Accred Qual Assur (2002) 7:480–487
DOI 10.1007/s00769-002-0544-1

GENERAL PAPER

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How autoverification through the expert system VALAB can make your laboratory more efficient

Received: 9 October 2001
Accepted: 22 July 2002

Presented at the European Conference on Quality in the Spotlight in Medical Laboratories, 7–9 October 2001, Antwerp, Belgium

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Abstract For over 10 years now various expert systems have been on the market, but very few have reached the level of performance of Validation Assistée pour les Laboratoires d'Analyses Biologiques (VALAB). Over 25,000 rules are combined through an inference engine to reproduce human reasoning in the complex "biological validation" process. After a review of the product concept and its development program, we will see how this "intelligent" tool can bring quality to clinical laboratories, from a production as well as legislation point of view. With more than 140 laboratories using VALAB in Europe in daily routines, our designer and vendor experience in installation, maintenance, upgrading, reliability, efficiency, and liability is excellent.

Keywords Autoverification · Expert system · Post analytical phase

Introduction

Last year, an excellent paper by Edwards [1] described the role of expert systems (ESs) in clinical laboratories. Ten years ago, the boom in information technology (IT) promised the development of ESs to help in decision making processes. But it appears to be more difficult than expected to develop such systems for the following reasons:

- The rules of reasoning must be well defined and not likely to change.
- The result must be of interest to the user.
- It is not easy to come to a consensus on reasoning, and then on rules.
- One can face individual or political reticence if one tells a practitioner what test to prescribe, or suggest a diagnosis.
- Authors and vendors risk liability in the case of an unexpected result.
- The technology transfer is not easy to implement: the final product must be fast, reliable, user friendly, easy to maintain and upgrade, not requiring a lot of knowledge or equipment, etc.
- The necessity to convince potential users of the quality of the product and the benefits it brings.

For these reasons, most ESs that have appeared on the market have narrow market niches, or are of a "tool box" type, in which the users have to develop their own sets of rules. This is also why it is not easy to give a good definition of an ES, as they can range from a set of basic tables or independent rules, up to a very complex, combinatory process, close to human reasoning and decision making. Let us say that an ES is a database linked to a computer tool allowing a more or less complex decision making process.

The Validation Assistée pour les Laboratoires d'Analyses Biologiques (VALAB)ES

Database

Initiated in 1986 by Valdiguié and his team (Rangueil Hospital, Toulouse, France), headed by Rogari, the first system was developed for only 10 parameters in bio-

chemistry, and had over 100 rules (see below for some examples of rules). The quality of the database is very important, because it is the heart of the system, which provides the basic source of knowledge., Rogari, who is also a cognitive engineer, led the pathologists to perform "reverse engineering" of the validation process, going back to all the basic rules used for each parameter. Only rules that did not depend on personal, local or technical influences were accepted and retained in the database. This is important in order to make the system acceptable and applicable in any situation, whether a private or hospital laboratory, in the south, north or even outside of France. Today, the VALAB database has over 25,000 rules for 126 parameters in 4 different (but correlated) fields: biochemistry, hematology, coagulation, and blood gases. The user cannot modify the rules, but is able to personalize default settings to fit their habits.

The type of data used in the expertise are:

- Age
- Gender
- Origin of report (ward, prescriber)
- Hospitalized and/or emergency request
- Inter-parametric correlation
- Dynamic changes from last previous result
- Medical information: cirrhosis, human immunodeficiency virus (HIV), vitamin K antagonist (VKA) treatment, etc.
- Technical information: hemolyzed sample, air in syringe, blasts, etc.

Software design

From the beginning, VALAB has been developed using an inference engine (IE) in artificial intelligence (AI).

The preferential applications for AI are:

- Symbolic representation
- Complex and combinatory phenomena
- Uncertain and imprecise data.

