WHONET

Advanced analysis

WHO Collaborating Centre for
Surveillance of Antimicrobial Resistance

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WHONET Tutorial – Expert system

The WHONET 5.4 Expert System consists of a number of components:

Part 1.   Isolate alerts
   -   Microbiological alerts
   -   Statistical alerts

Part 2.   Expert antimicrobial interpretation rules

Part 3.   Selective antimicrobial reporting

Part 1.   Isolate alerts

WHONET now permits the user to take advantage of pre-defined or user-defined expert rules that can benefit the user in data entry and in clinical reporting. An additional unique feature of the WHONET expert system is the integrated use of expert rules in data analysis.

At present, WHONET 5.4 includes approximately 200 microbiological rules. In this first version of the expert system, pre-defined expert rules cannot be edited, but individual rules can be turned on or off by the user. In addition, users are also free to develop their own expert rules for reporting and analysis.

Rules are flagged according to the following alert categories.
   -   Quality assurance
      -   Unlikely resistance
      -   Unlikely susceptible
      -   Unlikely phenotype
      -   Disk diffusion is not recommended for this organism and antibiotic
      -   Other problem
   -   Microbiological alerts
      -   Important microbial species
      -   Important antimicrobial resistance
      -   Save the isolate
      -   Send the isolate to a reference laboratory
      -   Other alert
   -   Clinical alerts
      -   Alert the infection control team
      -   Therapy comment
   -   Priority
      -   High priority
      -   Medium priority
      -   Low priority
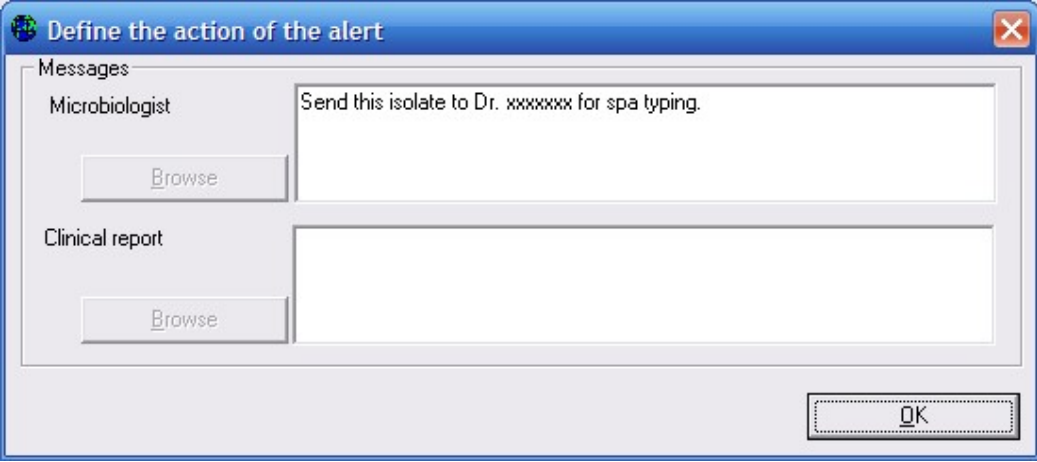
1A.   Configuration of microbiological alerts

