MIC SYSTEM AS A TOOL FOR RESPONSIBLE ANTIBIOTICS USAGE

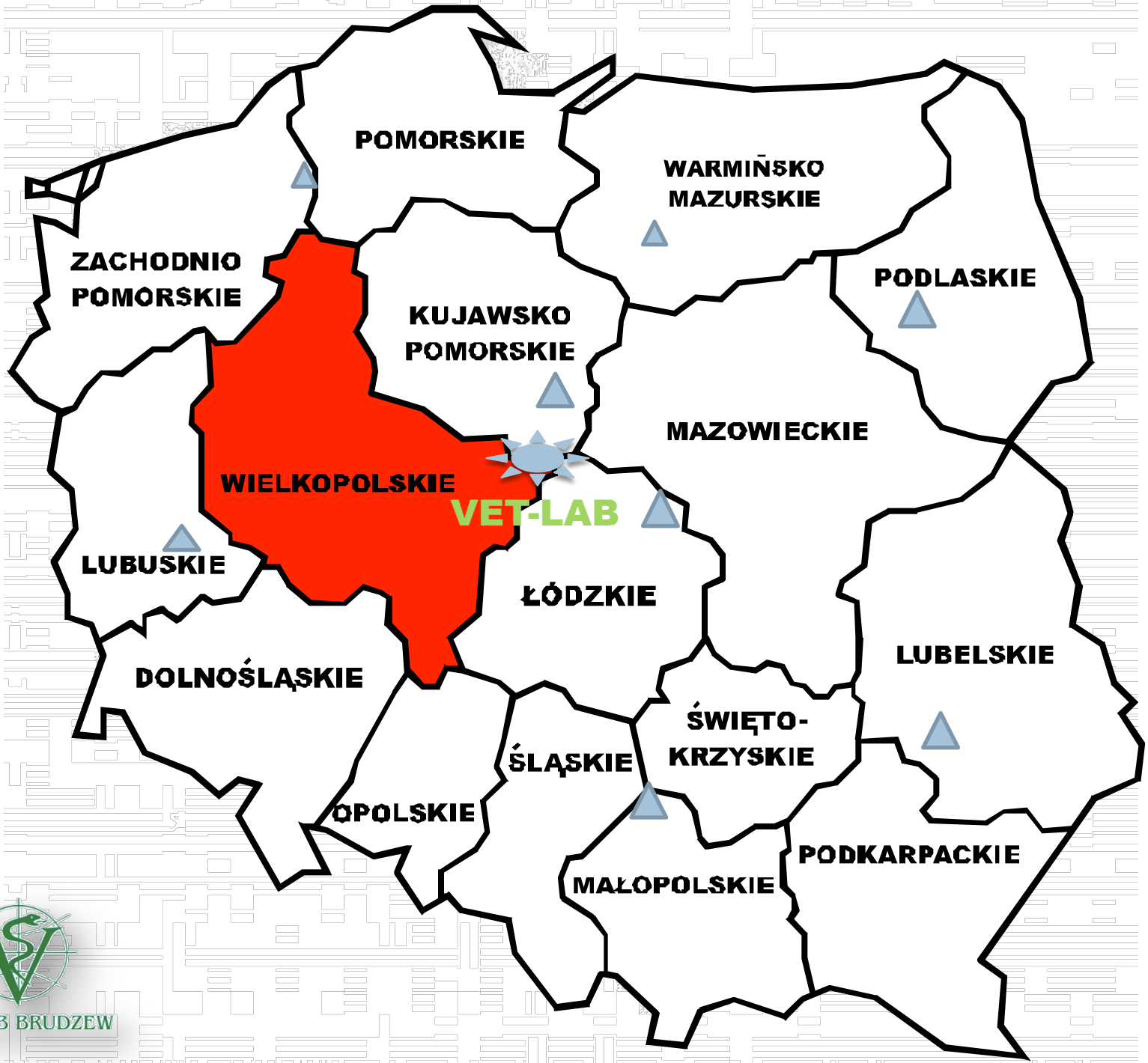
dr PIOTR KWIECIŃSKI

VET-LAB BRUDZEW

as an example of private veterinary practice focused on farm animals

VET-LAB BRUDZEW

VET-LAB BRUDZEW
ul. Turkowska 58 C
62-720 Brudzew
www.vetlabbrudzew.pl



VET-LAB BRUDZEW

what is VET-LAB?

- Clinic (1990)
- Laboratory (2003)
- Warehouse (2009)

DIAGNOSICS + CLINIC + PHARMACY = SUCCESFUL VET

A MORE COMPLETE SERVICE

VET-LAB BRUDZEW

VET-LAB *team*

VET-LAB team is composed of 35 people:

- 11 veterinary doctors, specializing in poultry, swine and ruminants
- 12 microbiologists – specialists in laboratory medicine
- 10 veterinary technicians
- 1 accountant
- 1 cleaner
- auxiliary group of field vaccinators

VET-LAB BRUDZEW

VET-LAB
clinic's main fields of activity

- POULTRY FARMS
- SWINE FARMS
- COW FARMS

Services include:

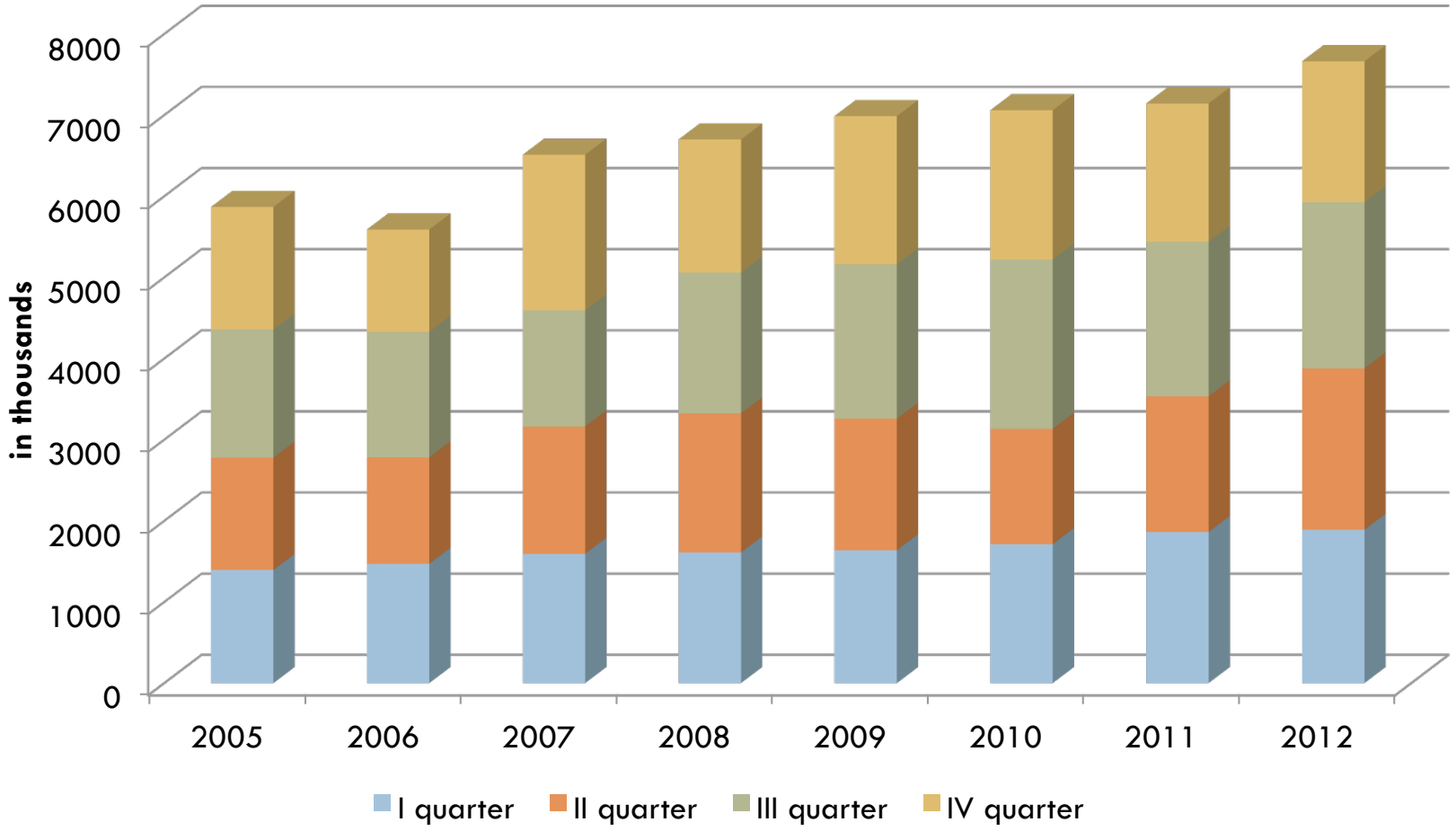
- creating prophylactic programmes
- treatment of animals
- analysis of performance
- nutritional advisory service

VET-LAB BRUDZEW

AGENDA

- POLISH POULTRY MARKET
- WHAT IS MIC
- MIC IN PRACTICE
- RESONABLE USE OF ANTIIOTICS
- CURRENT HEALTH PROBLEMS OF POULTRY IN POLAND

Introduction of broiler breeders in Poland



(The National Poultry Council - Chamber of Commerce)

Introduction of broiler breeders in Poland

- 2013 --- 8.096,32
- 2014 --- 8.933,70 2015 --- ???

- At the moment Poland is the leader in broiler breeders production

- Estimated number of flocks in Poland - 950
- Average number of birds in a flock – 8,500

Hatching eggs in Poland

COUNTRY	NUMBER OF HATCHING EGGS (in mln)			% IN OVERAL EU PRODUCTION		ANNUAL CHANGE	
	2009	2010	2011	2010	2011	2010	2011
FRANCE	1.087,7	1.048,9	1.151,2	13,5	15,4	+2,8	+9,8
G B	1.058,1	1.105,5	1.078,4	14,2	14,6	+4,5	+2,6
POLAND	854,3	906,8	956,2	11,7	12,8	+6,1	+5,4
CZECH REP.	241,8	249,2	237,4	3,2	3,2	+3,1	-4,8
UE-27	7.496,4	7.758,1	7.458,5		-	+3,9	-3,9

2012 – number of hatching eggs in Poland was 989,7 mln which was 2,6% higher than in the same period in 2011

2013 – 1099,4 mln

2014 - 1157,7 mln

Ministry of Agriculture 2012

Production of commercial broilers

COUNTRY	HATCHING OF COMMERCIAL BROILERS (mln)			% IN OVERAL EU PRODUCTION		ANNUAL CHANGE	
	2009	2010	2011	2010	2011	2010	2011
G B	843,8	903,6	896,6	15,1	15,4	+7,1	-0,8
FRANCE	816,5	778,3	848,9	13,0	14,6	+4,7	+9,1
POLAND	662,1	711,7	746,4	11,9	12,8	+7,5	+4,9
CZECH RE.	191,1	196,4	184,4	3,3	3,2	+2,6	-6,1
UE - 27	5.738,1	5.991,8	5.828,0		-	+4,4	-2,7

JAN-JUN 2015 – the number of hatched commercial broilers 502 mln, that is 5,1% increase in relation to the same period in 2013.