In the case of VALAB, the tool allows one to combine basic rules so that they are similar to the complex and combinatory process used in biological validation. Also, using an IE guarantees two major aspects in the database:

- *Consistency* is the verification that there is no contradiction between any set of rules and all other existing rules.
- *Completeness* means that the system will be able to make a decision, in all cases, by either accepting or rejecting the patient report.

At last, the IE used in VALAB is second generation. This means that the rules can have different "weights", so that we can express tendencies to obtain the final decision, whilst traditional algorithms can only use "yes or no", "black or white" or "1 or 0". To conclude, we can say that the creator declares and organizes the knowledge, and the IE builds the right decision tree needed for each report by itself.

The expertise process

Being a deterministic system, VALAB will always build exactly the same decision tree for one report. This allows us to reproduce any previous case, even months later, and implement accreditation procedures.

For each report, there will be a hierarchical entry for the expertise: for example, hemoglobin will be analyzed before white cells, sodium and potassium before lipids or uric acid. VALAB looks at the value, situates it as normal, high or low (already taking into account, if justified, the age and gender). Then, the system looks at all the other correlated information for this parameter. If the value is normal, and there is no discordance (no "negative" rules) in the report, this value is validated.

If the value is out of normal range, VALAB will need to find enough reasons to accept it. The further it is from normal range, the more the system will look for "positive" rules, in order to accept low or high values.

For example, in the case of a high and increasing creatinine:

- If urea and potassium are also high and have increased
- If protein and/or calcium are low and have decreased
- If it is an emergency request
- If the patient is in a nephrology ward.

All this information has a positive influence on accepting the high creatinine value.

When all the values are validated, the global report is validated. If at least one parameter is rejected, the total report is not validated, and VALAB puts in flag(s) to indicate for which parameter(s) and for which reason(s) it has not been accepted.

Integration with the laboratory information system (LIS)

Laboratories applying "technical" and "biological" validation

Technical validation is defined as being complementary to other technical controls like quality control (QC), standard deviation, Levey-Jennings diagram and Westgard rules: it is a mono-parametric filter using limits (normal range, panic values) and delta-check (rate of variation with previous result) control. It can be done at the analyzer level or on a data management system (DMS).

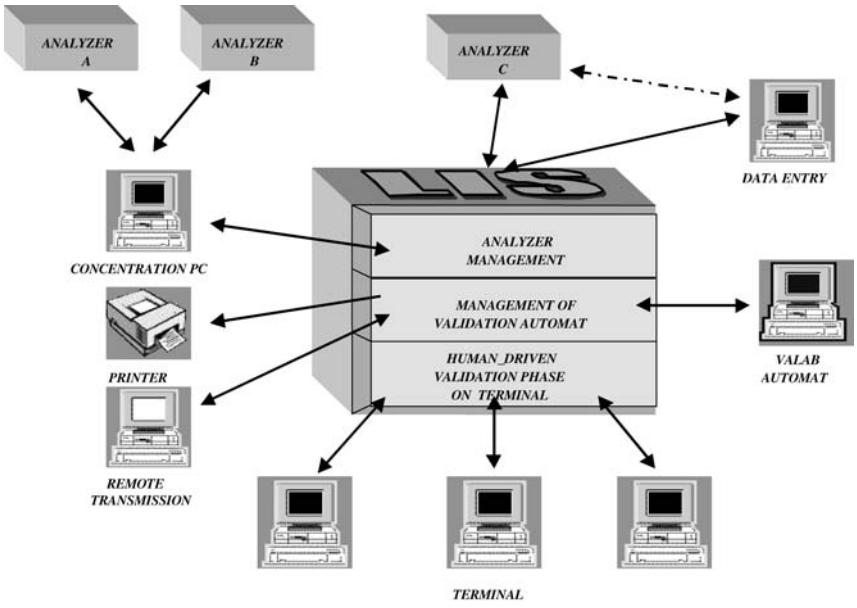

Fig. 1 Position of the Validation Assistée pour les Laboratoires d'Analyses Biologiques (VALAB) expert system (ES) in relation to the laboratory information system (LIS), analyzers and terminals

Those involved within the particular laboratory setting are:

- A prescriber: the physician, clinician or specialist ordering the tests.
- A technician: also called scientist in some countries, who works at the analyzers level.
- A pathologist: the clinical pathologist, also biochemist or biologist.