Begin WHONET, select your laboratory, and click on "Modify Laboratory". You will see a new button on the screen for "Alerts". Click on this button, and you will see the following screen.
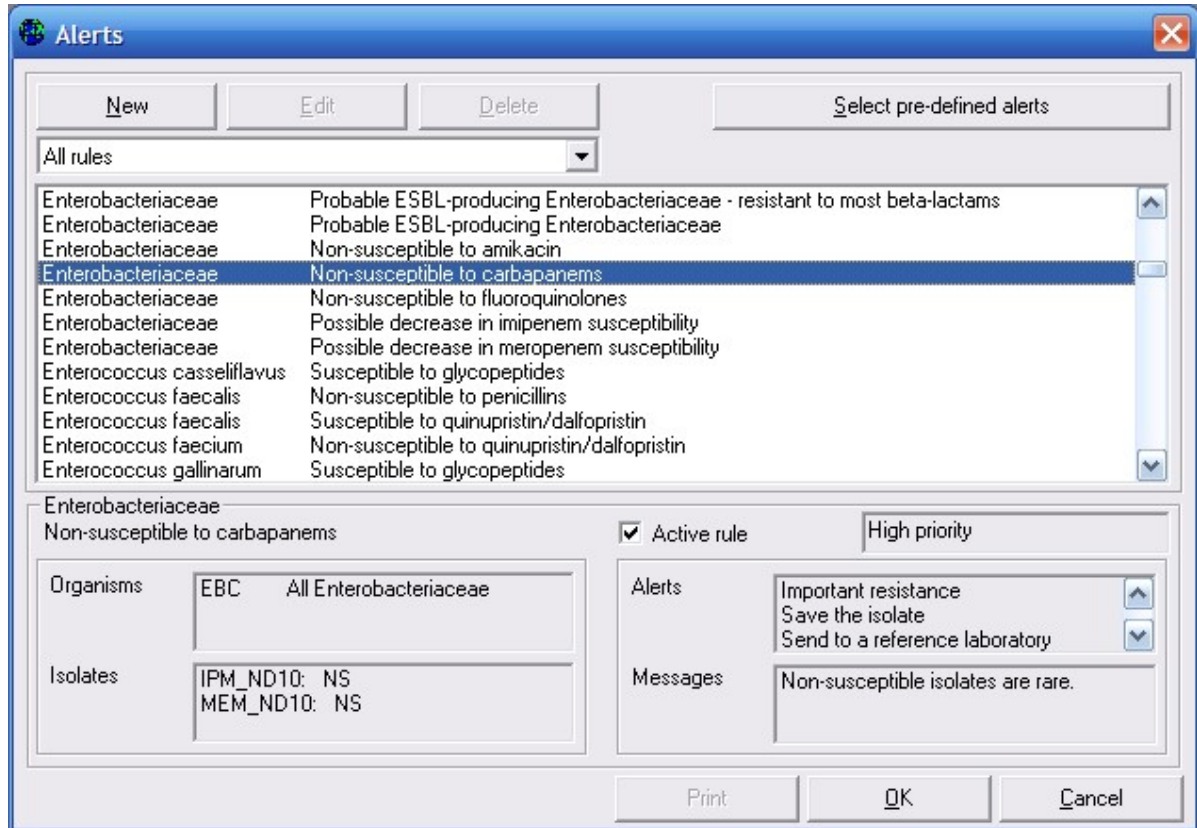
Predefined alerts

In the example, a rule for *Enterobacteriaceae* non-susceptible to carbapenems has been selected. Details of the rule appear below. The software customizes the rules depending on the antimicrobials which you test in your laboratory. You can click on "Active rule" to activate or deactivate the rule. At the top of the screen, you can decide whether you want to view all rules, or only rules of a particular type, for example Quality control rules.

There is also a button called "Select pre-defined alerts". At present, there is only one set of expert rules defined in WHONET, but it is anticipated that in the future, some countries or projects may wish to create their own pre-defined sets for use in the surveillance network.

