

# An Intelligent Medical System for Microbiological Data Validation and Nosocomial Infection Surveillance

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## Abstract

*We describe a knowledge based system for microbiological laboratory data validation and bacteria infections monitoring. The knowledge base has been obtained from international standard guidelines for microbiological laboratory practice, from experts' suggestions and from data mining. In this work, we evaluate the system in terms of accuracy on a test dataset.*

## 1. Introduction

This work is part of a project for monitoring nosocomial infections, jointly started by DEIS University of Bologna and Dianoema S.p.A. [13], an Italian information technology company operating in the Health Care market. In this work, we describe an Expert System [3] for Microbiological Data Validation and Surveillance called ESMIS. We have described in details the ESMIS specifications and features in [14]: in this paper we show the overall system, its prototypical implementation and its performances obtained on a testing trial. For bacterial infections, the stored data usually includes: information about the patient (sex, age, hospital unit where the patient has been admitted), the kind of material (specimen) to be analysed (e.g., blood, urine, saliva, pus, etc.) and its origin (the body part where the specimen was collected), the date when the specimen was collected (often substituted with the analysis request date) and, for every different bacterium identified, its species and its antibiogram. The antibiogram [1] represents its resistance to a series of antibiotics and it is usually represented by a vector of couples (antibiotics, resistance), where four types of resistance to antibiotics are possibly recorded: R when resistant, I when intermediate, S when sensitive, and null when unknown.

ESMIS adopts a rule-based approach to identify critical situations and correspondingly generate alarms. Its knowledge base has been obtained from NCCLS guidelines, from experts' suggestions and from data mining [2]. NCCLS [4][5] is an international standard organization recognized by almost all laboratories as the reference in routinely work, that publishes an annual compendium containing testing guidelines for microbiological laboratories.

ESMIS is able to provide automatic data validation and real-time alarming, performing a series of controls. Given a newly isolated bacterium and the related antibiogram, the system performs five main tasks: validates the culture results, reports the most suitable list of antibiotics, issues alarms regarding the newly isolated bacterium, issues alarms regarding the patient clinical situation and identifies potential epidemic events inside the hospital.

In order to let ESMIS validations be more reliable, we have tuned its knowledge base by performing tests on 6-month real microbiological data collected by the Clinical, Specialist and Experimental Medicine Department - Microbiology Section of the University of Bologna (Italy). This work was performed comparing ESMIS evaluations on raw antibiogram results with expert evaluations and considerations on the same data set. In the paper, we describe the results we have obtained in terms of accuracy and specificity.

## **2. An Expert System for Microbiological Surveillance**

ESMIS has been realized using an Expert System programming approach. This Artificial Intelligence programming technique has been applied to the medical field since 1980. In an Expert System [3], also called Knowledge Based System (KBS), knowledge about the problem is translated into special data structures and rules. An inference engine applies these rules to the available data to perform some specific tasks.

### **2.1. Specifications and Features**

Given a newly isolated bacterium and the related antibiogram, ESMIS performs five main tasks: validates the culture results, reports the most suitable list of antibiotics, issues alarms regarding the newly isolated bacterium, issues alarms regarding patient clinical situation and identifies potential epidemic events inside the hospital. In the validation of culture results, the system finds antibiotics not tested but necessary (rack test task), identifies impossible antibiotic results for particular species, and tests common relations between antibiotic results (validation task). In the intelligent reporting of antibiotics results, the system associates to each antibiotic a suitability, obtained considering some antibiotic characteristics: cost, infection site, bacteria specie and hospital ward (intelligent reporting task). In single analysis alarms, the system provides information regarding the bacteria (dangerous resistance, multiresistant bacteria, etc.). In single patients alarms the system issues alarms considering the infection history of the patient. For example:

- Polimicrobial population: if two or more bacteria species were found in two different (consecutive) time points in the same sample material;
- Resistance Acquisition: if the newly identified bacteria has more antibiotic resistances than the previous one of the same species.

The system will also provide information regarding the hospital ward (contagion) and epidemic breakout alarms: the system architecture is ready but these tasks are not implemented yet.

### **2.2. Knowledge elicitation**

For knowledge elicitation we selected the NCCLS guidelines [4][5]: they are basically composed, for each species, of: a table that specifies antibiotics to be tested, a table that specifies antibiotic test interpretation and a list of exceptions regarding particular antibiotic test results. ESMIS knowledge base (KB) now contains rules regarding three species or group of species: Staphylococcus, Enterobacteriaceae, Pseudomonas and other non-Enterobacteriaceae.