As shown in Fig. 1, VALAB works on a regular PC (minimum requirement is Pentium 90 with any Windows OS), connected to the LIS through a bi-directional connection.

When the technical validation has been completed by the technician, the LIS sends the report to VALAB. When the report is received back in the LIS, there are three possibilities:

- The report is validated. It can then be printed, transmitted, etc., with no further control.
- The report is not validated. It awaits further validation following the traditional path in the LIS.
- There are abnormal extra-parameters in the report seen on the LIS validation screen, or an extra-parameter in the report that is not sent to the ES.

Laboratories applying only "technical" validation

When the validation is done on a concentrator PC or on the LIS, there are two ways to use VALAB:

- By sending VALAB only the results rejected by the DMS; a percentage of those results will be validated because a lot of "abnormal" values will be accepted with the dynamic and inter-parametric coherence
- By sending VALAB all results. Here the settings for rejected values and delta-checks in the DMS will be opened, and technicians will only have to verify reports that have been "flagged" by VALAB and/or the technical criteria.

In both types of integration, the whole process, reception plus expertise plus transmission, lasts less than half a second per report, whatever the number of parameters included. A report is defined as the request, or file, which is the complete request for one patient, whether it has one or several parameters. Another important point is that since one does not need to work on the VALAB PC, only one system is sufficient, even for thousands of reports a day, or in a multi-site laboratory with a central unit.

Installation and settings

VALAB has default settings integrated for each parameter:

- Normal and extreme limits for healthy adult males; variation depending on age, gender and origin of report are integrated in the ES.
- Normal delta-check reference (these values will increase or decrease depending on positive or negative rules).
- Time limit for previous result: if older, the previous result is not taken into account in the expertise.
- Correlation and anteriority sensitivity adjustment: the default value is 1. If you increase the sensitivity you give more weight to the rules and make the expertise more permissive, if you decrease it you make the

system more restrictive by reducing the weight of the rules.

That is why only 2 days are necessary to install the system completely:

– The first day for connecting the system, parameter settings and dictionary definitions. Then you can leave the system working overnight.
– The second day is dedicated to checking the first expertise reports, starting the fine tuning of the system, and training the users with the tool. One user is the "VALAB Administrator" or contact user who we consult once a week by phone, providing help and advice for adjusting the sensibility of the system to the exact level of requirements.

After only 3 or 4 weeks, the system is completely efficient. To update the system, the first of three diskettes is inserted in the PC and the user types "release". After a few minutes the new version is installed with all the current user settings and dictionaries.

Results and evaluation of the product

The mean rate of automatic validation by VALAB is around 70% for a general hospital (Table 1), ranging from 50% to 90%, depending on the following factors:

– Samples: outpatient or hospitalized.
– Ward: intensive care or general pathologies.
– Data available: the more you have the better the expertise: previous results, age, gender, technical and medical information.
– The number of parameters (Table 2).
– Specific field modules (biochemistry, hematology, blood gases or coagulation) or polyvalent activity (for example, for coagulation, automatic validation can exceed 85%).