User-defined alerts

Click on "New", and a screen similar to the following will appear. To define a rule, first give a name to the rule, for example "S. aureus and spa typing". You can indicate whether this is a high, medium, or low priority rule. In the area "Define the selection criteria", use the "Organisms" and "Isolates" buttons in the same way that you would in WHONET data analysis to select the organism/isolate criteria for the alert.
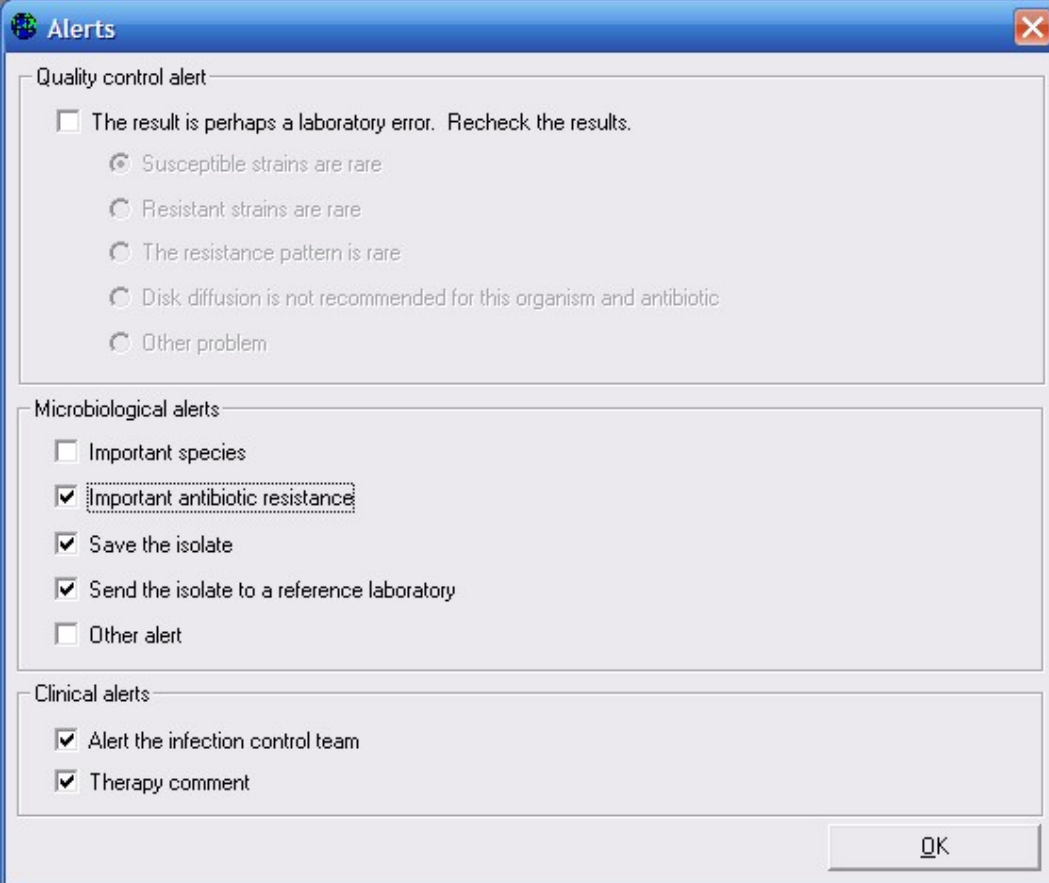
Now that you have defined the criteria which will trigger the alert, you can indicate that details of the alert back to the user. Use "Alerts" to indicate that category and type of alert, and select "Messages" to enter any messages you wish to display back to the microbiologist or to the clinician. If you click "Alert", you will get the following screen:

Indicate the flags which you wish to apply to the new alert, and click "OK".

If you click on "Messages", you will get the following. Indicate any messages you wish to send to the microbiologist or clinician, and click "OK". When you complete all details of your new alert, you can return to the main configuration screen to save your modifications.

1B.   Alerts and Data entry

Alerts are a significant enhancement to the data entry program. They can assist in the identification of typing errors, prompt notification of resistance results, and educational information on recommended laboratory testing practices.

Go to the Data Entry program, and process with normal entry of information. As you begin to enter results, any alerts triggered will appear automatically in the lower right-hand corner of the screen, as in the figure below.

If there is a "High priority" alert, you will receive an alert similar to the following.