### **2.3. System Architecture**

ESMIS is ready to work in real-time in the final on-line environment which is composed by: a database (containing configuration data and antibiogram data), the analytical

instruments (that automatically sends antibiogram results to the database) and the ESMIS system itself. The system interacts with the environment in four ways: checking for changes in the configuration data (composed by antibiotic data, bacteria data, testing protocols), importing from the database a set of non validated antibiograms, validating these antibiograms, issuing alarms and returning evaluations back to the database together with their comments and explanations. Another application will present these information to the laboratory personnel during the validation task.

A laboratory information system called Italab C/S developed by Dianoema S.p.A. [13] manages and stores all the information concerning patients, analysis requests and analysis results in an Oracle database and transfers in real-time microbiological data to a dedicated database called Epidemiological Observatory (see Figure 1). Data are organized in a set of database tables, specially designed for ESMIS.

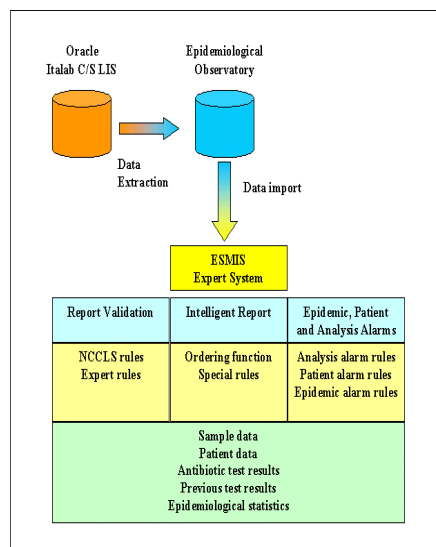


Fig.1 – Databases and Data types

The NCCLS compendium contains a table that specifies antibiotics to be tested on a specific species subdivided in: Main reporting antibiotic groups (basic, advanced, specific and for urinary tract infections), Antibiotic subgroups (antibiotics with similar characteristics) and Antibiotic equivalencies (antibiotics with the same bacteria test result).

All this data plus data regarding bacteria (single bacterium data and bacteria classification) are stored in special tables. ESMIS checks if changes are made to information stored in these tables, and, if needed, updates its knowledge base in order to be always consistent with them.

Regarding database connectivity, the tool used for building ESMIS provides a library of functions useful for opening database connection and executing SQL command. These functions use the Microsoft ODBC database connectivity infrastructure provided by Microsoft operating systems.

#### 2.4. ESMIS reports and graphics user interface

Figure 2 shows an example of ESMIS evaluation report in which we find the results of the controls executed on a Staphylococcus Aureus bacterium. For each ESMIS result there is an associated note explaining the name of the rule applied and its description. Please note that in

Figure 2, an inconsistency arises between NETILMYCIN (belonging to the AMINOGLYCOSIDE antibiotic group) and OXACILLIN. The validation note about this inconsistency is N\_VALI1:

**VALIDATION NOTE:** N\_VALI1 --> 1: ( Vali\_Stafi\_23\_5)  
 If OXACILLIN test result is Resistance (R) then test results for AMINOGLYCOSIDE should be Resistance too. The expected test result is R.

REP. GRP.	ANTIBIOTIC	STRUM. RES.	ESMIS RES.	DER. RES.	TO REPORT	RACK NOTE	VALID. NOTE	REPORT NOTE
C41	RIFAMPIN	S	S	no	no	--	--	N_REP1
B41	VACOMYCIN	S	S	no	*	--	--	--
B21	CLINDAMYCIN	R	R	no	*	--	--	--
B11	CLARITHROMYCIN	R	R	no	*	--	--	--
---	NETILMYCIN	S	>R<	no	*	N_RACK1	N_VALI1	--
A11	OXACILLIN	R	R	no	*	--	--	--
A21	PENICILLIN	R	R	no	*	--	--	--
B31	SULFA/TRIMETH	R	R	no	*	--	--	--
---	CLOXACILLIN	-	>R<	*	no	--	--	N_REP2
---	DICLOXACILLIN	-	>R<	*	no	--	--	N_REP3

Fig.2 – Antibigram results after ESMIS evaluation

One important aspect of ESMIS is interaction with the laboratory personnel. The main objectives regarding this problem are: to simplify the overall laboratory work, to help in finding antibiotic test errors, to help the generation of reports and to aid in the early detection of dangerous infection events. In order to achieve these goals, we have proposed the following procedure:

The user interface, which is under development, for each time t will show the following information:

- Instrumental results (read only);
- Last test results proposed by the user, called USER(t) (read only);
- Actual test results proposed by ESMIS (read only);
- Validation alarms issued by ESMIS evaluating USER(t);
- New test results proposed by laboratory personnel: USER(t+1) (changeable)

### 3. Implementation

We developed ESMIS using the Expert System Tool Kappa-PC 2.4 by Intellicorp [6] which offered a good ratio cost/features and a simple and powerful programming language. Moreover, it works in interpreted and compiled mode, and can reason both forward and backward.