Table 1 A qualitative study on 310,000 reports shows the global impact of Validation Assistée pour les Laboratoires d'Analyses Biologiques (VALAB) versus a laboratory information system (LIS)

VALAB	LIS (Cronos) traditional evaluation		
	Validated	Not validated	Total
Validated	20,1%	49.9%	70.0%
Not validated	1.2%	28.8%	30.0%
Total	21.3%	78.7%	100%

Table 2 Influence of the number of parameters on the validation percentage by VALAB versus LIS

N = number of test results	% Files validated		
	1<N<3	4<N<9	10<N<21
% Files validated by VALAB	84.72	71.68	58.83
% Files validated by LIS (Cronos)	53.31	22.80	7.37
improvement VALAB over LIS Cronos	31.41	48.88	51.46

Table 3 Active VALAB sites as of October 2001 (in France and abroad. Versions: B= biochemistry, C= coagulation, G= blood gases, and H= haematology

	Type	Versions	LIS	Country
Laboratories in hospitals				
94	Broad spectrum	B 10 BG 17 CH 9 BCH 11 BCGH 37 H 4 Other 6	11	France
Private laboratories				
25	SEL 6 LABM 19	BH 6 BCH 10 BCGH 9	13	France
Laboratories abroad				
46	Broad spectrum	B 1 Unknown 12 BCGH 33	11 home system 9	Belgium Switzerland Italy Luxembourg The Netherlands Spain

– Sensibility of parameter settings: the level of automatic validation greatly depends on what the user wants to see: only really abnormal values (compared to others in the report) or major analytical and medical problems that may need attention. Requirements can be very different from one country to another, or between one individual and another, depending on whether their role is only to deliver correct results, or also to intervene as a counselor to the practitioner.

Many evaluations and tests have been done in France and other countries by users (before or after buying the system) and also by the National Center for Hospital Equipment (CNEH): an epidemiological evaluation in 1992 and a medico–economical evaluation in 1998 and 1999 [2–10]. Table 3 gives an impression of the extent to which VALAB is used.

Examples of expertise

Here some examples of positive and negative rules (from the 25,000 of the database) are given. It is noticable that they do not all have the same "weight", some just "modify" original settings of a value whilst others reject the value.

Strategy of reasoning example

If there is a high value of glutamate oxaloacetic acid transaminase (GOT) (e.g. >300 IU/l to 37°):

– Search for information which could justify this value.
– Infarction disorders: high or very high value of creatine kinase isoenzyme MB (CKMB), creatine kinase (CK), myoglobin; patient in intensive care unit, clinical information on infarction.
– Liver disorders: high value of glutamic pyruvic transaminase (GPT), high or very high value of conjugated bilirubin, high value of C reactive protein, patient in gastrointestinal ward, information on infectious disease or acute hepatitis.
– Or other context: liver or pancreatic disorder.
– Or chemotherapy context.
– Check if no negative rule is triggered, which could prevent acceptance of such a GOT value, e.g. low GPT value.

Positive anteriority rule for serum calcium

If there is a decrease of serum calcium with low serum calcium.
If there is a result and a previous result for creatinine.
If the creatininemia is above 300 µmol/l.
If the value of creatininemia increases.
If this increase is above 100 µmol/l.
Then *increase the delta-check* of calcium by 10%.