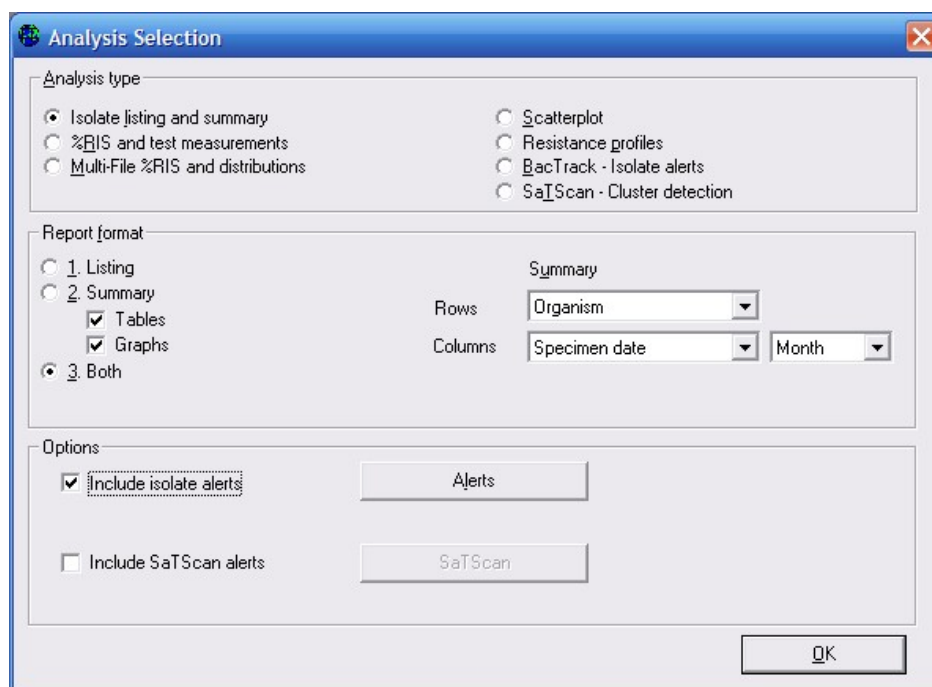When you save the isolate, you will get a summary of all of the alert messages.

1C.   Alerts and Data analysis

One of the powerful features of the expert system is the integration of microbiological alerts into analysis tools. This will facilitate a quick review of large amounts of data, highlighting possible laboratory errors or important resistance findings. For national data managers, this feature can facilitate the prompt feedback to laboratory participants and further identification of problems identified.

In Data Analysis, microbiological alerts are integrated into a two main areas: 1. isolate listings and 2. BacTrack – Isolate alerts. To test out the new features, you may use the WHO Test Hospital sample database or your own. The following screens were prepared with the WHO Test Hospital data.

Isolate listings: Go to Data Analysis, and choose "Analysis Type". Click on "Isolate listing and summary". Click on the new option: "Include isolate alerts".
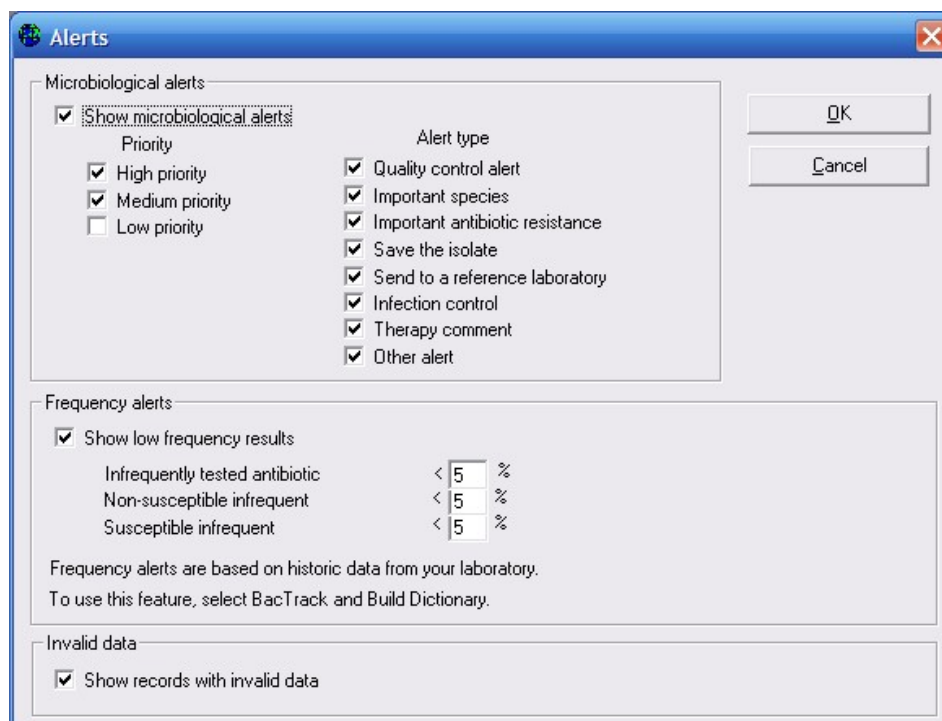
Click on "Alerts" to see additional options. As you can see in the below screen, you can include all alerts in the analysis, or only certain categories of alerts of interest to you. By default, WHONET will include all High and Medium priority isolate alerts from all alert types. Indicate the alerts that you want included in your analysis. Then click "OK", and then "OK" again to return to the main analysis screen.