Since NCCLS compendium guidelines can change each year, ESMIS rules are designed as templates: rules are general and are dynamically instantiated referring to NCCLS table entries, so they can be updated with the last guidelines version by simply updating the table. Thus the problem of continuous knowledge update by qualified people is avoided since it is sufficient to update NCCLS table entries which are stored in an Oracle database. We have also implemented in ESMIS exception rules, representing particular cases not considered in NCCLS tables. Of course these exception rules need to be changed if the specific cases change.

### 4. ESMIS Evaluation

The rule set is composed by: 9 culture result validation template rules, 24 culture result validation exception rules for the *Staphylococcus* species, 29 culture result validation exception rules for the *Enterobacteriaceae* species, 15 culture result validation exception rules for the *Pseudomonas* and other non-*Enterobacteriaceae* species, 8 single patient alarm rules, 6 single analysis alarms rules and 1 rule for contagion identification.

In order to evaluate ESMIS performance, we compared ESMIS results with expert results on raw antibiotic test results provided by laboratory instruments. The prototype has been tested off-line on 6 months culture results collected from the Clinical, Specialist and Experimental Medicine Department - Microbiology Section of the University of Bologna (Italy).

The available dataset is composed by 368 antibiograms and has the following features:

- 6 months from 14-JUN-00 to 25-NOV-00;
- 367 positive samples;
- 35 different species;
- 8904 antibiotic test result available for the Rack test task and Intelligent reporting task reliability evaluation;
- 3638 antibiotic test result available for Validation control reliability evaluation;
- 334 patients.

Performance evaluations have been performed on the rack test, validation and intelligent reporting tasks. The evaluation results regarding each specific task, have been aggregated in four different performance indexes following an approach similar to the one explained in [15]. These indexes are generally used for characterizing the reliability of a system in correctly classifying a set of samples previously classified by a domain expert. Consider, for example, a set of samples that may be classified as positive or negative. In the rack test task, a positive sample is an antibiotic that ESMIS requires to be tested while a negative sample is an antibiotic that ESMIS does not require to be tested. In the validation task, a positive sample is an antibiotic result that is changed by ESMIS while a negative sample is an antibiotic result that is not changed by ESMIS. In the reporting task a positive sample is an antibiotic whose result is reported by ESMIS while a negative sample is an antibiotic that ESMIS does not report. Performing the comparison between Expert and System classification of dataset samples, we calculate: Accuracy, which describes System's ability to correctly classify positive the samples (number of samples correctly classified positive divided the total number of samples classified positive by System); Sensitivity, which describes System's ability to correctly find positive samples (number of samples correctly classified positive by System divided the total number of samples classified positive by Expert); False Alarm Rate, strictly related with Specificity, which describes the percentage of negative samples which System incorrectly identifies as positive.

In our tests, ESMIS is the System, the laboratory expert is Expert, the samples are the antibiotic test results and each task is considered as a sample classification.

The first evaluation is the reliability of the rack test task (for example, the ability to correctly identify the set of antibiotics to test, identify significant antibiotic erroneously not tested). Executed tests regard the antibiotic results added and reported by the expert, because considered necessary, in order to identify the percentage of them also added by ESMIS. The Expert added 49 results and ESMIS also added all of them so the system achieve 100% of rack test reliability in this first evaluation.

The second evaluation regards the validation task reliability. Now the comparison is focused on instrumental antibiotic test result changes performed by ESMIS and laboratory expert. ESMIS, according with its knowledge base, classify a result as "to change" or "normal" (to not change). Changes are performed when a result is considered abnormal.

These classifications have been compared with the ones performed by Laboratory Experts. In this evaluation, when both ESMIS and Laboratory Expert change a result, is important to verify if the new proposed result value is the same or different: Ccorr is the number of matching results and Cerr is the number of mismatching results.

Performance evaluation data are collected in Table 1.