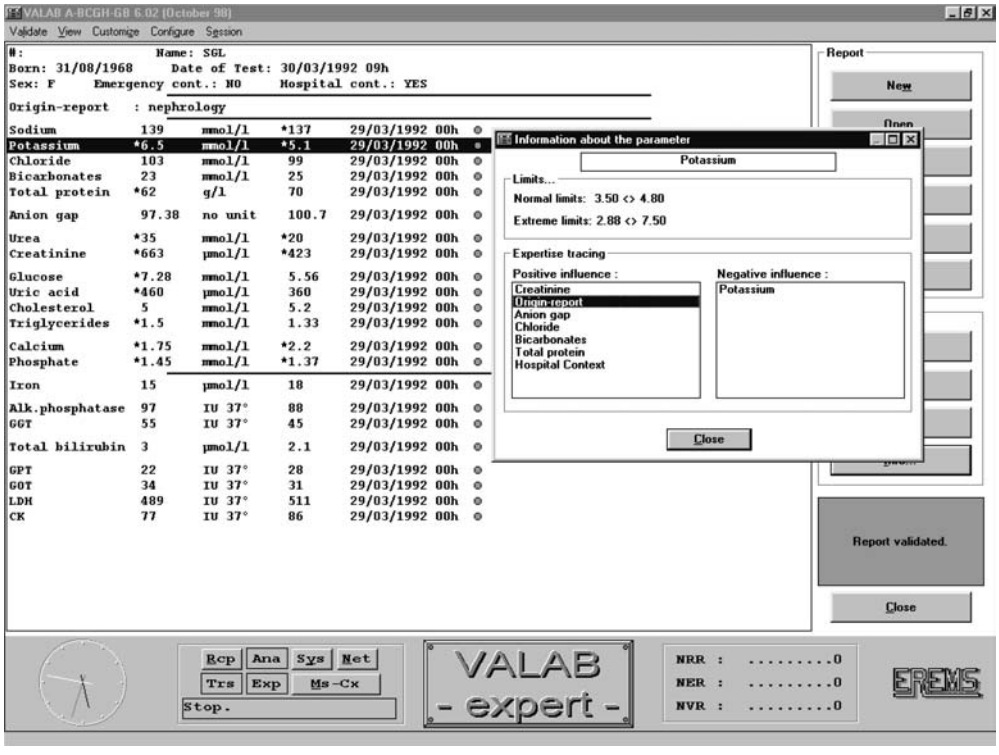

Fig. 2 Validation report, VALAB example 1 (biochemistry).Report validated: the highly abnormal values of this report (urea, creatinine, potassium) are perfectly integrated into the progressive context of renal failure. The foreground window shows the data which influence the validation of potassium

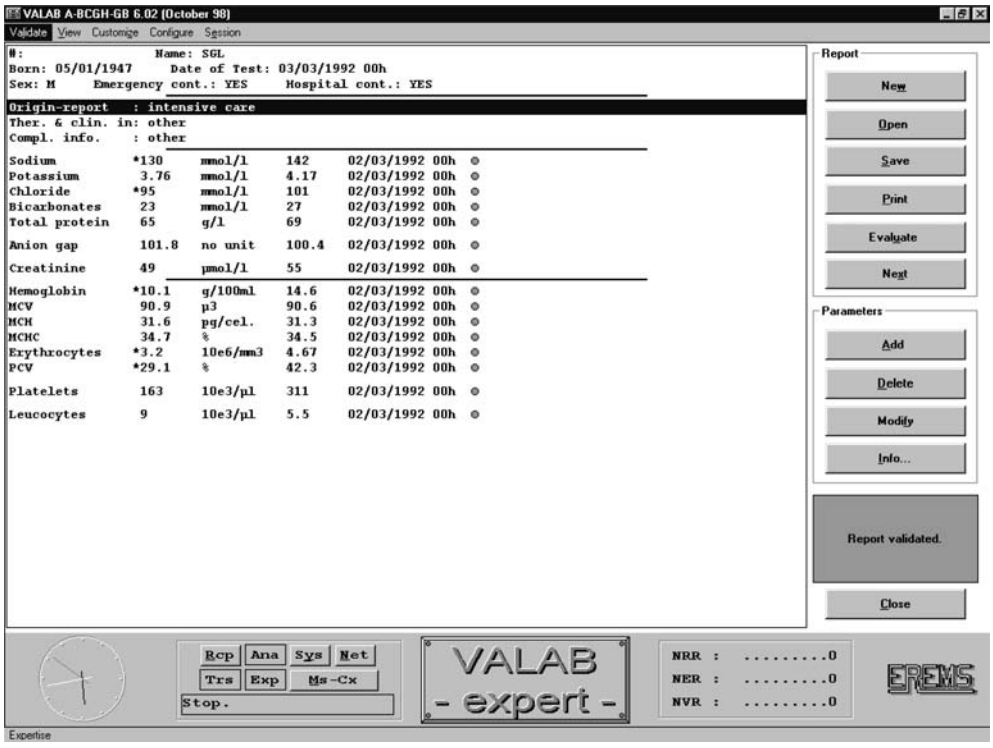

Fig. 3 Validation report, VALAB example 2 (hematology). Report validated: profuse bleeding and dilution in the case of major surgery or intensive care

Negative anteriority rule for serum calcium

If there is a decrease of serum calcium with low serum calcium.
If there is a result and a previous result of total proteins.
If the value of the total proteins increases.
If this increase is above 5/10 g/l.
Then *decrease the delta-check* of serum calcium by 5/10%.

