharmacopeias)
- The organisms used are: **5 …3bacteria**
- **2fungi**

Pseudomonas aeruginosa	Candida albicans
Staphylococcus aureus	Aspergillus braziliensis
Escherichia coli	Zygosaccharomyces rouxii

Preservative efficacy testing (Challenge Test)



Preservative efficacy testing

1. After inoculation of the products in their final containers they are stored under specified conditions for 28 days
2. During this period samples are removed at intervals of time and neutralized before enumerating the survivors using plate counts
3. Bacteria are incubated at 30-35C for 18-24 hours
4. Candida and Zygosaccaromyces at 20-25C for 48 hours
5. Aspergillus at 20-25C for one weeks

يعني نعمل تثبيط لل chemical biocide

Fungi and Yeast

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Table 16.3 EP performance criteria for preservative efficacy tests.

Product type	Challenge organism	Acceptance criteria	Log reductions specified					
			6 h	24 h	48 h	7 days	14 days	28 days
Parenteral/ophthalmic	Bacteria	A	2	3				NR
		B		1		3		NI
	Fungi	A				2		NI
		B					1	NI
Topical, nasal, ear and inhaled products	Bacteria	A			2	3		NI
		B					3	NI
	Fungi	A					2	NI
		B					1	NI
Oral and rectal products	Bacteria						3	NI
	Fungi						1	NI

NI = no increase; NR = no recovery.

- Acceptance criteria are given the pharmacopeias

اذا تم التحقق من هدول الشروط بقدر انزل مستحضري على السوق

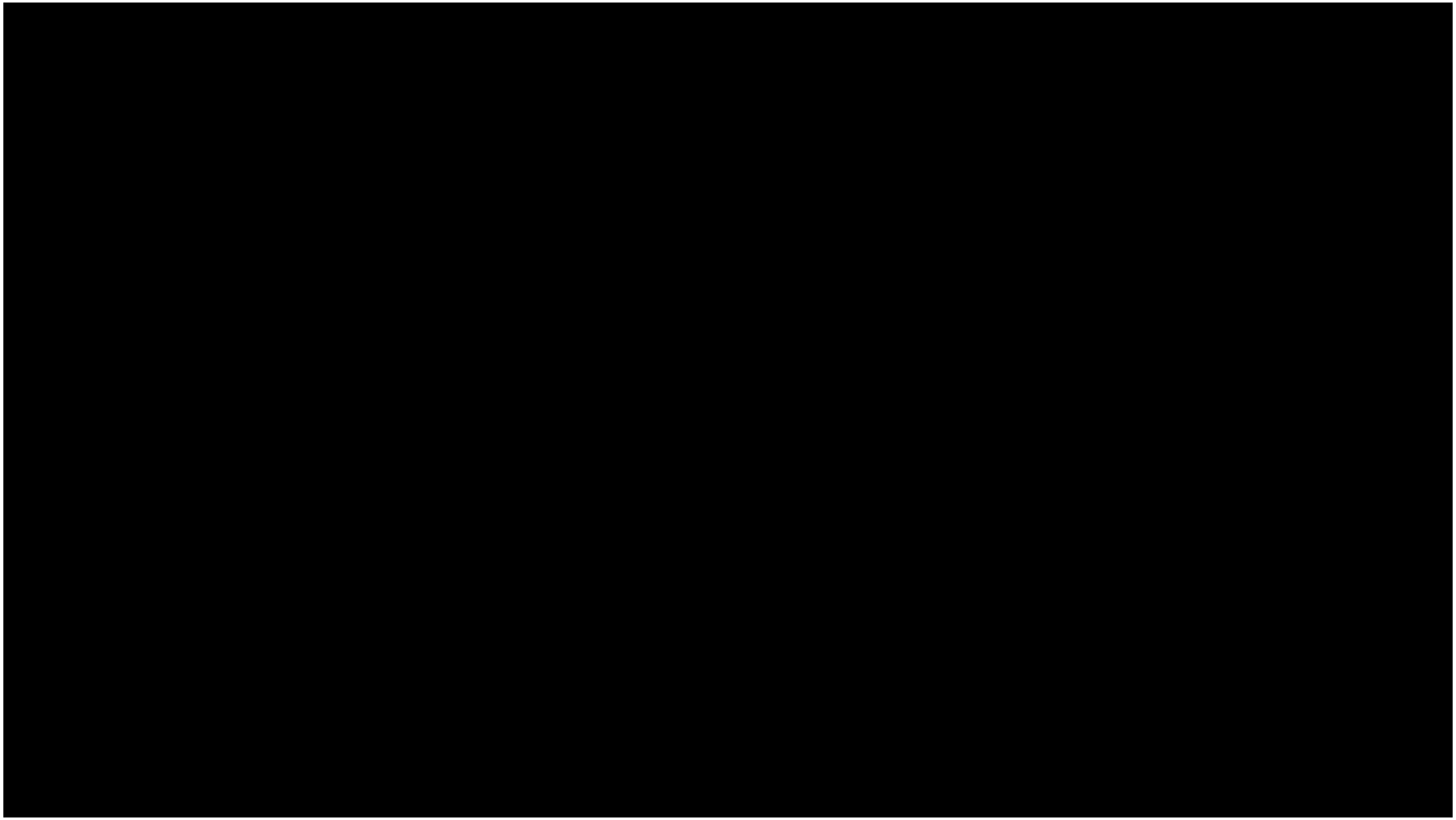
- A vs B criteria: A more demanding, generally applied and B less stringent if there is a risk of toxicity if conc. of preservative is too high