For "Organisms", select "ALL" organisms. For "Data files", select "w0195who.tst". Then "Begin analysis".

The left portion of the screen will look like the below. This is unchanged from earlier versions of WHONET. WHONET will display test interpretations for this analysis rather than zone diameters of MIC values.

The right portion of the screen looks like the following.

The usual line-listing from earlier versions of WHONET has now been supplemented with microbiological comments about potentially incorrect or important results. By clicking on any column heaing, the results table can be sorted by that column. In this way, it would be easy to see a list of isolates that should perhaps be repeated and sent to a reference laboratory if necessary.

BacTrack – Isolate alerts

In the isolate listing and summary, this user view results from all isolates, many of which may have alert comments. In the "Isolate alerts" feature, only strains with alerts are presented to the user. Alerts include a combination of microbiological rules, as described above, as well as statistical alerts for isolates occurring in low frequency according to the historical data of that laboratory.

To take advantage of the statistical "low frequency" alerts, you should first create a BacTrack reference dictionary with historical data from this laboratory – for example, the 2005 data file. You will then compare your new data file against this historical data. Alternatively, you could create the BacTrack dictionary using the new data file.

For this example, choose "BacTrack – Isolate alerts" and "Create dictionary". Then click "OK". For Organisms, WHONET will automatically include "ALL" isolates. For data files, select "w0195who.tst". Then "Begin Analysis". When the analysis is finished, you will receive a message "BacTrack has completed the dictionary."

Now return to "Analysis Type" and select "BacTrack – Isolate alerts", "Isolate alerts". As earlier, you can click on "Alerts" to select those alerts you would like included in the analysis. You may also set the percent of isolates to be used as a threshold for the determination of "infrequent" results. The default is 5% for each option. To increase the number of flagged isolates, you can increase this percentage. To decrease the number of flagged isolates, then lower the percentage. You can put the percentage at 0% if you want to turn a particular feature off.

Alerts

Microbiological alerts

☑ Show microbiological alerts

Priority
☑ High priority
☑ Medium priority
☐ Low priority

Alert type
☑ Quality control alert
☑ Important species
☑ Important antibiotic resistance
☑ Save the isolate
☑ Send to a reference laboratory
☑ Infection control
☑ Therapy comment
☑ Other alert

OK   Cancel

Frequency alerts

☑ Show low frequency results

Infrequently tested antibiotic	< 5 %
Non-susceptible infrequent	< 5 %
Susceptible infrequent	< 5 %

Frequency alerts are based on historic data from your laboratory.
To use this feature, select BacTrack and Build Dictionary.

Invalid data

☑ Show records with invalid data

When finished your selections, click "OK" to return to the main analysis screen, and "Begin analysis".