Negative correlation rule for prothrombin time/quick time (PT/QT)

If the PT/QT increases by more than 8 s.
If there is a result of activated partial thromboplastin time (APPT).
If there is an increase of APPT of less than 3 s.
Then *it is not possible to validate* such a value of PT/QT.

Two example reports for chemistry and hematology are given as Figs. 2 and 3, respectively.

Quality and productivity benefits

A comparison of VALAB with technical tools and tool boxes was performed. With an ES one is much closer to human reasoning than with traditional tools. Here are the main differences between VALAB and the limits and delta-check systems:

- Inter-parametric correlation. The main feature of VALAB lies in cumulative treatment of all rules (positively or negatively) to increase or decrease the acceptability of each parameter according to all elements related to it.
- Control of pathological and normal values. Even a normal result must be coherent with all other correlated data of the report.
- Analysis of the variation of a parameter with the variation of correlated parameters.
- Taking into account age, gender, origin of report, clinical and therapeutic information.
- The plausibility of a value is considered with biological and/or medical reasons to accept or reject it.
- Dynamic delta-check: the default value changes with positive or negative influences. This rate will also have different meanings if you are in or out of the normal range, if the value increases or decreases, if the patient's condition declines or gets better.
- As for human reasoning, the more information you have, the better the system works.
- Easy implementation with default values included.
- Possibility to adjust the sensitivity of expertise on correlation or anteriority for any parameter.

Nevertheless, classical technical tools still remain useful, because ES will never be able to cover 100% of the parameters. With tool boxes, the user has the possibility to write their own rules. In addition, the database will have to evolve without internal contradiction. Rules stay inde-

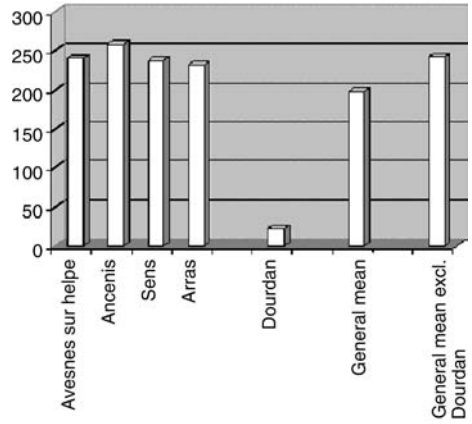

Fig. 4 Results of the study of CNEH in 1999 (2 private and 3 hospital laboratories): savings of the clinical pathologists (h/years)

pendent with no cumulative weight. This type of tool is specific to each laboratory and is complementary to VALAB.

Savings could be gained depending on the volume of activity of the laboratory and how the pathologist works. Automatic validation with an ES will save:

- Money, for those who use only technical validation, by reducing the number of controls on parameters.
- Time, for those who do biological validation. The second evaluation by the CNEH has shown a saving of more than 200 h per year for a laboratory treating about 300 reports a day (Fig. 4).

And if we consider that time is money, we summarized the prime benefits in Table 4.

The quality of validation was evaluated in depth. The pathologist does not waste time anymore on coherent reports and can spend more time on those requiring attention. This means that there is a decrease in the risk of transmitting an abnormal result, but also the pathologist is more available to work and communicate with the prescribers, which is not of secondary importance.

The organizational structure needed was minimal with regard to complexity, and clear with regard to the IT environment requested. The automatic validation is done in "real time", so there is a quicker delivery of results, and the pathologist can perform other activities without worrying about validation.