2013 – 871,5

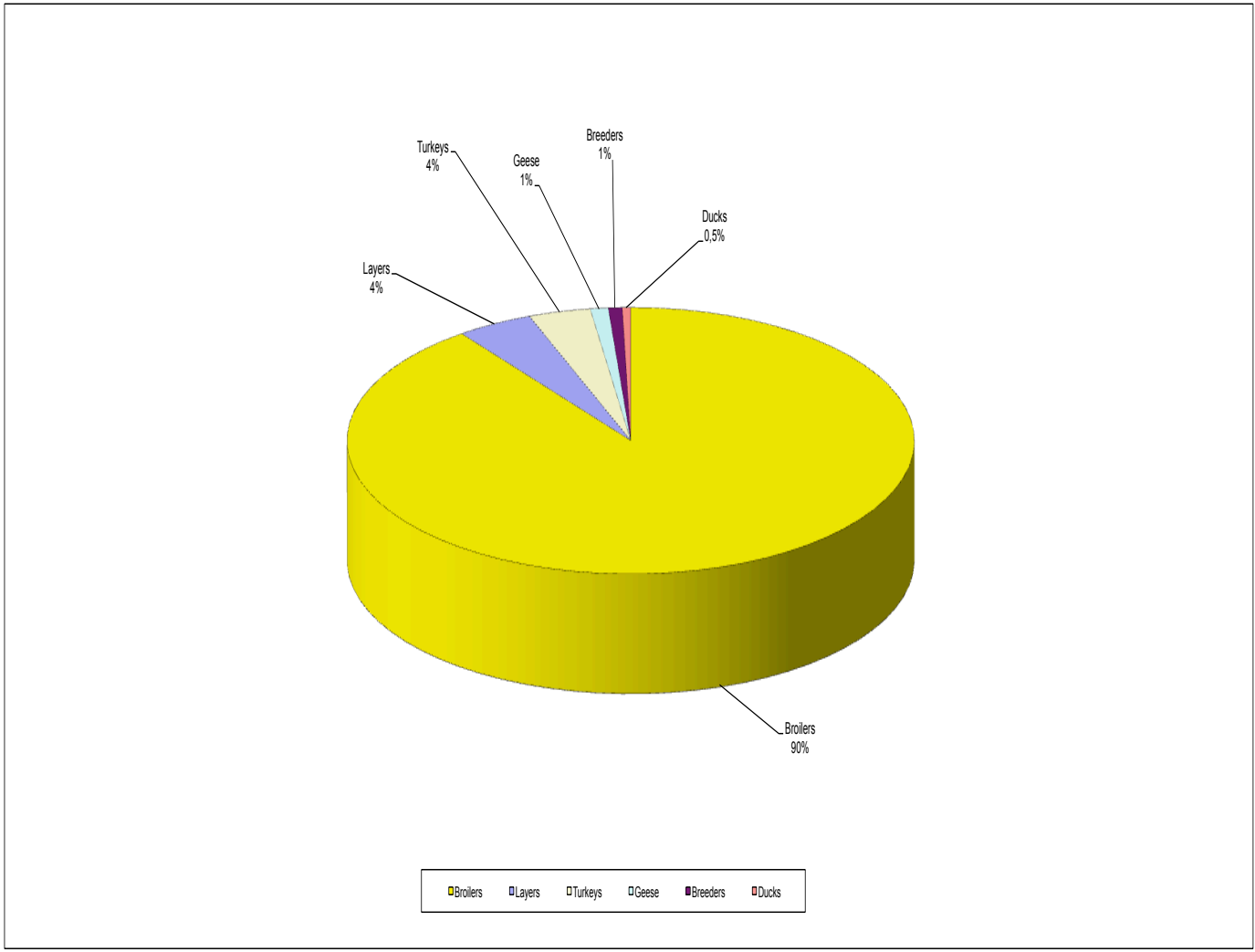
2014 --- 926,9 mln

EU – 6.256,2

Ministry of Agriculture 2012

Poultry market in Poland 2014

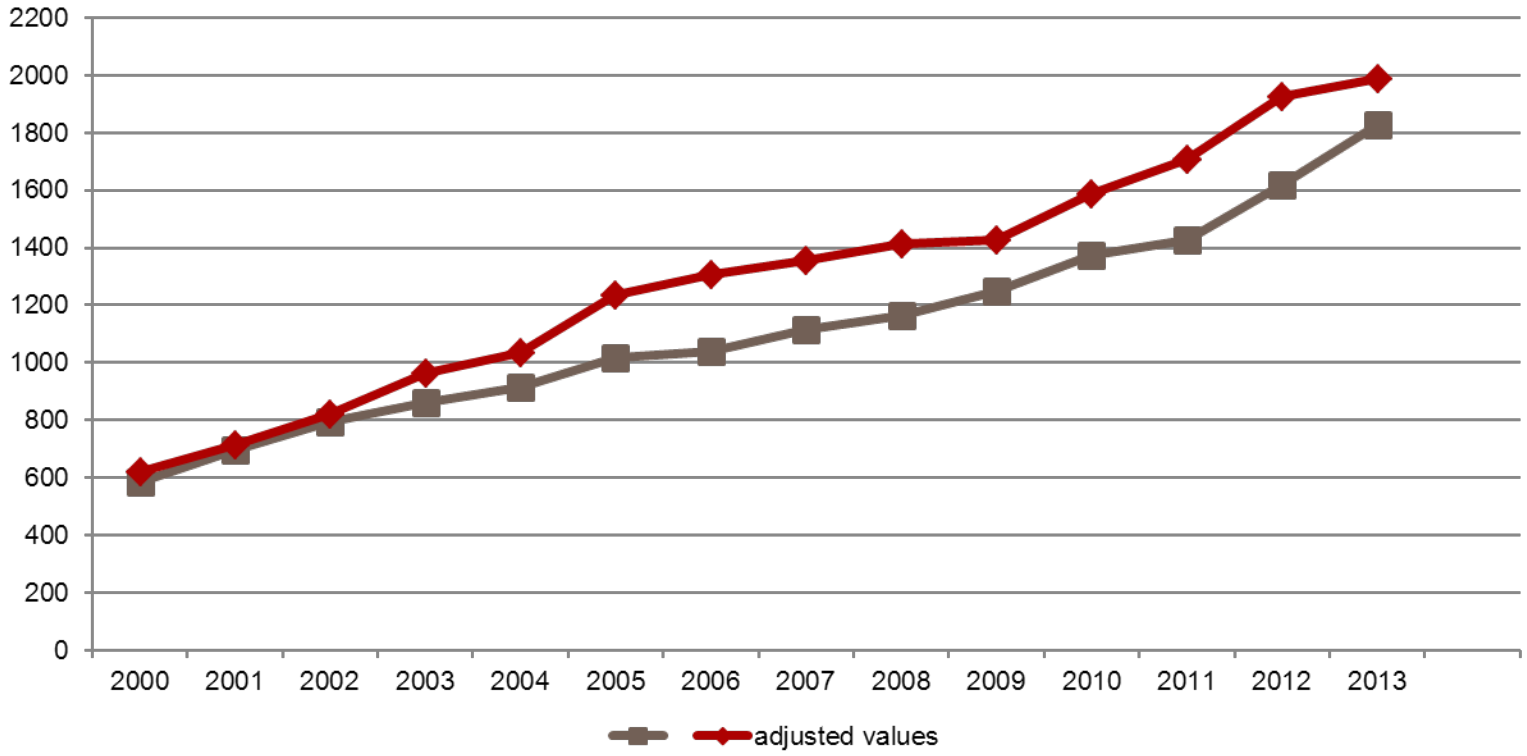
Broilers	840 000 000
Layers	32 000 000
Turkeys	35 000 000
Geese	7 500 000
Breeders	8 900 000
Ducks	4 800 000
TOTAL	928 200 000



Eurostat data

POULTRY MEAT PRODUCTION, THS TONS

(INSTITUTE OF AGRICULTURAL AND FOOD ECONOMICS-NATIONAL RESEARCH INSTITUTE)



GROWTH DYNAMICS 2005-2013 (2005=100%)

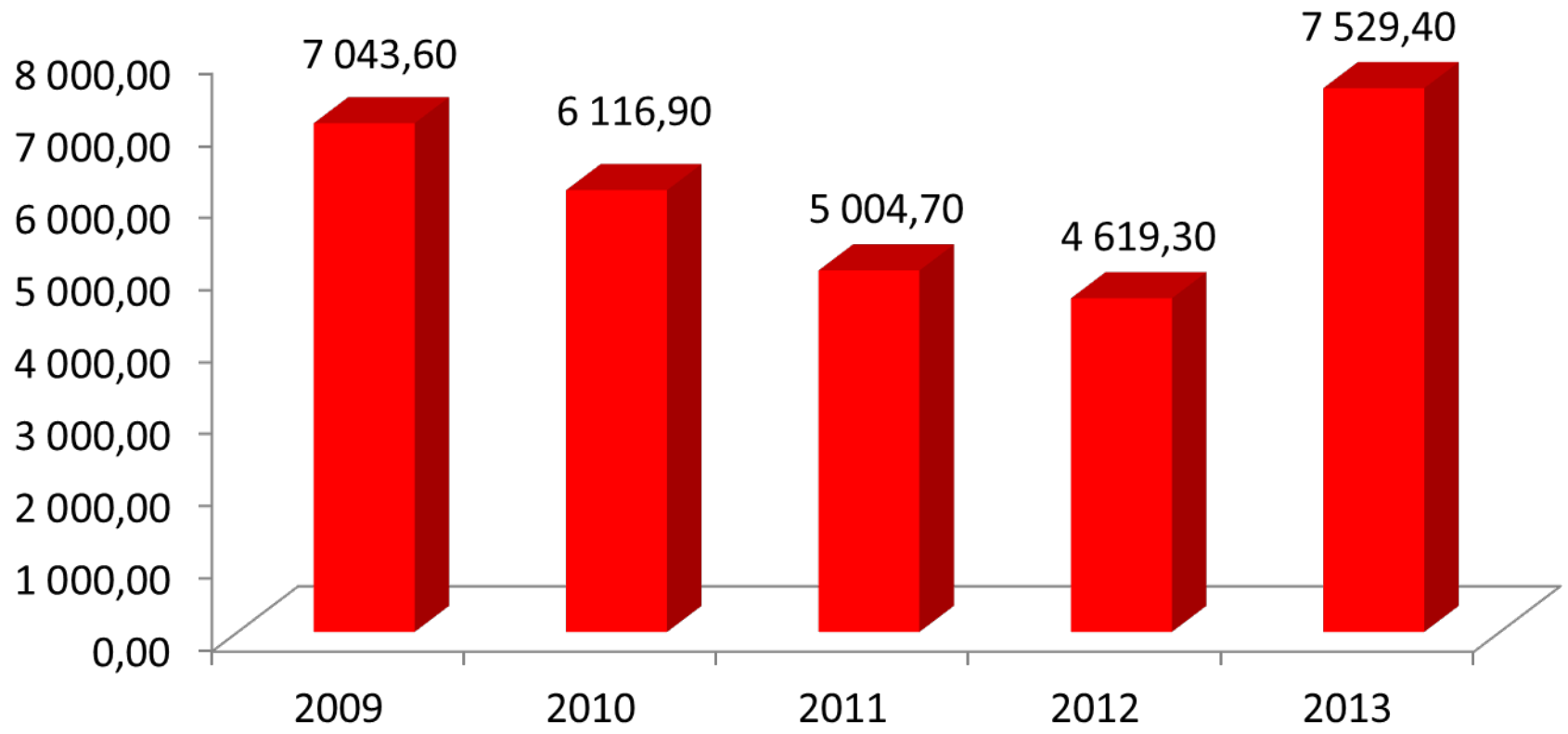
Number of birds slaughtered	
broiler chickens	155
turkeys	114
ducks	309
geese	115
Poultry meat production	180
Increase in the body weight of slaughtered birds	

AVERAGE BODY WEIGHT AT SLAUGHTER (2013)

Broiler chickens $\frac{1940000}{760833} \approx 2.55$ kg

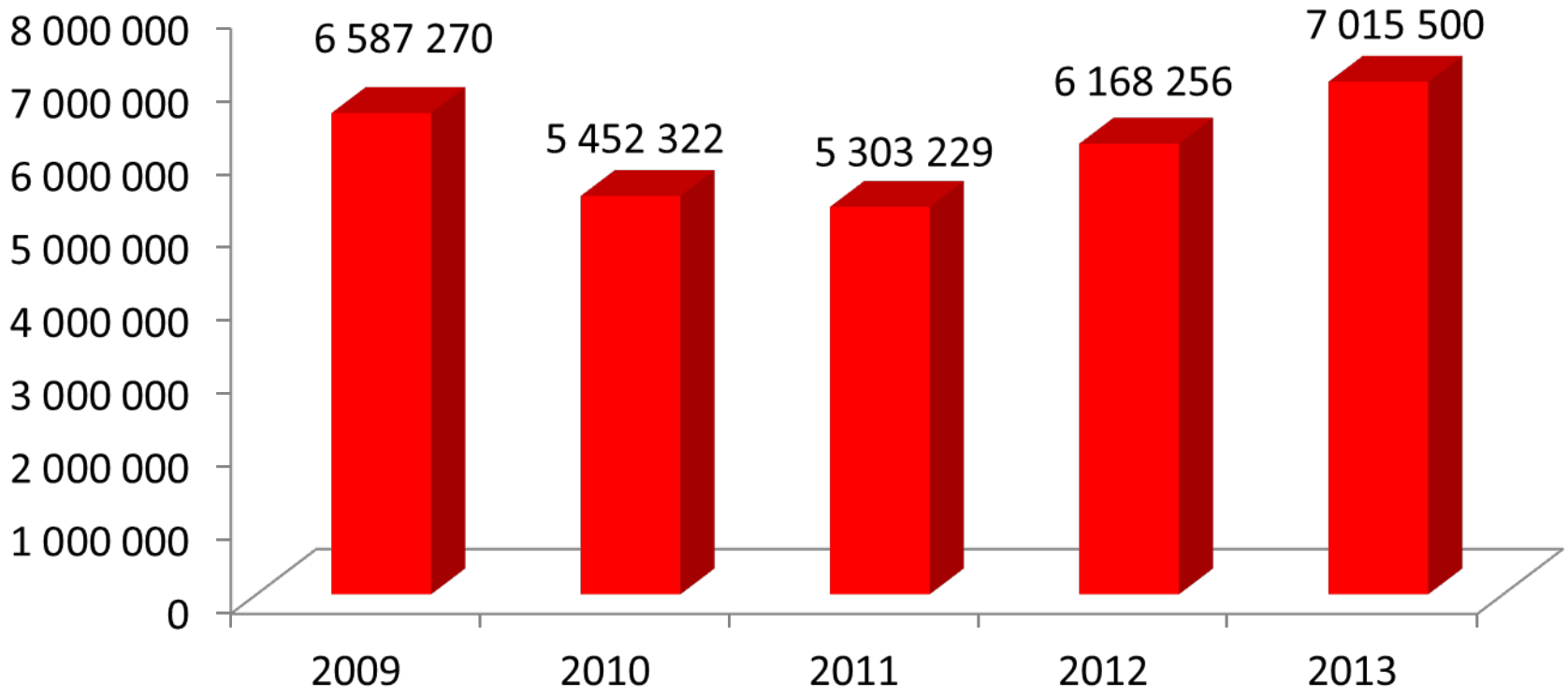
Turkeys $\frac{350\,000}{27287} \approx 12.835$ kg !?