Analysis Results

File   Edit   Data

Copy table   Copy graph   Print table   Print graph   Continue   Organism = All organisms   (n=57 Isolates)
☐ Show hidden columns

Identification number	Organism	Organism type	PEN	ERY	TCY	CHL	NIT	TOB	CLI	CEP	AMP	AMK	OXA	GEN	CRB	VAN	SXT	F(
531949	bsb	+	S	S	R	S	S		S		S		R			S	?	
549472	bsb	+	S	S	R	S			S		S		R			S	?	
406304	bsf	+	S	S	S	S			S		S		R			S	?	
460939	cfr	-					S			R	I			S			S	
549060	dxe	+	S	S	S	S			S		S		R			S	?	
237010	eae	-								R	R			S			S	
	eae	-								R	R			S			S	
275268	eae	-					S			R	R			S			S	
441326	eae	-					I			R	R			S			S	
237010	ecl	-								R	R			S			S	
508335	ecl	-					R			R	R			S			S	
546931	ecl	-								R	R			S			S	
	ecl	-								R	R			S			S	
204613	eco	-								R	R			S			S	
243833	eco	-						S			I	S			S			S
546471	eco	-						S		R	R			R*			R	
549471	eco	-						S			S	S			R*			S
358710	efa	+	S	I					R	R	S			S			I	
204613	ent	+	S	I					R	R	S						I	
	ent	+	S						R	R	S						I	
232196	ent	+	S	R				S		R	R	S			S			I
243746	ent	+	S	I					R	R	S			S			I	
324858	ent	+	S	I					R	R	S						I	
	ent	+	S	I					R	R	S						I	
334873	ent	+	S	R				S		R	R	S			R			
401142	ent	+	S	S					S#	R	S					S		
482498	ent	+	S	R			S		R	I	S						I	
533493	ent	+	S	I			S		R	R	S			S			I	
546339	ent	+	S	I					R	R	S			S			I	
509619	hin	-									R						R*	
542522	kpn	-								S	R			S			I*	
437077	mmo	-					R			R	R			S			S	
530709	mmo	-					R			R	R			S			S	
413521	nme	-									S						S	
544160	nme	-			I						S						S	
203262	pae	-				R		S				R*		R		I	R	
221791	pae	-				S		R*					S	R		I	S	
337951	pmi	-				R				S	S			I*			S	
50835	pmi	-				R				S	R*			S			S	
376140	pr-	-				R				R	R			S			S	
	pr-	-				R				R	R			S			S	

Every isolate included in this printout has at least one alert flag. Statistical "low frequency alerts" are found to the left of the listing, and are marked by a special symbol: 1. "*" – the observed resistance is infrequent, based on the hospital's local data; 2. "#" – the observed susceptible result is infrequent, based on the hospitals' data; and 3. "+" – the antibiotic indicated is not frequently tested for this organism, based on the hospital's data.

In this particular example, examples of "infrequent" results include: *E. coli* resistant to gentamicin; *Enterococcus* spp. susceptible to clindamycin; *H. influenzae* resistant to trimethoprim/sulfamethoxazole; *P. aeruginosa* resistant to amikacin; *P. aeruginosa* resistant to tobramycin; and *P. mirabilis* resistant to ampicillin. While such findings may be common in other institutions, the alerts indicate that these findings are rare (<5%) for the results of organisms in this laboratory. Findings of low frequency may perhaps be due to laboratory error, so should be confirmed; or they may reflect important new resistant strains still present at low levels in the institution.

In contrast to the fixed, pre-defined, globally relevant microbiological expert rules described earlier, a great advantage of the "low frequency" alerts is that alerts are automatically adjusted to the past experience of this particular laboratory for all tested organisms and antibiotics.

After viewing the isolate alert listing, click "Continue" to proceed to the isolate alert summary. The summary tabulates every alert that was encountered in the scanned data. Totals are provided, as well as the type of alert – "quality assurance", "send to a reference laboratory", *etc.* If results from more than one laboratory are scanned, the summary also includes the breakdown of alerts by laboratory, as illustrated in the screen below.