For private laboratories, it can also be useful to have the printed results folded in envelopes and posted without the classical overload of work before closure of the post office.

From an intellectual point of view, in the beginning, VALAB was compared to a "black box" because one had no idea of the rules. For some years now, it has been possible to look at a report treated by VALAB within 2 days, and have details for any specific parameter and all the data that have had positive or negative influence on its expertise. Many users have told us how much this has helped them to auto-evaluate their own biological validation, because they had never previously had an opportunity to really compare their work with that of their colleagues.

Table 4 Benefits to the organization through the use of the VALAB: GBEA, Guide de Bonne Exécution des Analyses

	Relative improvement
Time saving/validation of residual reports	+++++
Absence of delay/absence of clinical pathologists	++++
Absence of delay/numerous incoming reports	++++
Increase in results security	++++
Time saving in secretarial work	+++
Less phone calls	++
More free time/other tasks (GBEA...)	++
Higher productivity/laboratory's staff	++
Impact on the various stages of production	++
Last signature earlier in the day	+

Harmonization is reached gradually because the large disparities between biologists in their degree of permissiveness when validating is made obvious. One individual does not have the same sensibility and vigilance level depending on the time of the day or night, workload or psychological pressure. Here also, many users told us how much they appreciated VALAB with its common initial level of validation, not only for their quality procedures, but also in the case of discord among staff.

ESs and legislation

In France the biological validation of reports is a legal requirement and the official guide for quality procedures is the Guide de Bonne Exécution des Analyses (GBEA). The first edition in 1994 did not cover ESs. We can now say that the expertise of VALAB exactly fits the definition of "biological validation" according to the GBEA. This document also says: "the biological validation must be done by a biologist", however, the second edition (1999) says that the use of validation tools does not release the pathologist from their responsibility to validate every report (le recours à un système d'aide à la validation ne décharge pas le biologiste de sa responsabilité en matière de validation biologique pour chaque compte rendu)". Further on it says that reports can be delivered only if they have been validated, which is very constricting. So the pathologists have to decide:

- Either to look at all reports, meaning an overload of work and a real risk of error
- Or to use tools to screen results, i.e., limits and delta-check, or VALAB.

In practice, when implementing quality procedures, pathologists are obliged to use tools even if this could be considered as a misinterpretation of present legislation.

Many countries don't have such explicit requirements about "biological validation". In these countries, laboratories, particularly those which treat thousands of reports a day, have to implement high-level quality procedures, including limits and delta-checks for technical validation. Here, the interest of VALAB is mainly productivity, by increasing the number of validated reports, thus reducing the costs.

In contrast to technical products, there are no references to intellectual procedures, particularly for biological validation processes, in the European Norms. Today, the best criteria to validate a product like VALAB is the continuously increasing number of users, and the absence of problems reported after more than 10 years of daily use. In the near future, we intend to ask for an official "quality label" from the authorities.

We have written a document describing the procedure to answer accreditation requirements. VALAB is a deterministic system, containing an audit trail that keeps track of all modifications of settings. Thus, in case of a problem we can reset the exact configuration to that on the date of the report and reproduce the same expertise for the report.

Conclusions

The profound differences between ESs and traditional technical validation tools and tool boxes has been shown. These provide benefits in quality, economy, organization, and human harmonization. According to Edwards improvement in human intervention by adding a higher level of automatization is also a way of "restoring and invigorating the clinical role of pathologists".

With 10 years experience, we can prove that computer-assisted validation (CAV) using VALAB introduces quality into the validation process by giving the same attention to all reports and by using pre-qualified procedures. At present, of the 140 laboratories using VALAB, 20 are private and two are accredited. In a recent survey listing the 50 best hospitals in France, we noticed that 50% of them use VALAB in their laboratories. This proves that ES has become a valid part of the procedures for pathologists who implement quality.

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