NUMBER OF GOSLINGS HATCHED (THS BIRDS)



EUROSTAT, General Veterinary Inspectorate, Central Statistical Office, National Poultry Council – Chamber of Commerce; based on Adamski, 2014

NUMBER OF GEESE SLAUGHTERED (BIRDS)



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THE ROLE OF MICROBIOLOGICAL LABORATORY AND THE EFFICIENCY OF CHEMOTHERAPHY

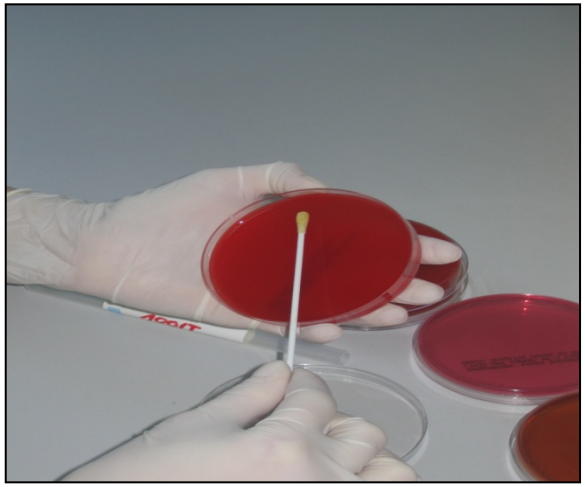
LABORATORIUM MIKROBIOLOGICZNE

One of the most important steps in routine microbiological diagnosis of microbial infection is to assess the susceptibility of the bacteria to a particular medicine.

METHODS OF ASSESSING SENSITIVITY

- IMMUNODIFUSION METHOD
- MIC METHOD – (Minimal Inhibitory Concentration)

IMMUNODIFUSSION METHOD



- The standarized suspension of the bacteria is transferred to the surface of the media.
- Antibiotic diagnostic discs are applied to the surface of the media
- The diameter of lack of growth is measured.

RESULT INTERPRETATION

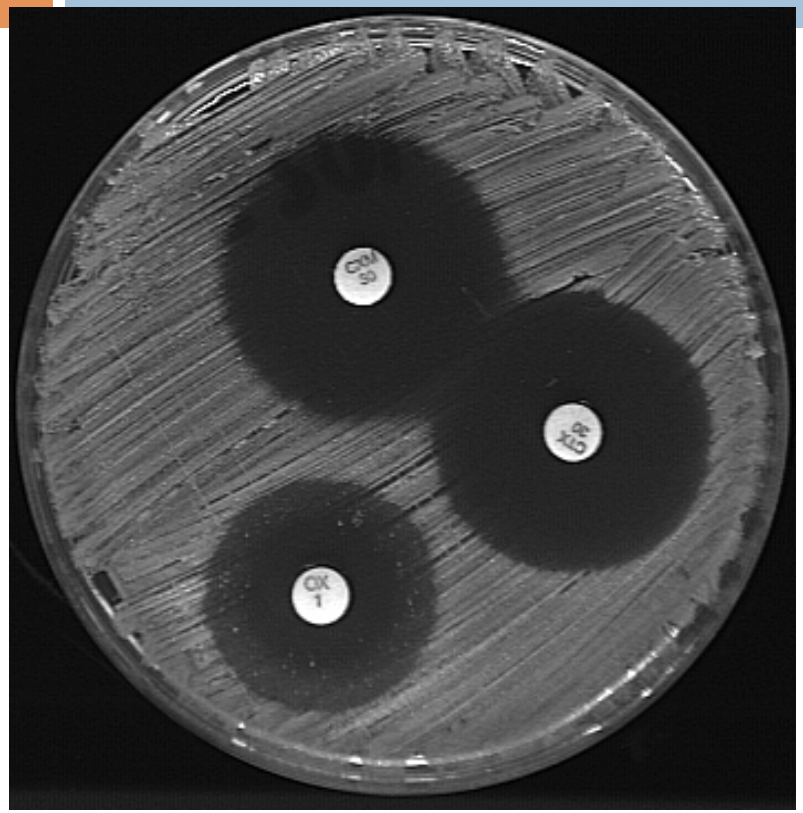
Basing on the measured zone of inhibited growth the microorganism is classified as:

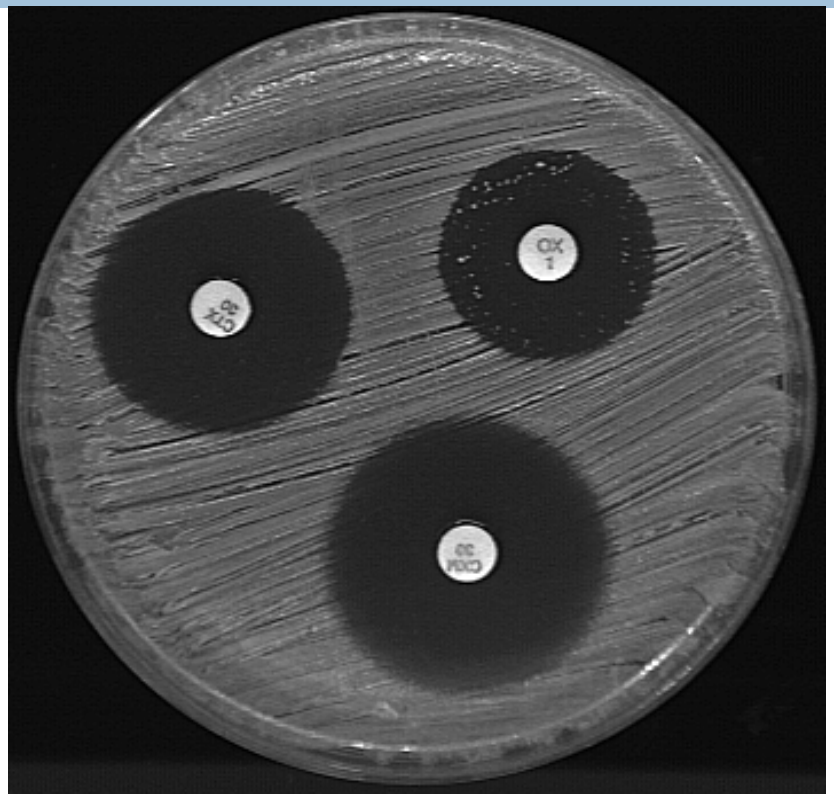
- Susceptible (+++)
- Intermediate (++)
- Resistant (-)

Bacteria	Antibiotic	Growth inhibition zone [mm]		
		R	I	S
E. coli	Gentamicin	≤12	13-14	≥15
S. aureus	Penicillin G	≤28	-	≥29

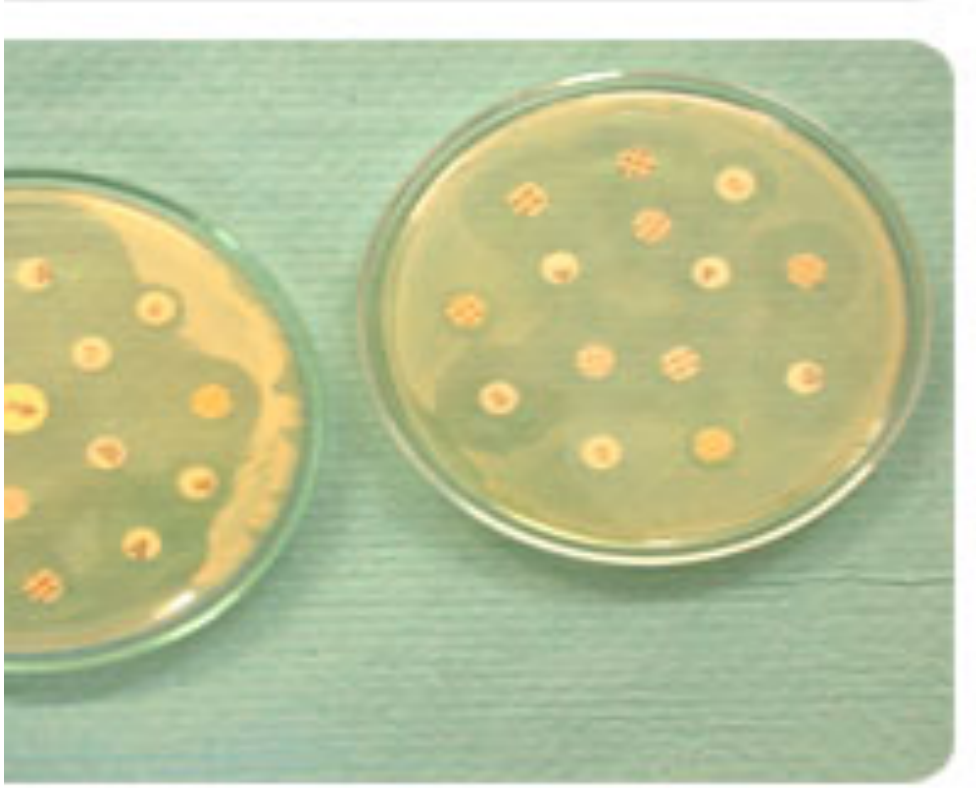
Method developed in the 60s

RESISTANT OR SUSCEPTIBLE?



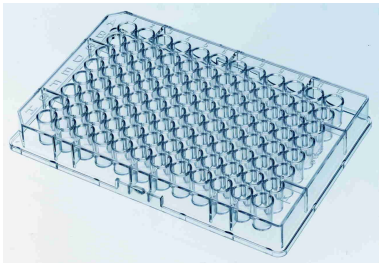


RESISTANT OR SUSCEPTIBLE?