		ESMIS	
		Changed	Normal
Laboratory expert	Changed	Ccorr = 132   Cerr = 0	EN = 8
	Normal	EC = 2	TN = 3496

Table 1 - Comparison between Expert and ESMIS validation

Ccorr = Number of results changed by laboratory expert, correctly changed by ESMIS

Cerr = Number of results changed by laboratory expert, erroneously changed by ESMIS

EN = Number of results changed by laboratory expert, erroneously considered normal by ESMIS

EC = Number of results considered normal by laboratory expert, erroneously changed by ESMIS

TN = Number of results considered normal by laboratory expert, correctly considered normal by ESMIS

Accuracy, Sensitivity, Specificity and False Alarm Rate of this control are obtained thanks to these formula:

$$Accuracy = \frac{Ccorr}{TPC} = 98.5\% \quad Sensitivity = \frac{Ccorr}{TCR} = 98.5\%$$

$$Specificity = \frac{TN}{TNR} = 98\% \quad FalseAlarmRate = 1 - Specificity = 2\%$$

TPC = Total number of Result Changed by ESMIS = Cerr + Ccorr + EC

TCR = Total number of Result Changed by Laboratory Expert = Ccorr + Cerr + EN

TNR = Total number of Result considered Normal by Laboratory Expert = EC + TN

The third evaluation is the reliability of intelligent reporting task (for example, the ESMIS ability of masquerading, among antibiotics that resulted sensitive, those relating to dangerous and last generation antibiotics). In this evaluation, the focus is not on the value of the test result, but in the comparison between the composition of antibiograms provided by instruments, ESMIS and laboratory experts. ESMIS, according with its knowledge base, classify a result as “to report” or “to not report”. These classifications have been compared with the ones performed by Laboratory Experts.

These evaluation results are collected in Table 2.

		ESMIS	
		Reported	Not Reported
Laboratory expert	Reported	Crep = 2164	Enorep = 1475
	Not Reported	Erep = 217	Cnorep = 5048

Table 2 – Comparison between Expert and ESMIS reporting

Crep = Number of results reported by laboratory expert, reported by ESMIS  
 Enorep = Number of results reported by laboratory expert, not reported by ESMIS  
 Erep = Number of results not reported by laboratory expert, reported by ESMIS  
 Cnorep = Number of results not reported by laboratory expert, not reported by ESMIS

Accuracy, Sensitivity, Specificity and False Alarm Rate of this control are obtained thanks to these formula:

$$Accuracy = \frac{Crep}{TRES} = 91\% \quad Sensitivity = \frac{Crep}{TREx} = 60\%$$

$$Specificity = \frac{Cnorep}{TNEx} = 96\% \quad FalseAlarmRate = 1 - Specificity = 4\%$$

TRES = Total number of results Reported by ESMIS = Crep + Erep

TREx = Total number of results Reported by Laboratory Expert = Crep + Enorep

TNEx = Total number of results Not reported by Laboratory Expert = Erep + Cnorep

To summarize, notice that as concerns the rack test task the system reaches 100% of reliability.

As concerns obtained Accuracy, Specificity and Sensitivity for the validation task, the system reaches an Accuracy of 98.5%, Sensitivity of 98.5% and a Specificity of 99%. This is a very satisfactory result. The executed test provided many insights to expert too (we discovered some mistakes done by them).

As concerns the intelligent reporting task, both Accuracy and Specificity are very good. The value for Sensitivity (60%) is low since one of the purpose of the system is to reduce as much as possible the number of antibiotic results proposed to clinicians.

## 5. Related work

During the last few years, many surveillance systems have been developed in order to monitor microbiological analysis results and to early identify infection and epidemiological events. All these systems have peculiar features that make them not suitable for efficient and correct analysis of Italian data. Significant examples of these systems are WHONET 5 [7], GermWatcher [8] and TheraTrac 2 [9]. WHONET 5 is a database software for the management of microbiology laboratory test results. GermWatcher is an expert system, which applies both local and international culture-based criteria for detecting potential nosocomial infections. TheraTrac 2 is a system for microbiological data validation and real-time alarming. It directly interacts with Vitek [10] an expert system for test results validation, that is integrated in particular analytical instruments. All systems use international standard guidelines in order to define controls to be executed on laboratory test results. WHONET is an off-line tool useful for medium and long term data analysis but it is not suitable for real-time monitoring and alarm generation. GermWatcher works on-line but in order to work correctly needs a lot of data not available in Italy. TheraTrac 2 works on-line but is designed

for USA hospital organization (focused on pharmacists) that is different from Italian hospital organization.

In the past, DEIS University of Bologna and Dianoema S.p.A. have designed and implemented an expert system for the validation of biochemical analysis [11].

## 6. Conclusions and Future work

In this paper we have described a system for microbiological laboratory data validation and bacteria infections monitoring. We also described the first results we have obtained with a prototype that adopts a knowledge-base approach to identify critical situations and to correspondingly issue alarms.

Summarizing, the ESMIS control evaluation test shows that the rack test control, the validation control and the intelligent reporting control reliability is very good. The system is also able to identify mistakes done by laboratory experts.

In the future we plan to integrate ESMIS real-time evaluations with batch statistical ones performed by another module we are realizing within our project.

## 7. Acknowledgements

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