Analysis Results

File Edit Data

Copy table	Copy graph	Print table	Print graph	Continue	Organism = All organisms (n=835 Isolates)						

	Number	Organisms	Alert	Number of isolates	Priority	061	TST	FFF	GEP	Quality control	Imp sp
▶	8	All organisms	Discordant penicillin and beta-lactam-+inhibitor resul	12	Medium priority		12			☑	
	25	Enterobacteriaceae	Probable ESBL-producing Enterobacteriaceae	249	Medium priority	131	6	104	6	☐	
	26	Enterobacteriaceae	Non-susceptible to amikacin	1	Medium priority		1			☐	
	28	Enterobacteriaceae	Non-susceptible to fluoroquinolones	4	Medium priority		4			☐	
	30	Enterococcus casseliflavus	Susceptible to glycopeptides	12	Medium priority	12				☑	
	31	Enterococcus faecalis	Non-susceptible to penicillins	43	Medium priority	41		2		☑	
	32	Enterococcus gallinarum	Susceptible to glycopeptides	10	Medium priority	10				☑	
	33	Enterococcus sp.	VRE - Vancomycin-resistant Enterococcus	15	Medium priority	1	11	3		☐	
	54	Listeria monocytogenes	Important species	3	High priority			3		☐	
	58	Neisseria gonorrhoeae	Important species	29	High priority	13		16		☐	
	62	Neisseria meningitidis	Important species	3	High priority		2	1		☐	
	75	Pseudomonas aeruginosa	Discordant amikacin and aminoglycoside results	1	Medium priority		1			☑	
	81	Salmonella sp.	Important species	33	Medium priority	20		13		☐	
	84	Salmonella sp.	Non-susceptible to third-generation cephalosporins	1	High priority	1				☐	
	94	Staphylococcus aureus	MRSA - Methicillin-resistant S. aureus	9	Medium priority		9			☐	
	98	Staphylococcus aureus	VISA - Vancomycin-intermediate S. aureus / Glycop	6	High priority	5		1		☐	
	99	Staphylococcus sp.	Intermediate to vancomycin, teicoplanin	7	High priority	6		1		☐	
	100	Staphylococcus sp.	Non-susceptible to vancomycin, teicoplanin by disk	1	Medium priority		1			☐	
	104	Staphylococcus sp.	Non-susceptible to vancomycin, teicoplanin	10	High priority	7	2	1		☐	
	111	Streptococcus pneumoniae	Beta-lactams tested by disk diffusion (except for oxa	2	Medium priority		2			☑	
	114	Streptococcus pneumoniae	PNSSP - S. pneumoniae Non-susceptible to penicill	358	Medium priority	222		130	6	☐	
	118	Streptococcus sp.	Non-susceptible to vancomycin, teicoplanin	3	High priority	2	1			☐	
	120	Streptococcus viridans	Non-susceptible to penicillin, ampicillin	22	Medium priority	20		2		☐	
	123	Streptococcus, beta-hemolytic	Non-susceptible to penicillins	21	High priority	16	2	1		☐	
	124	Streptococcus, beta-hemolytic	Non-susceptible to third-generation cephalosporins	6	High priority	5				☐	

Part 2.   Expert interpretation rules

The microbiological rules described above provide alerts of various sorts to the user. These rules do not change the antimicrobial test interpretation. There are a few additional rules which actually do change test interpretations given certain findings, for example, an isolate of MRSA should be considered resistant to all beta-lactam agents, irrespective of the *in vitro* test measurements.