Micronaut
System for evaluation of bacterial susceptibility

Microplate with antibiotic suspension

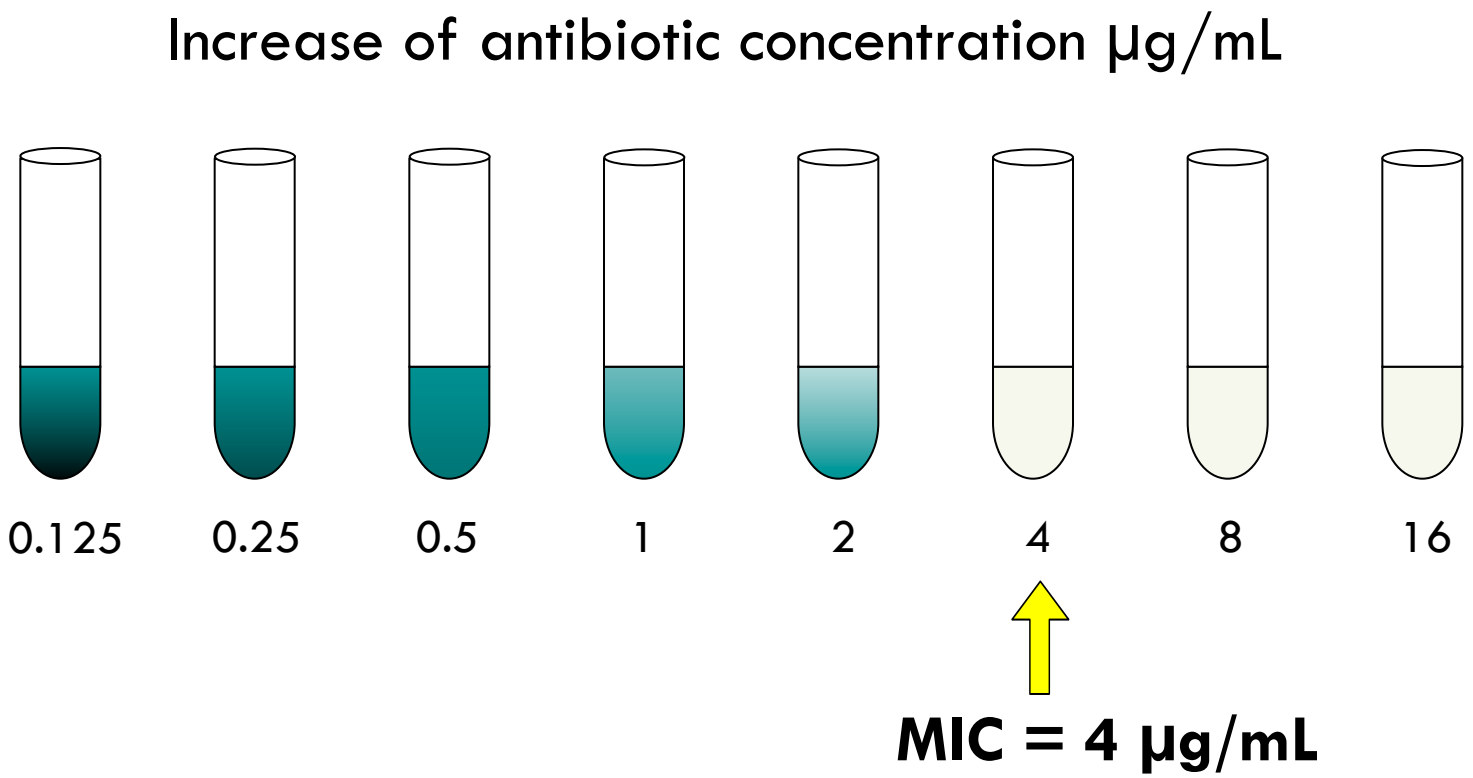


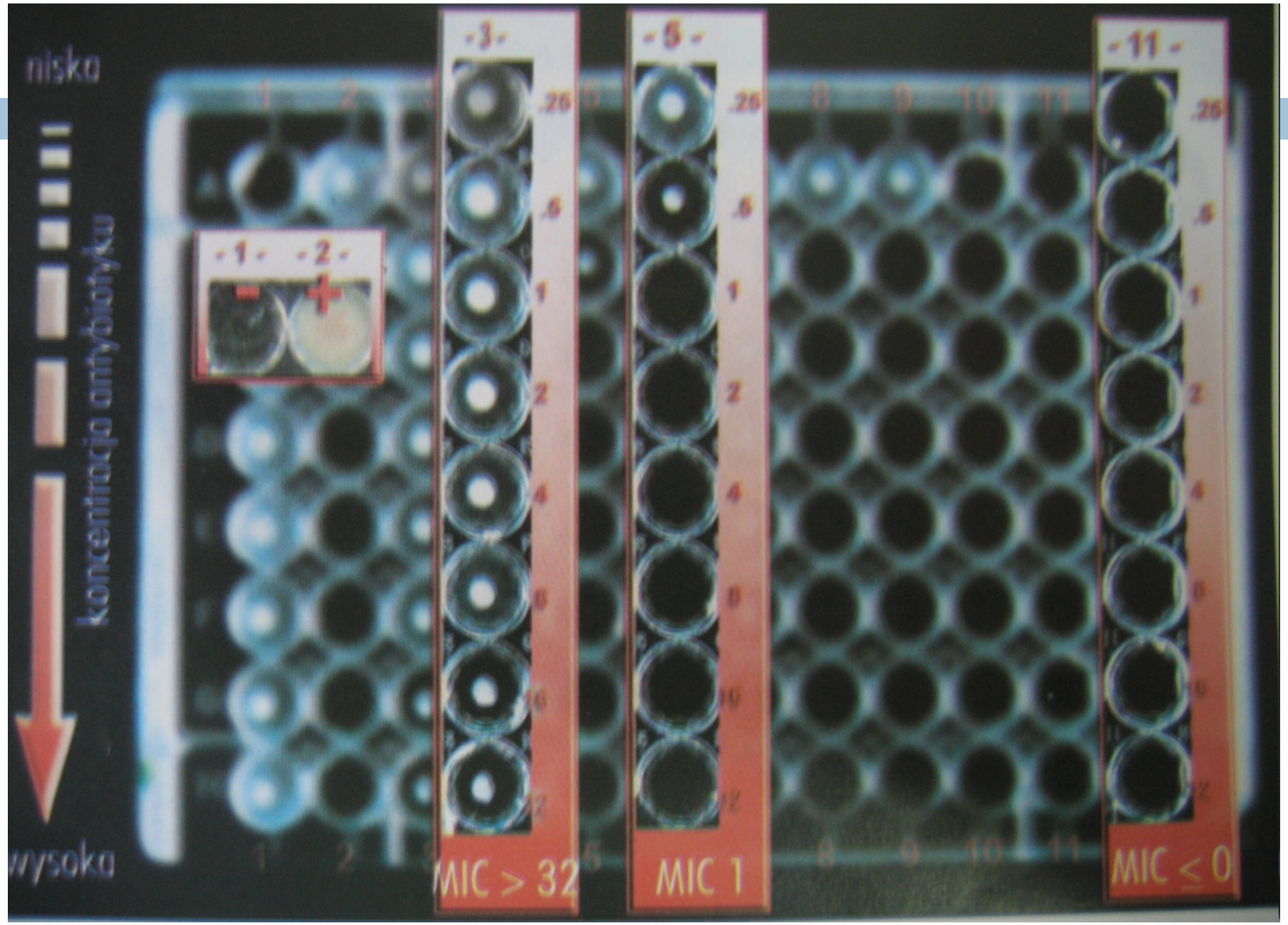
Preparing the Microbial suspension And plate inoculation

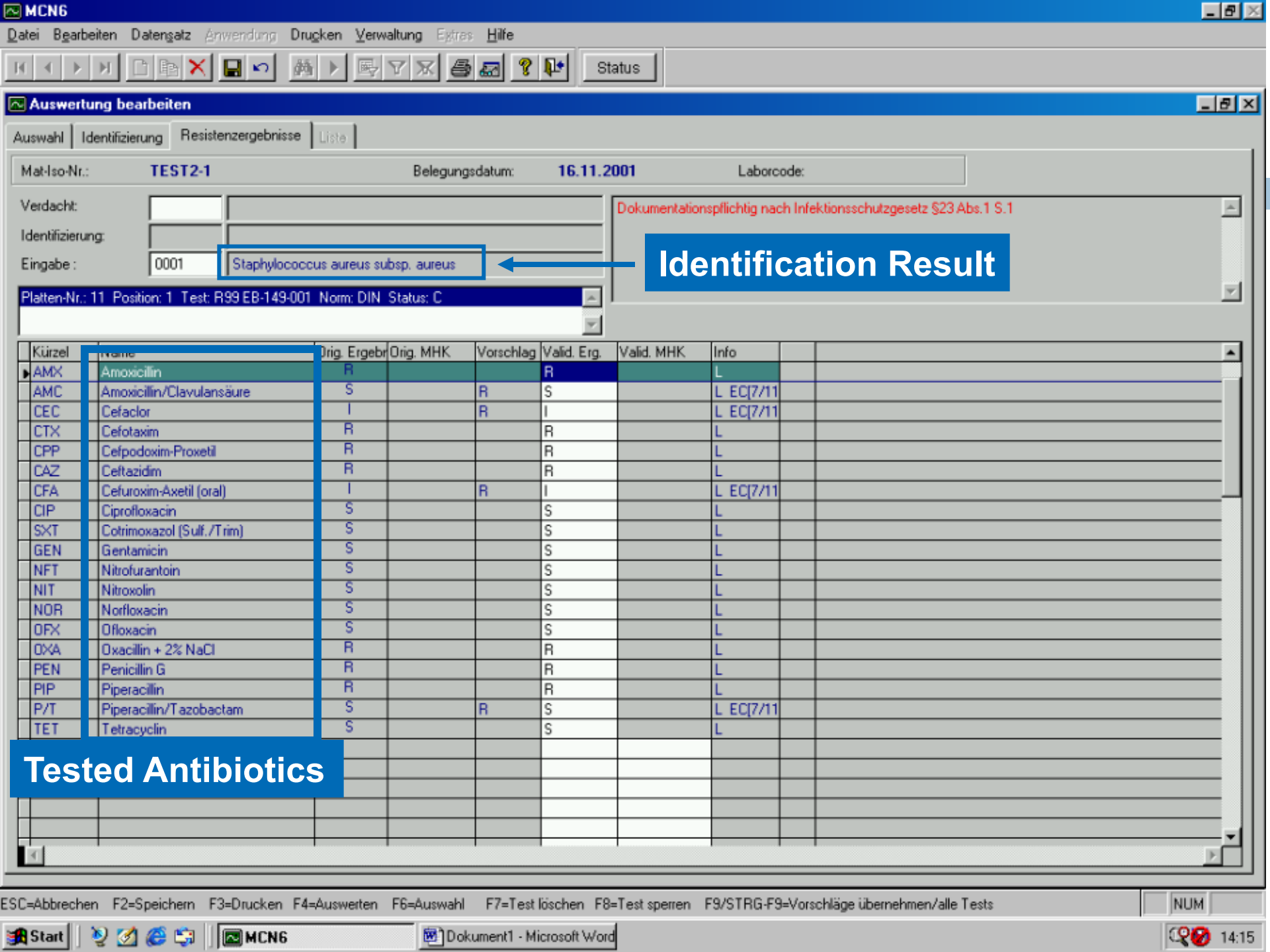
Photometric reading

Results displayed by computer system

MIC = Minimum Inhibitory Concentration




niska
koncentracja antybiotyku
wysoka
-1-
-2-
-3-
-5-
-11-
MIC > 32
MIC 1
MIC ≤ 0


MCN6
Datei Bearbeiten Datensatz Anwendung Drucken Verwaltung Extras Hilfe
Status
Auswertung bearbeiten
Auswahl Identifizierung Resistenzergebnisse Liste
Mat-Iso-Nr.: TEST2-1 Belegungsdatum: 16.11.2001 Laborcode:
Verdacht:
Identifizierung:
Eingabe : 0001 Staphylococcus aureus subsp. aureus
Dokumentationspflichtig nach Infektionsschutzgesetz §23 Abs.1 S.1
Identification Result
Platten-Nr.: 11 Position: 1 Test: R99 EB-149-001 Norm: DIN Status: C
Kürzel Name Orig. Ergebr Orig. MHK Vorschlag Valid. Erg. Valid. MHK Info
AMX Amoxicillin R R L
AMC Amoxicillin/Clavulansäure S R S L EC[7/11
CEC Cefaclor I R I L EC[7/11
CTX Cefotaxim R R L
CPP Cefpodoxim-Proxetil R R L
CAZ Ceftazidim R R L
CFA Cefuroxim-Axetil (oral) I R I L EC[7/11
CIP Ciprofloxacin S S L
SXT Cotrimoxazol (Sulf./Trim) S S L
GEN Gentamicin S S L
NFT Nitrofurantoin S S L
NIT Nitroxolin S S L
NOR Norfloxacin S S L
OFX Ofloxacin S S L
OXA Oxacillin + 2% NaCl R R L
PEN Penicillin G R R L
PIP Piperacillin R R L
P/T Piperacillin/Tazobactam S R S L EC[7/11
TET Tetracyclin S S L
Tested Antibiotics
ESC=Abbrechen F2=Speichern F3=Drucken F4=Auswerten F6=Auswahl F7=Test löschen F8=Test sperren F9/STRG-F9=Vorschläge übernehmen/alle Tests
NUM
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MCN6
Dokument1 - Microsoft Word
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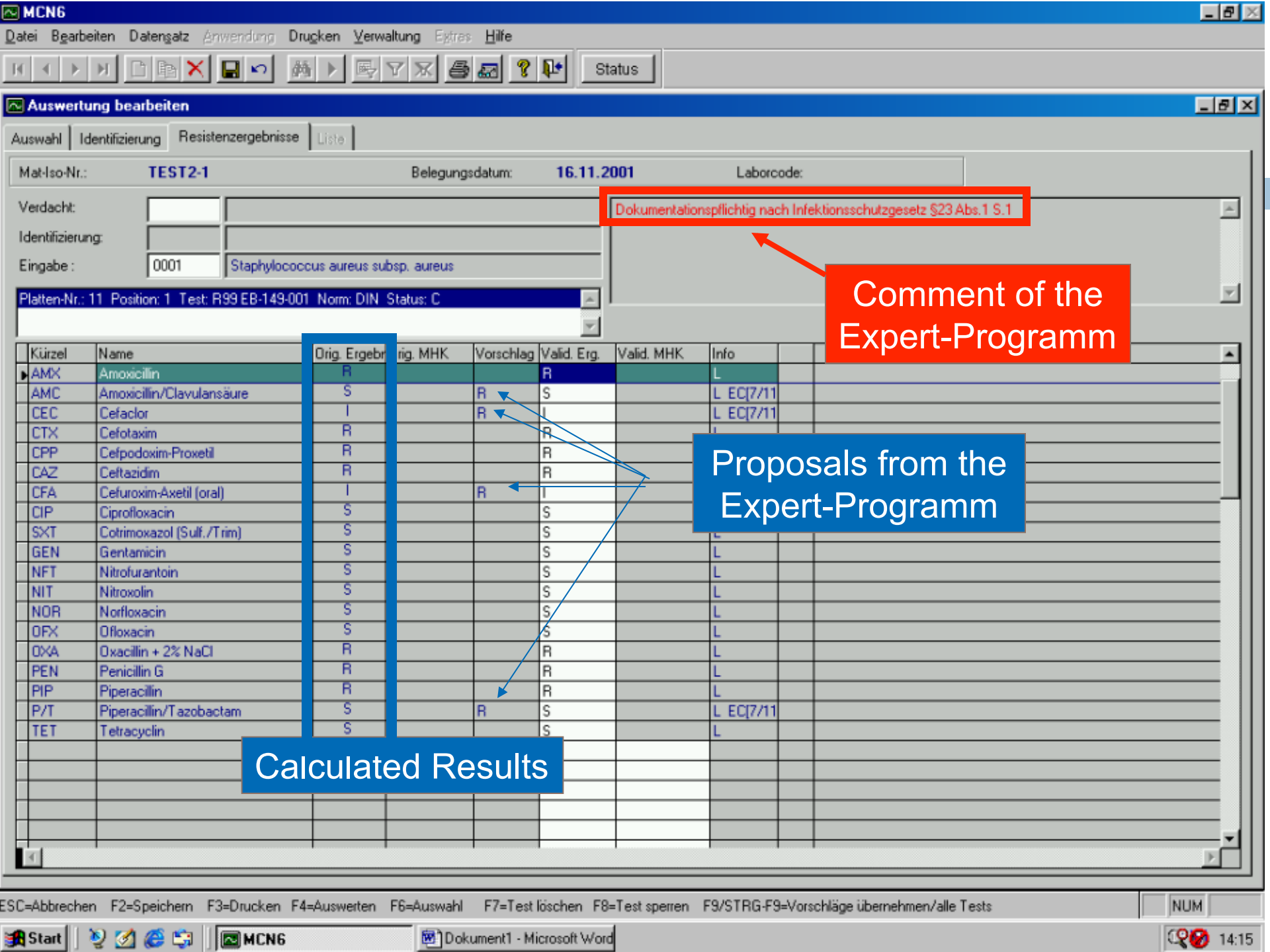
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Comment of the Expert-Programm
Proposals from the Expert-Programm
Calculated Results
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CFA Cefuroxim-Axetil (oral) I R I
CIP Ciprofloxacin S S
SXT Cotrimoxazol (Sulf./Trim) S S
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NFT Nitrofurantoin S S L
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OFX Ofloxacin S S L
OXA Oxacillin + 2% NaCl R R L
PEN Penicillin G R R L
PIP Piperacillin R R L
P/T Piperacillin/Tazobactam S R S L EC[7/11
TET Tetracyclin S S L
ESC=Abbrechen F2=Speichern F3=Drucken F4=Auswerten F6=Auswahl F7=Test löschen F8=Test sperren F9/STRG-F9=Vorschläge übernehmen/alle Tests
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MCN6
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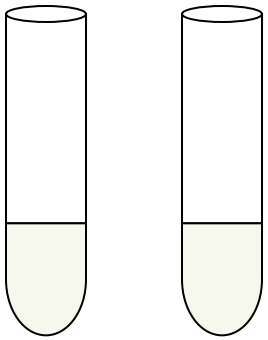
SIR Evaluation

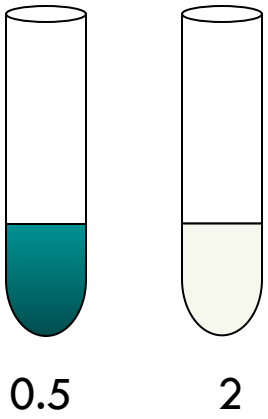
Susceptible (S)



The “susceptible” category implies that an infection due to the strain may be appropriately treated with the dosage of antimicrobial agent recommended for that type of infection and infecting species, unless otherwise contraindicated

NCCLS M7-A6-2005

SIR Evaluation



I = Intermediate

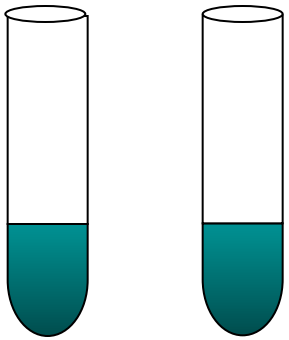
Intermediate (I)

The „intermediate“ category includes isolates with antimicrobial agent MICs that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates.