Disinfectant testing

زي الديتول مكتوب انو يقتل 99% وبناءا على disinfectant لحتى testing اعرف قديه requirement of different M.O properties

- Disinfectants are intended for use within diverse environments thus there is requirements that they possess bactericidal, sporicidal, fungicidal, and virucidal properties
- The basic approach is to add MOs to a disinfectant and remove samples at interval of time, neutralizes the biocides and assess the survivors

بجيب M.O disinfectant وبعمل remove sample at interval of time فبزرع الي عملته وبوخذ a time point من البكتيريا وبزرعها واشوف اكم ضايل بعد وقت معين من exposure of disinfectant وطبعا نكون عاملين neutralize for antibiotic



هون المصنع لازم يكون اله procedureمعين حتى اعمل

Non-sterile Regulations: Microbial Control

- 21CFR 211.113 – Control of Microbiological Contamination
  - "Appropriate written procedures, designed to prevent objectionable organisms on drug products not required to be sterile, shall be established and followed."

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

كل component. containerاستخدمه بصناعه المستحضر لازم يكون خالي من اي M.O

- 21CFR 211.84
  - "Each lot of component, drug product container, or closure with potential for microbiological contamination that is objectionable in view of its intended use shall be subject to microbiological tests before use."
- 21CFR 211.165
  - "There shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms"

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

- USP Testing methods:
  - <61> - Microbiological Examination of Non-sterile Products - Microbial Enumeration TVC
  - <62> - Microbiological Examination of Non-sterile Products - Tests for Specified Organisms OBJECTIONAL M.O
  - <51> - Antimicrobial Effectiveness Test

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

- USP <61>
- Purpose of the test:
  - To determine the overall bioburden of the non-sterile product – Bacterial and Mold/Yeast
  - Quantitative result
  - Monitor in-process testing
  - Lot release
  - Harmonization
    - USP/EP/JP Methods

مش بس للمنتج النهائي ولكن ايضا
ثناء علمليه التصنيع

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

- USP <61>
  - Media used for testing:
    - Preparation
      - Buffer solution
      - Soybean Casein Digest Broth
    - Total Aerobic Microbial Counts (TAMC)
      - Soybean Casein Digest Agar
    - Total Yeasts and Mold Counts (TYMC)
      - Sabouraud Dextrose Agar

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

- USP <61>
  - Sampling and sample size
    - 10 gram/milliliters/ patches of sample recommended
    - 1% for smaller batches
    - Amount tested should have a justification and included in sampling scheme
    - Must represent the entire lot tested

اذا عندي مثلا 100gما يزبط كل شوي اوخذ 10gعشان اشيك عليهم لانهم رح يخلصو لهيك بوخذ 1g

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s

- The sampling scheme should include:
  - Follow 21CFR 211.84 requirements
    - What and where to sample –
      - Beg, mid, end
      - Top, mid, bottom
    - Amount of sample needed
    - How often the sampling should be performed
    - Very specific sampling methods/procedures (training, precautions to avoid cross contamination)
      - Equipment use – Sterile
    - Sampling labeling, handling, storage and shipping

الاماكن الي لازم اخذ منهم عينه عشان الفحص

المصنع يحددها

Microbiology Testing for Non-sterile Products
https://www.youtube.com/watch?v=2RsuPBZK058&t=966s