To review the current expert interpretation rules, choose "Modify laboratory" to enter the configuration area, "Antibiotics", "Breakpoints". You will see the following screen. Click on "Expert interpretation rules.
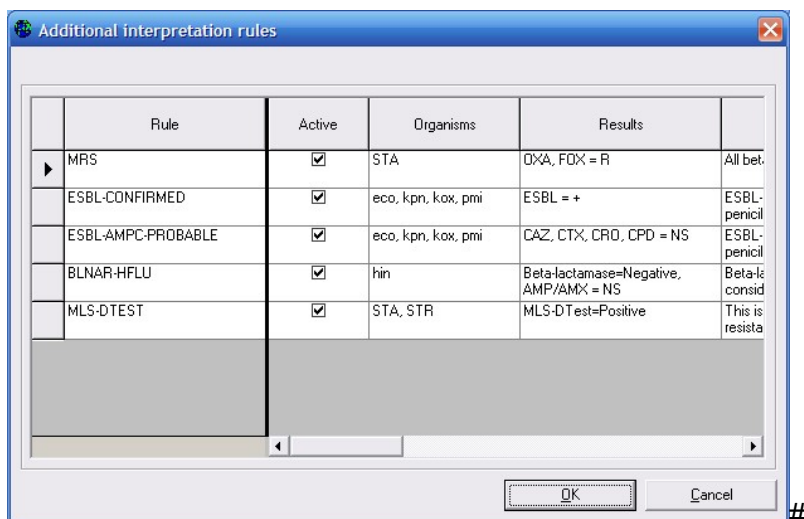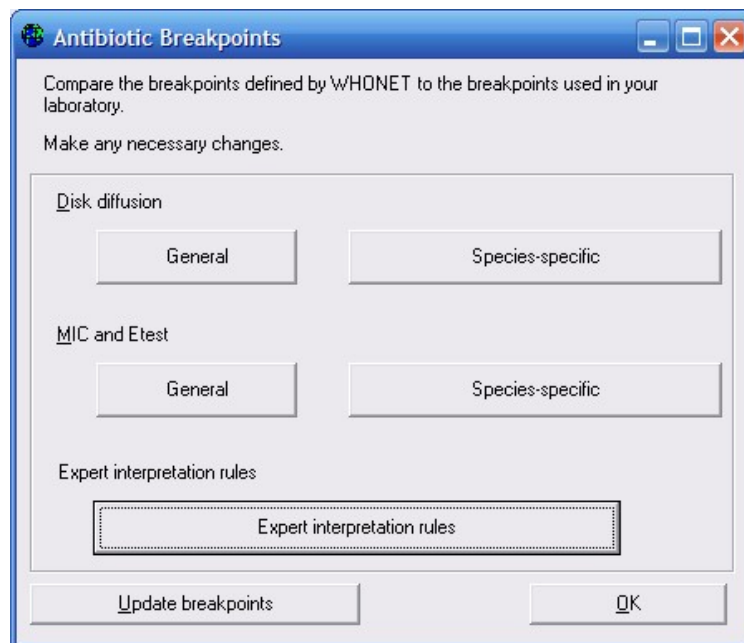
You will see the five expert interpretation rules currently defined, adapted from CLSI recommendations: 1. methicillin-resistant *Staphylococcus*; 2. confirmed ESBL-producing *E. coli, K. pneumoniae, K. oxytoca,* or *P. mirabilis*; 3. probable ESBL-producing *E. coli, K. pneumoniae, K. oxytoca,* or *P. mirabilis;* 4. beta-lactamase negative ampicillin-resistant *H. influenzae*; and 5. DTest positive strains of *Staphylococcus* and *Streptococcus*.

At the present time, users cannot create new interpretation rules or edit existing ones. Rules can be activated or deactivated by the user.

It is important to understand when WHONET applies these expert rules. For Data Entry and clinical reporting, ***these rules are always applied*** (unless specifically deactivated by the user). In Data Analysis, ***these rules are are never applied until the option is turned on by the user.***

In the Data Analysis program, if you want to apply these expert interpretation rules, go to "Options" and click on "Use expert interpretation rules". It is the first option listed on the screen.

Part 3.   Selective antimicrobial reporting

For laboratories using WHONET as a clinical reporting system, the ability to selectively report or suppress certain antimicrobials can be important in supporting rational drug use and guiding clinical therapy decisions.

To configure the selective reporting rules, click on "Modify laboratory", "Antibiotics", "Panels", and click on "Conditional antibiotic reporting".

In the screen below, you can indicate your standard First-line agents, which should typically be reported for all isolates. You can indicate Second-line agents, which will be included in the clinical report under certain conditions (if the result itself is resistant or if the isolate is resistant to multiple First-line agents). For drugs that are principally used only for organism identification (optochin, novobiocin, *etc.*), you can choode "Do not print" to exclude these isolates from clinical reports.

In addition to the results described on this screen, you can enter "Additional rules" to define additional reporting criteria.

The responses that you enter in these screens will set the default behavior for clinical reporting. During data entry, you can change these selections manually by including or excluding additional antimicrobials by using the F8 and F9 keys. In the below screens, antibiotics appearing in gray to not appear in the clinical report.