The „intermediate“ category implies clinical applicability in body sites where the drugs are physiologically concentrated (e.g. quinolones and ß-lactams in urine) or when a high dosage of a drug can be used (e.g. ß-lactams)

SIR Evaluation

Resistant (R)

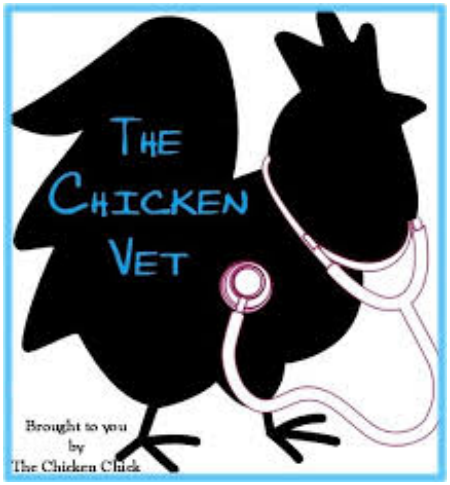


0.5 2

R = Resistant

Resistant strains are not inhibited by the usually achievable systemic concentrations of the agent with normal dosage schedules and/or fall in the range where specific microbial resistance mechanisms are likely (e.g.,ß-lactamases) and clinical efficacy has not been reliable in treatment studies. NCCLS M7-A6-2005

MIC IN SCIENCE



PHARMACOKINETICS (PK)

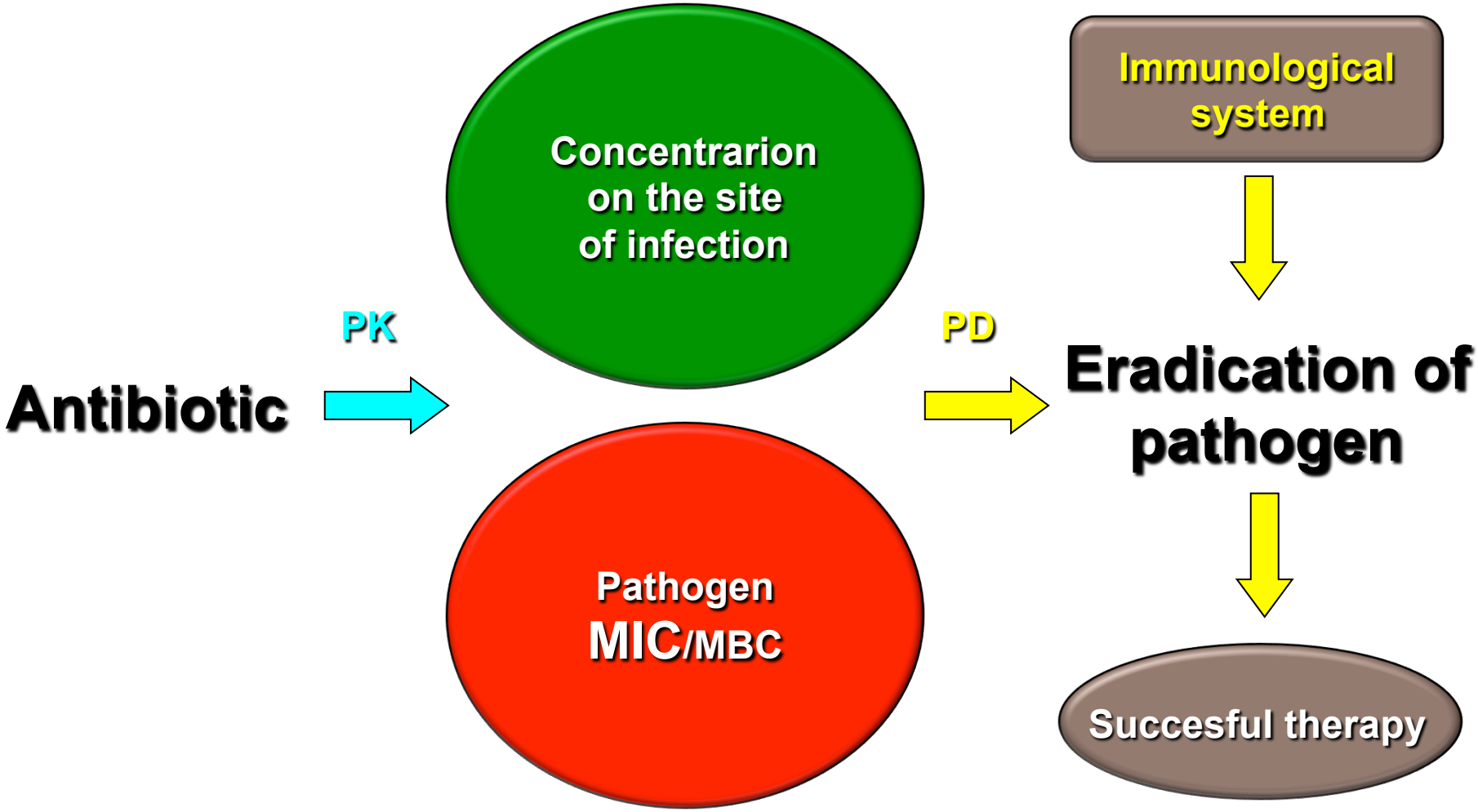
„ something what organism does with the drag”

PHARMACODYNAMICS (PD)

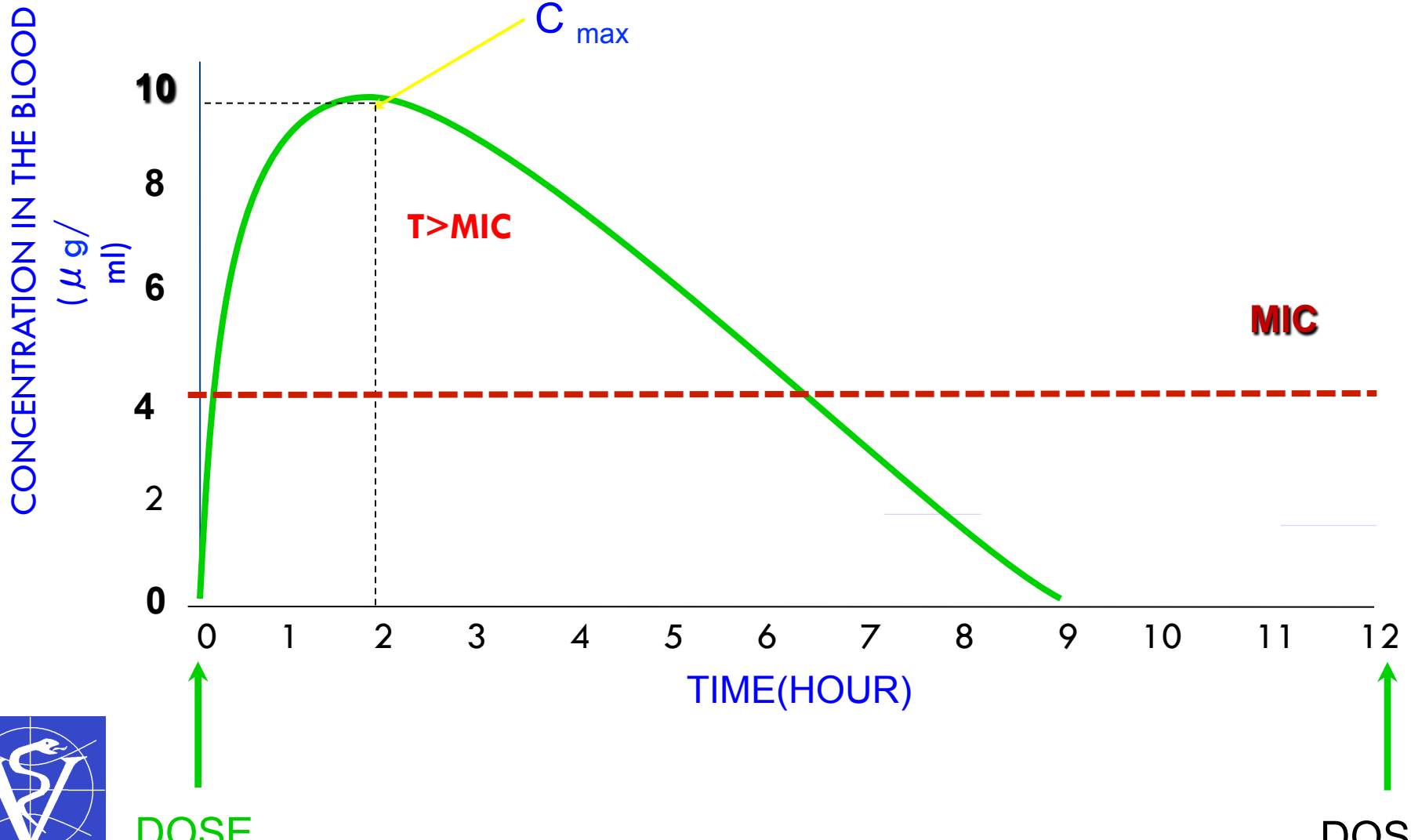
„ how the drag fighting with pathogen ”

Jacobs MR Clin Microbiol Infect 2001; 7: 589-596

Optimal antibiotic therapy



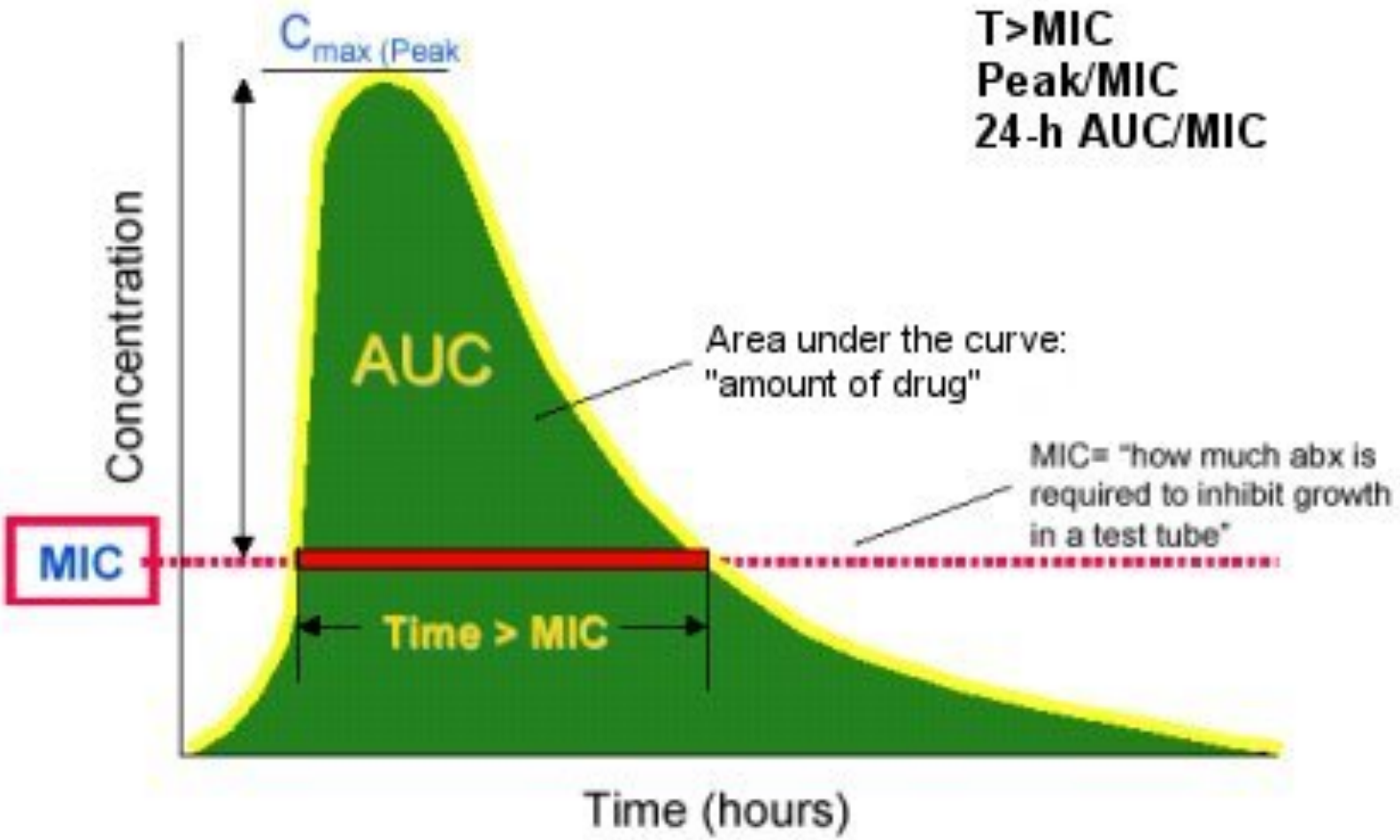
CONCENTRATION IN THE BLOOD



Pharmacokinetic/Pharmacodynamic Predictors of Efficacy

PK/PD parameters

T>MIC
Peak/MIC
24-h AUC/MIC



Pharmacodynamic abilities of different groups of antibiotics

Antibiotic	PD profile	Optimal PD parameter	Goal of treatment
Aminoglycoside Fluoroquinolone Metronidazole	Concentration dependant	C_{max}/MIC	high concentration Cmax/MIC > 8
β-lactamase Macrolides TMP/SMX	Time dependant	T > MIC	Time of exposure T > MIC = 100% (at least 60%)

Clin Pharmacokinet 2006; 45 (8)

Presentation of major groups of antimicrobials for oral use

Drug class	Pharmacokinetic Parameter	Optimal Dosing Regimen
Beta-lactams	Time above MIC	Serum concentration continuously above MIC
Aminoglycosides	Peak concentration	Peak serum > 8-10 times MIC
Fluoroquinolones	AUC; peak concentration	Peak serum > 10-12 times MIC or 24-hour AUC/MIC > 125
Pleuromutilins	Peak concentration and time above MIC, MBC	High tissue/serum concentration; > MIC through dosing interval
Macrolides Lincosamides	Time above MIC, MBC	High serum concentration; > MIC through dosing interval
Tetracyclines	Time above MIC	High serum concentration; MIC through dosing interval

Antimicrobial drugs

BACTERIOSTATIC:

- TETRACYCLINS
- **MACROLIDES**
- LINCOSAMIDES
- CHLORAPHENICOL ANALOGUES
- SULFONAMIDES
- TRIMETHOPRIM

BACTERICIDAL:

- β-LACTAMASE
- AMINOGLICOSIDES
- QUINOLONES
- POLIMYXINS

}

- METHOXASOL, TRIMSULFASOL
- NITROIMIDAZOLE DERIVATIVES

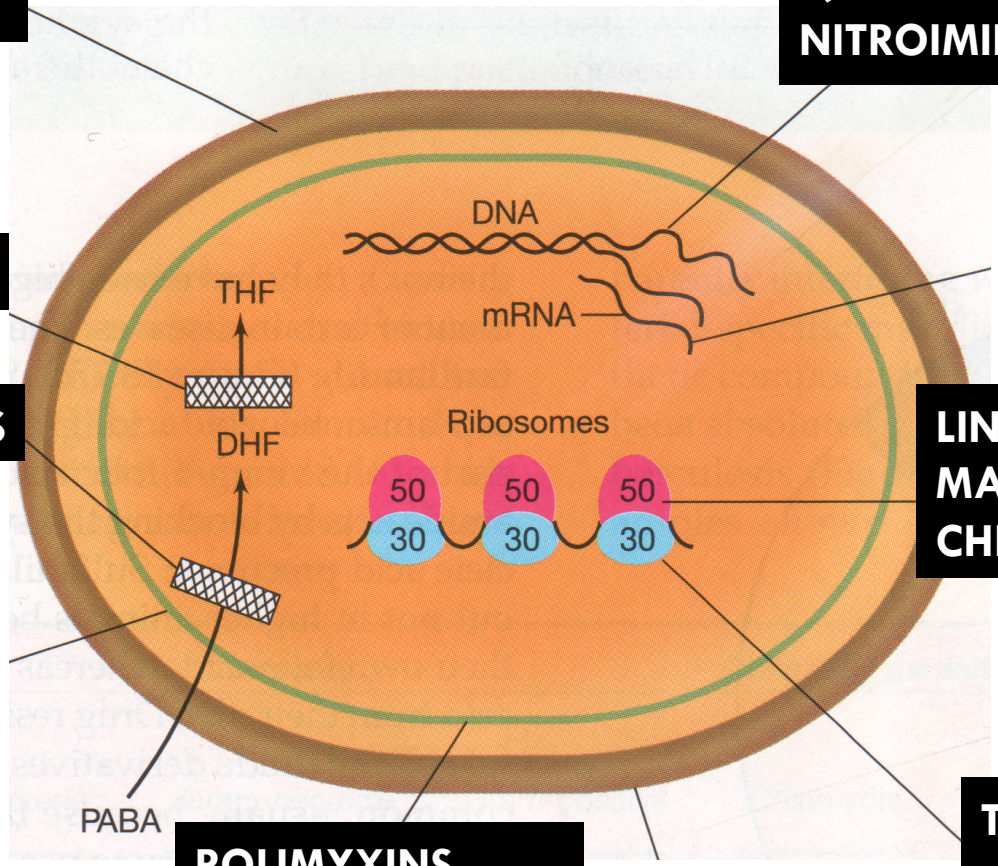
Different mechanisms of antibiotic activity

BETA-LACTAMASE

QUINOLONES
NITROIMIDAZOLE

TRIMETOPRIM

SULFONAMIDES



LINCOSAMIDES
MACROLIDES
CHLORAPHENICOL

CYTOPLASMIC MEMBRANE

POLIMYXINS

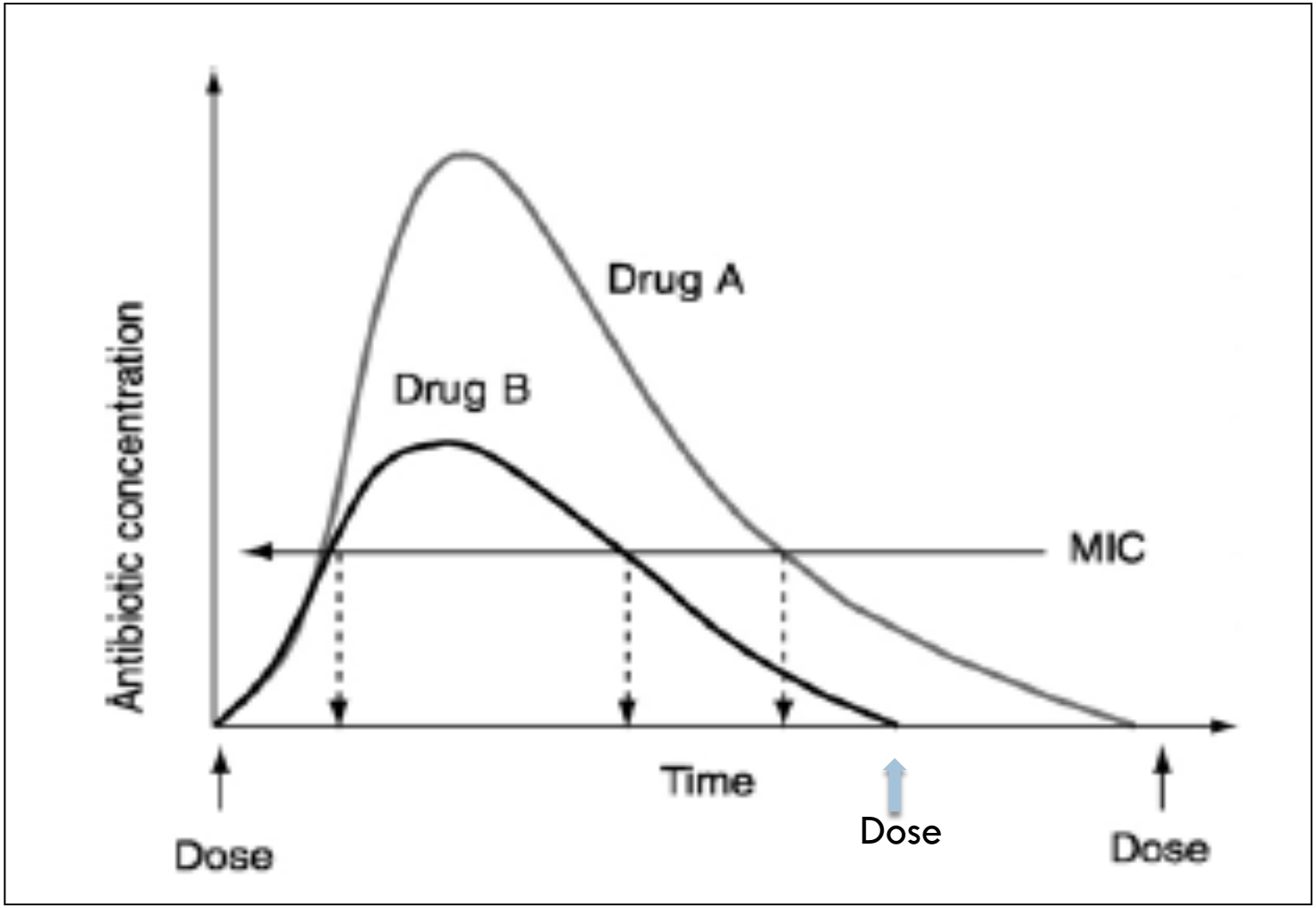
CELL WALL

TETRACYCLINES

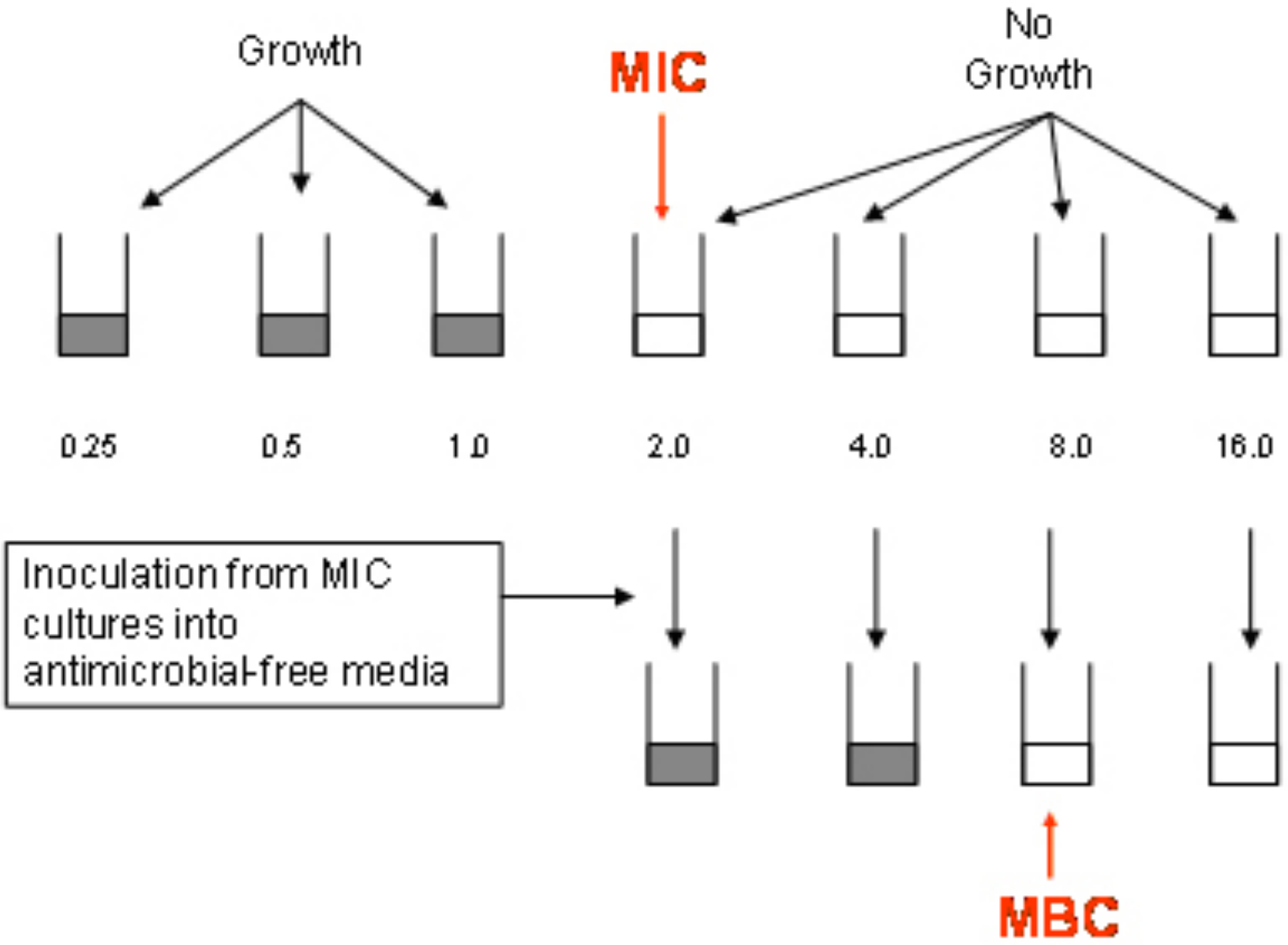
AMINOGLICOSIDES

wg. Brock IX ed.

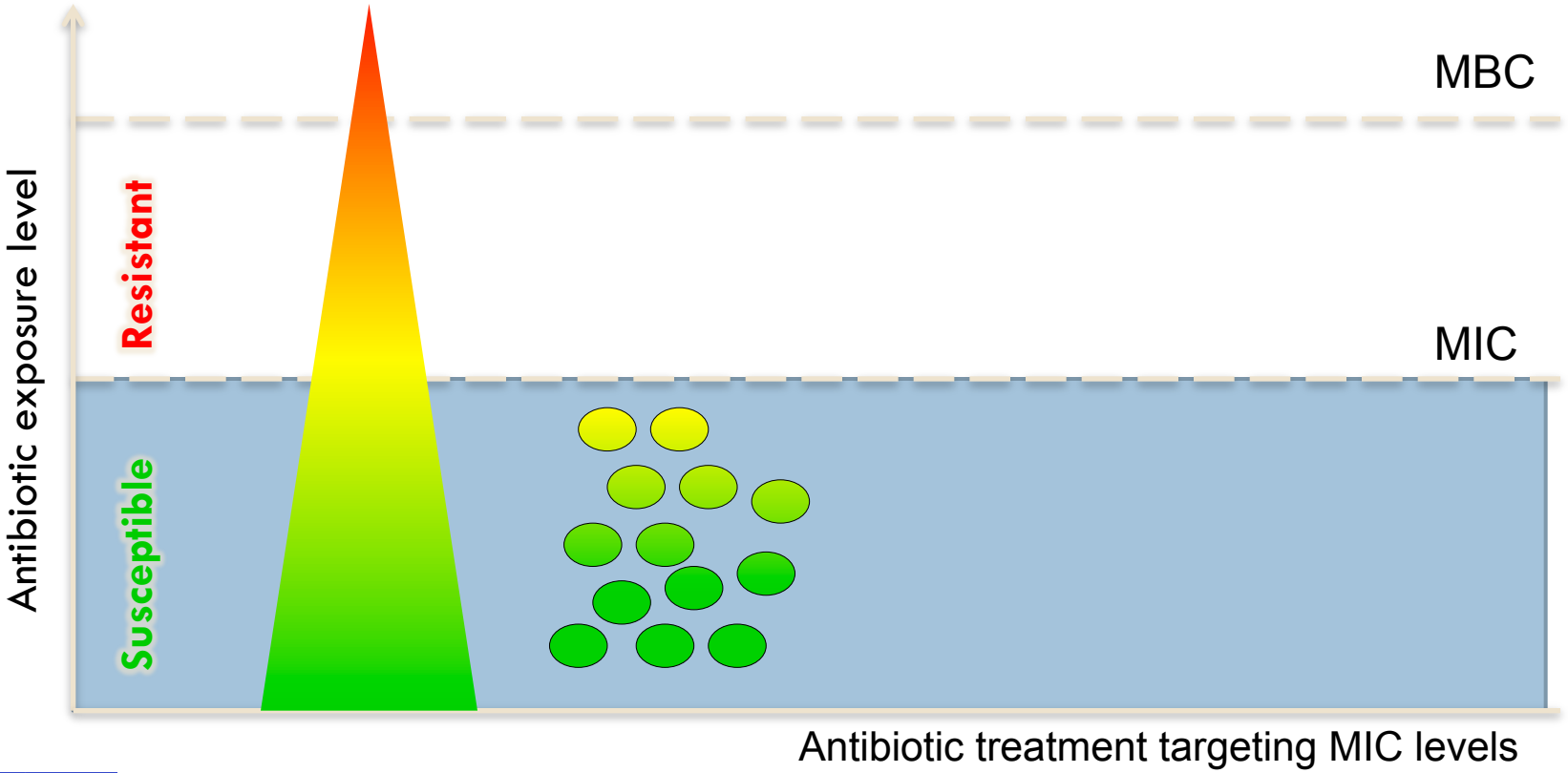
Beta-lactams



Serial Dilution Susceptibility Testing

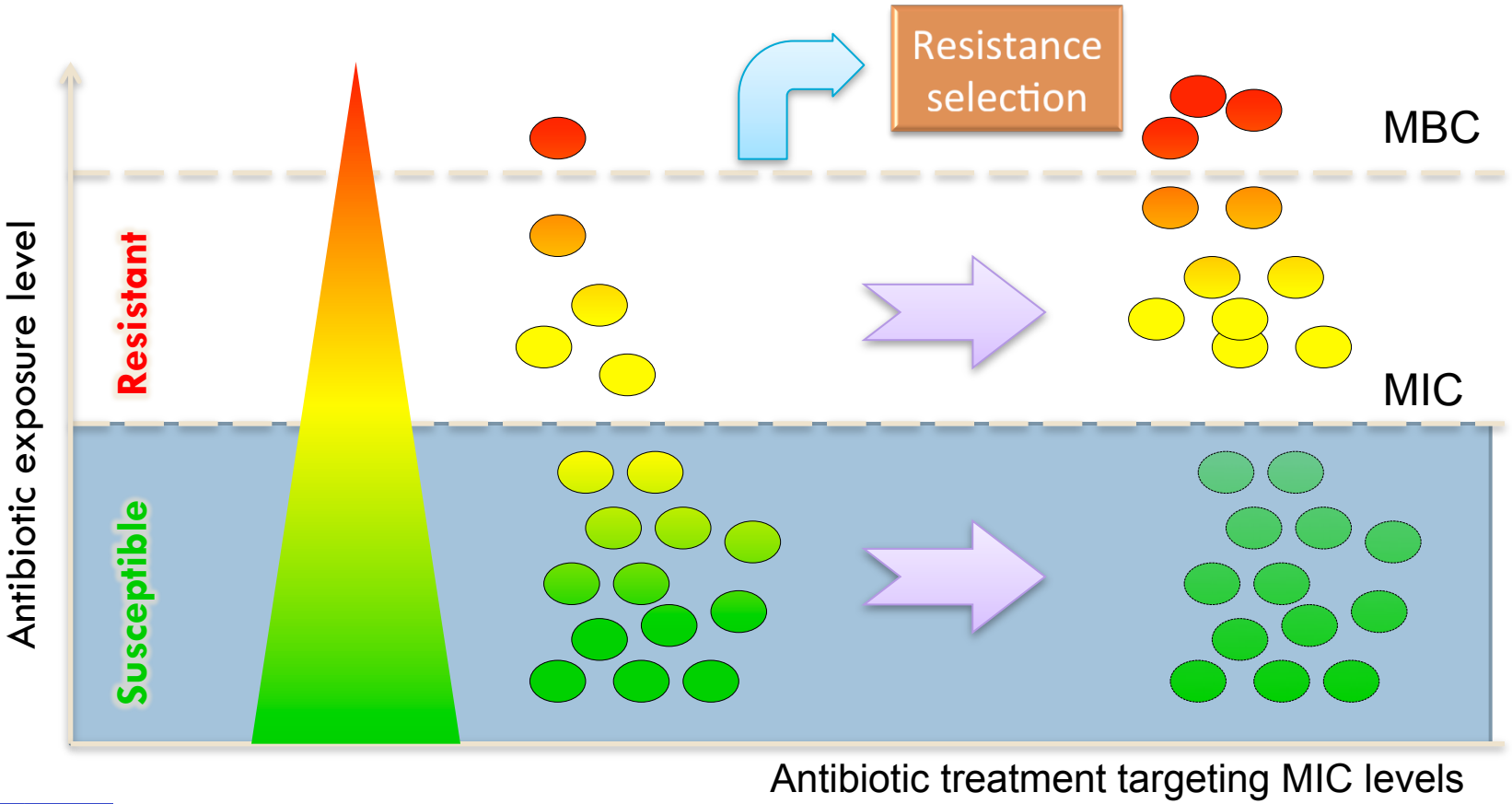


Infection: targeted therapy and eradication of pathogenes by the organism



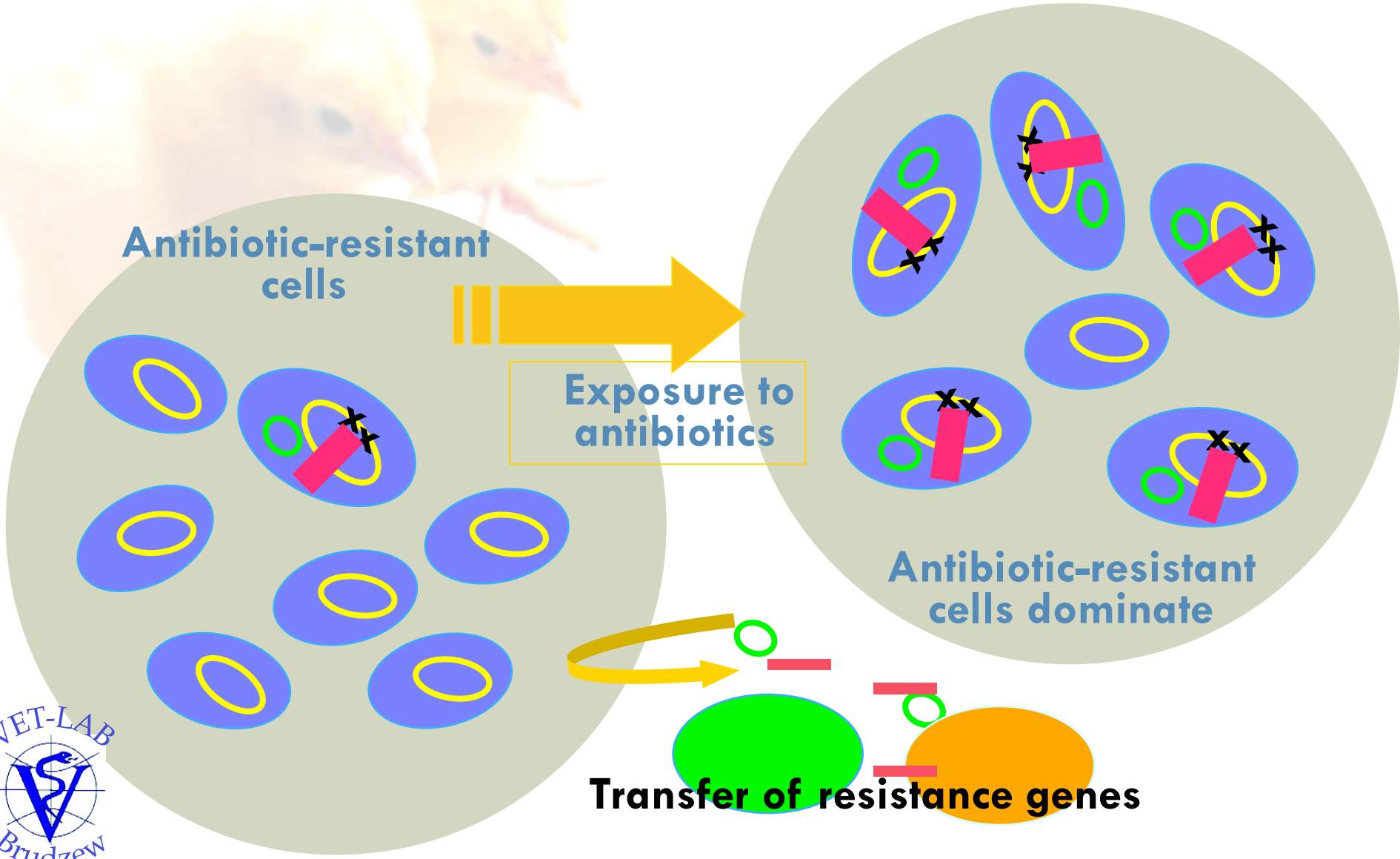
Adapted from Canton & Morosini, 2011 FEMS microbiol reviews

Infection: non-targeted (empirical) treatment – forming drug resistance

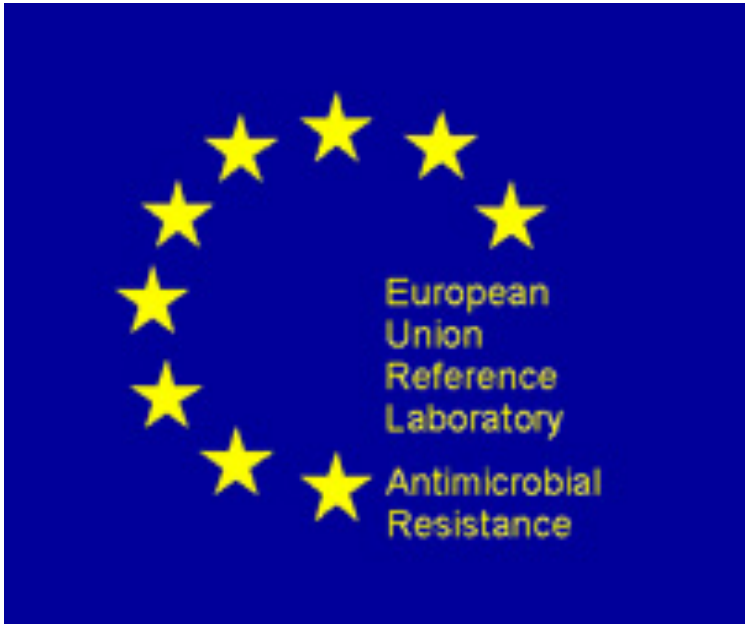


Adapted from Canton & Morosini, 2011 FEMS microbiol reviews

Antibiotics cause drug resistance



MIC – quantitative method



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- WHAT IS MIC
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- CURRENT HEALTH PROBLEMS OF POULTRY IN POLAND

Vet-Lab Brudzew
ul. Turkowska 58 C
62-720 Brudzew
tel./fax. 063 279 70 04

Laboratorium badawcze objęte systemem zarządzania według normy PN-EN ISO/IEC 17025

Próbka #: 331/13

Bieżąca data: 23.01.2013

Nazwa: Tujdowski Marek, Okrężna 1

Imię: Płoty, 66-016 Czerwieńsk

Typ próbki: wymazy z narządów wewnętrznych

Zlecający: lek. wet. Andrzej Janczewski

Identyfikacja: Izol. 6: B596 Enterococcus faecalis

Antybiotyk	Izol. 6 Interpretacja
Amoksycylina/ kwas klawulanowy	S
Amoksycylina	S
Cefquinom	R
Ceftiofur	R
Cefaleksyna	R
Kloksacylina	R
Kolistyna	R
Cephapirin	R
Doksycyklina	R
Enrofloksacyna	S
Erytromycyna	S
Florfenikol	S
Gentamycyna	R
Linkomycyna	R
Linkomycyna/ spektinomycyna	S
Nafcylina	R
Neomycyna	R
Norfloksacyna	I
Oksytetracyklina	R
Penicylina G	R
Streptomycyna	R
Trimetoprim/ sulfametoksazol	R
Tiamulina	R
Tylozyna	R
Tylvalosin	S

Legenda: R=oporny S=wrażliwy I=średniowrażliwy

MIC range (µg/ml) for mycoplasmas and ORT

TYPE	ENRO	ERY	TYLO	TIAM	OTC	TYLV
MG	0.5-32	>32	4- 32	< 0.03-1	0.5-1	0.007-0,2
MS	0.5-16	>32	8-32	<0.03-0.125	0.25-0.5	0.009-0,2
MI	8-32	>32	>32	>32	8-32	-
ORT	1-8	-	0,06-0,5	0,06-0,5	0,12-16	0,03-0,12

HIGH MIC LEVELS FOR ENRO ERY AND TYLO INDICATE GROWING RESISTANCE OF MYCOPLAMSMA TO THESE ANTIBIOTICS

An MIC VALUE OF 2.0 µg/ml AND HIGHER CAN BE CONSIDERED A RESISTANT STRAIN

AGENDA

- POLISH POULTRY MARKET
- WHAT IS MIC
- MIC IN PRACTICE
- RESPONSIBLE USE OF ANTIBIOTICS
- CURRENT HEALTH PROBLEMS OF POULTRY IN POLAND

WHY RESPONSIBLY

- A lot of effort is made to control diseases in broilers with antimicrobials (antibiotics, antivirals, antifungals, antiparasitics)
- However, many antimicrobials are used in vain
  - Due to inappropriate manner of administration
  - Inadequate dosage
  - Inadequate duration of therapy
- Successful treatment depends on whether antibiotics susceptibility and concentrations at the site of infection have been duly considered

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ANTIBIOTICS

- The correct treatment and administration of antibiotics is complicated
- As little as possible -as much as necessary
- For maximum benefit the following conditions must be fulfilled
  - Correct diagnosis based on laboratory tests
  - Correct way of administration
  - Correct dosage and interval between treatments

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Antibiotics cannot serve the purpose of:

- antipyretic drugs – for chickens
- sedatives – for farms owner and vet

Antibiotic therapy

Empirical therapy

Only if a suspicion of infection occurs; the suspicion must be based on a clinical and anatomopathological examination

Targeted therapy

After microbiological lab tests (MIC)

Choosing the right therapy

Targeted therapy is the best!!!

(MIC, antibiotic concentration)

Proper dosage, method of administration and duration of therapy

Fast and intense!!!

FBO….Vet….examination….diagnosis….intervention……..evaluation..

GLOBAL TRENDS IN ANTIBIOTIC THERAPY

- reducing the time of drug administration
- maximising the dosage of drug which ensures safe therapy

Amoxicillin degradation in the water at different pH at 35°C

pH	Half-life of amoxicillin content (hours)
1,1	6
3,8	14
5,5	64
7,1	30

STABILITY OF TETRACYCLINE ANTIBIOTICS IN WATER SOLUTIONS

- Doxycycline forms insoluble complex with iron ions more often than CTC/OTC
- CTC/OTC forms insoluble complex with calcium and magnesium ions more often than doxycycline
- All tetracyclines are sensitive to copper ions and degradation occurs rapidly in water solutions

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Doxycycline degradation in water at different pH at 35°C

pH	Half-life of doxycycline content (days)
1,0	4,5
2,5	5,5
4,6	3
5,5	2
7,0	1
8,5	1,5
10,0	0,5

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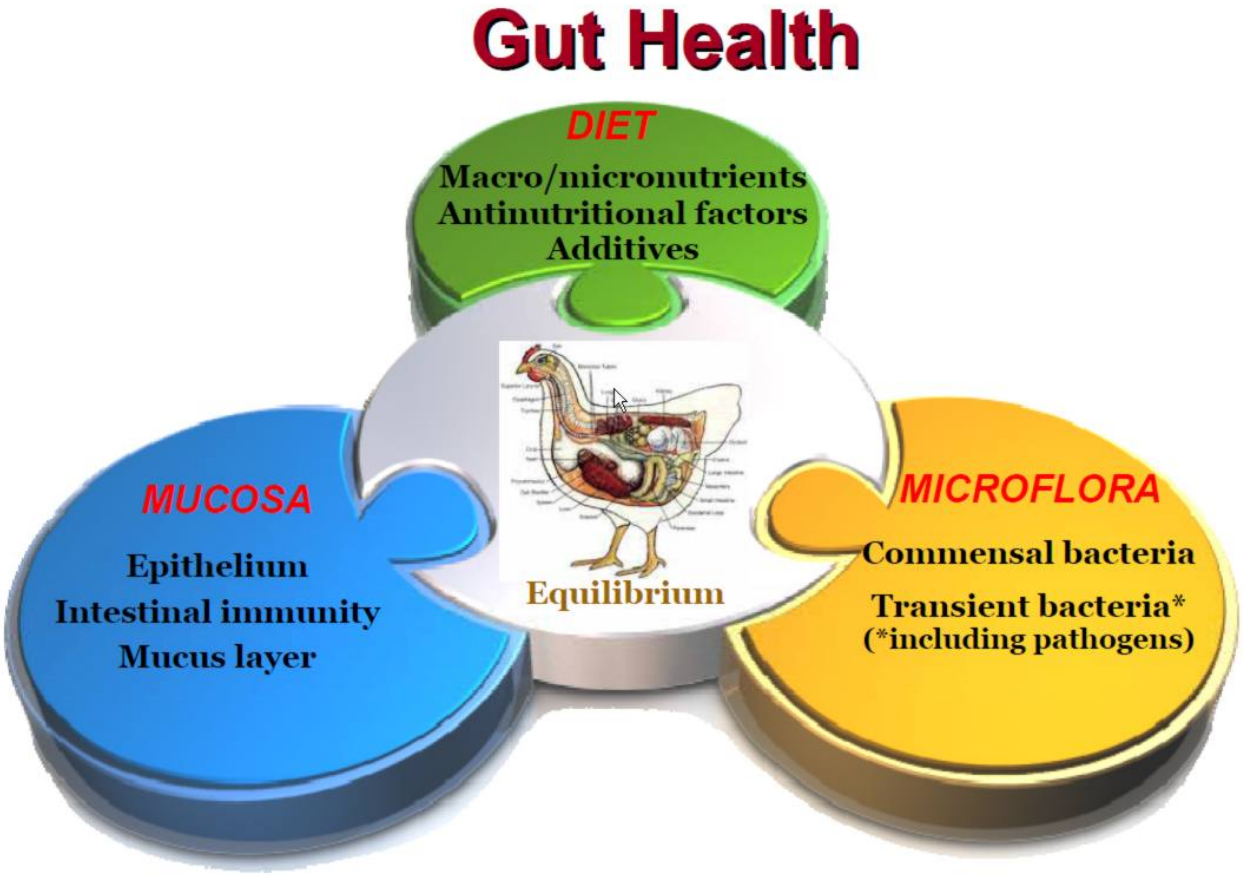
Antibiotics damage intestinal microflora

Functions of intestinal microflora

- Blocking receptors on the surface of epithelial cells
- Competing for nutritional factors with pathogens
- Production of substances stopping the growth of potential pathogens
- Stimulation of immune system

Antibiotics damage intestinal microflora



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RESPONSIBLE USE OF MEDICINES

- RESPONSIBLE USE OF MEDICINES IN AGLICULTURE ALLIANCE - RUMA
- ANTIMICROBIALS GUIDELINES BY RUMA:

RESPONSIBLE USE OF MEDICINES IN AGRICULTURE ALLIANCE

ruma

http://www.ruma.org.uk/antimicrobials.htm

European Antibiotic Awareness Day is marked annually on 18 November.

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Current problems of poultry pathology in Poland

- IB, REO, IBD, APV, FAV,
- COLIBACTERIOSIS, ORT, MS, ENTEROCOCCUS
- NECROTIC ENTERITIS
- COCCYDIOSIS
- FEED INTOXICATIONS-(MYCOTOXINE)

CURRENT TOPICS DISCUSSED AT EUROPEAN FORUMS

- RESPONSIBLE USE OF ANTIBIOTICS
- CASCADE
- MEDICATED FEED
- DECOUPLING

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Commission

CURRENT TOPICS DISCUSSED AT EUROPEAN FORUMS

- VMP
- ZINC-OXIDE
- INTERNET SALES
- HARMONISATION – etc.

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Commission

UEVP

Union européenne
des vétérinaires praticiens

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„NO ACTION TODAY, NO CURE TOMORROW"

POINTING OUT KIND OF PROBLEMS WHICH FVE COULD LOOK INTO

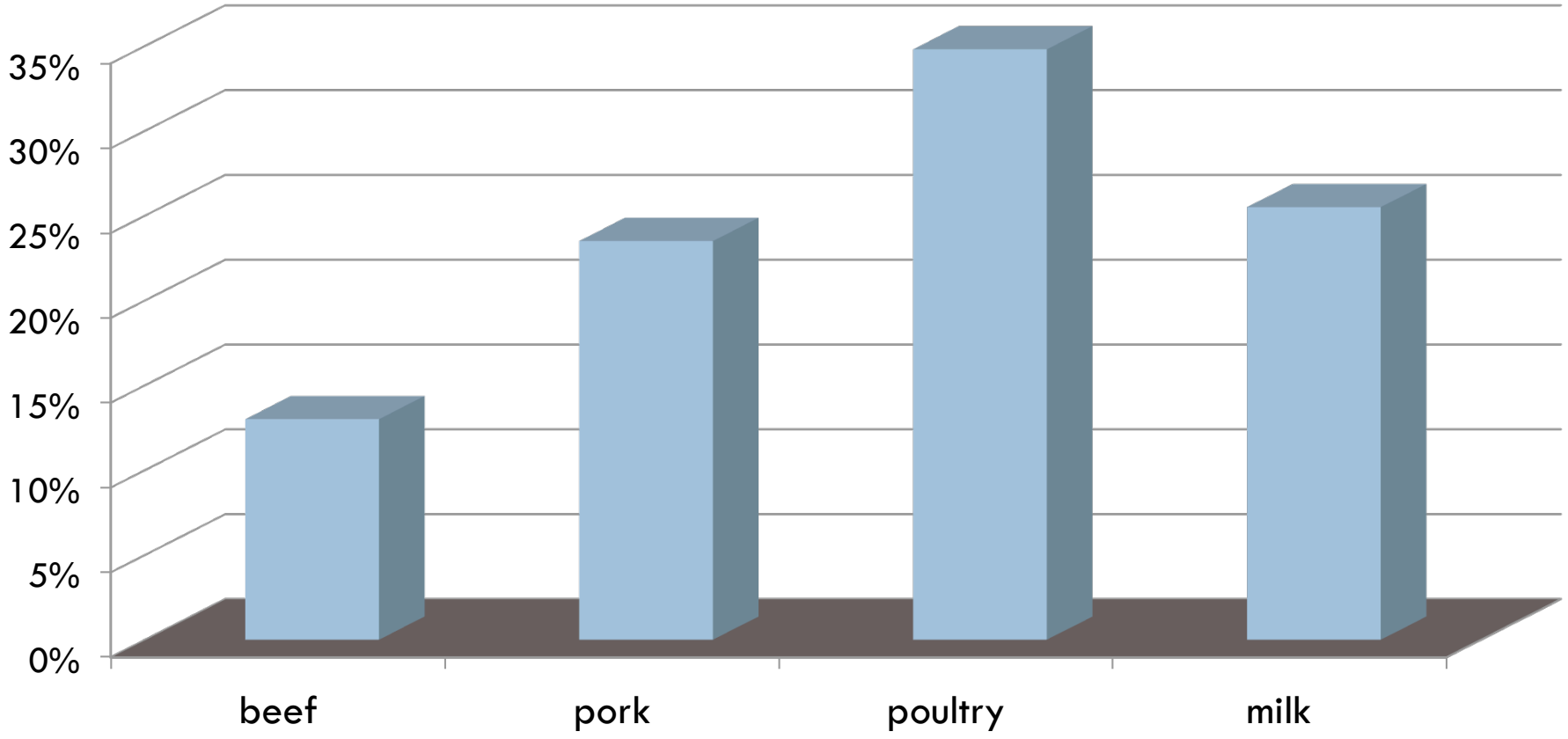
Current problems of veterinary profession in Poland

- DRUG RESISTANCE – MRSA AND ESBLs
- USE OF ANTIBIOTICS;

- HUMAN HEALTH + ANIMAL HEALTH + ENVIRONMENTAL HEALTH = ONE HEALTH

- ANIMAL WALFARE
- NEW MEAT INSPECTION REGULATIONS
- FEMINIZATION OF VETERINARY PROFESSION

Expected increase of demand for animal products in 2008-2018 (Mulder i Kennes, 2010)



CONCLUSIONS

- Food production has to increase by 100% by the year 2050 (important source of protein)

  IFAH
- 20% of animal productivity is lost due to diseases
- Treating existing diseases with antibiotics plays a huge role in safeguarding livestock to feed the world population

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Positive proof of global warming.
18th Century
1900
1950
1970
1980
1990
2006

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Animal medicine + Human medicine = One medicine