OPTION/BIO
L'ACTUALITE DU PRATICIEN BIOLOGISTE
62 RUE CAMILLE DESMOULINS
92442 ISSY LES MOULINEAUX CEDEX - 0171165500


APR 19,10
bimonthly

Approx. Surface (cm²): 1192
Page N°: 18-20

Analytical laboratories and diagnostics companies: a partnership approach

Companies are committed to supporting medical biology laboratories in their quality approach, in a context of compulsory accreditation. They ensure their customers of the CE marking of their products and provide ongoing information about the medical device vigilance and in vitro medical device vigilance, and of course a technical dossier of their equipment.

Whether in terms of the customer-supplier relationship in the normative and conventional sense or the respective share of each in the performance of methods, more than ever, exchanges between in vitro diagnostics companies and medical analysis laboratories are organized in partnership.

Diagnostics companies and the quality approach

To respond to the context of mandatory accreditation of medical analysis laboratories with respect to the ISO 15189 standard, a working group of industrialists who are members of the SFRL (In Vitro Diagnostic Industry Syndicate) has been formed. These suppliers have agreed on a charter that commits them to support their laboratory customers in the quality approach, in all matters relating to the use of their reagents, machines and other services.

I What are IVDMDs?

The abbreviation IVDMD or in vitro diagnostic medical devices refers to everything that is used to carry out an analysis, not only reagents, control and calibration specimens, but also automatons and on-board data processing equipment, consumables, devices and receptacles for biological samples. Annex II of the European Directive contains two lists, A and B, of so-called sensitive IVDMDs:

- List A: HIV, HTLV, hepatitis A, B, C viral serologies; ABO Rh anti-Kell blood groupings;
- List B: anti-Duffy, anti-Kidd, irregular anti-erythrocytic antibodies, congenital infections (rubella, toxoplasmosis), human infections (CMV, Chlamydia), hereditary disease (phenylketonuria), HLA tissue grouping, PSA tumor marker, trisomy 21 risk assessment, etc.).

The CE marking

These manufacturers are already involved in the quality approach, in particular through the CE marking system, which is compulsory for marketing any product on the European market. In fact, a manufacturer proposing a new product must accompany it with a dossier whose requirements are based on thirty to forty harmonized standards under directive 98/79 CE on in vitro diagnostic medical devices (IVDMD). The transposition of this directive into French law is the order 2001-198 of March 1, 2001 (L5222-3CSP). This directive includes requirements in terms of quality management and technical requirements.

Quality management requirements

In order to meet the first requirements, the supplier is usually certified according to ISO 9001 "Quality Management Systems - Requirements". If the supplier is a manufacturer, he may also be certified according to ISO 13485 "Medical devices - Quality management systems - Requirements for regulatory purposes". The main points of this standard concern:

- compliance with regulatory requirements;
- the control of special processes;
- risk analysis during product development;
- clinical trials and the long-term monitoring of these trials;
- the organization of the medical device vigilance;
- control of the traceability of the configuration of each medical device delivered.

Within the framework of this certification, the supplier/manufacturer implements the classic improvement tools (corrective and preventive action sheets, process reviews, management reviews...), as well as an information and information follow-up program with regard to analytical laboratories and concerning medical device vigilance and in vitro medical device vigilance, commercial conditions and customer laboratory complaints.

Technical requirements

The second set of requirements is of a technical nature and relates to the development, manufacture, storage and transport of IVDMDs. All the clinical trials conducted to meet these requirements are listed in a confidential technical dossier, which can only be submitted to the competent authorities (the Afssaps), and on their request.

Indeed, the CE marking is the result of a self-assessment or commitment of the supplier to comply with the requirements of directive 98/79 CE. Its declaration of conformity removes any prior control, i.e. before placing on the market, and its commitment is materialised by the "CE" logo appearing on the packaging and the product leaflet (non systematic issue of certificate).

However, the results of the clinical trials of this technical file are included in the package leaflet accompanying the products under the expression of sensitivity, specificity, linearity, interferences... Moreover, for the products of annex II of the directive (see box), each batch must meet the acceptance criteria defined by the notified body. In France, a product verified in this way bears the mention "CE 0459", 0459 being the code of the notified body.

ISO 15189 standard and method validation by the laboratory

It is not a question for the laboratory of "redoing the work of manufacturers",

OPTION/BIO
L'ACTUALITÉ DU PRATICIEN BIOLOGISTE
62 RUE CAMILLE DESMOULINS
92442 ISSY LES MOULINEAUX CEDEX - 01 71 16 55 00

APR 19, 10
bimonthly

Approx. Surface (cm²): 1192
Page N°: 18-20

namely redoing the tests which appear in the self- assessment technical file and whose results are included in the notices (see Cofrac's Technical Guide to Accreditation: GTA 04 for method validation in medical biology). The aim is to ensure and verify that the stated performances are indeed those that the laboratory finds in its daily practice, on the one hand, and that this is in comparison with acceptable criteria and limits chosen by the biologist and adapted to the needs of patient follow-up, on the other hand.

I Some definitions

Validation: Confirmation by examination and provision of objective evidence that the special requirements for a particular use are fulfilled.
Verification: provision of tangible evidence that a given entity meets specified requirements.
Validation is verification that the specified requirements are adequate for a given use.

Source

According to ISO/CEI Guide 99: 2007 International Vocabulary of Metrology - Basic and General Concepts and Associated Terms (IVM).

The charter "Support to the accreditation approach"

In a concern for mutual understanding of the needs and constraints of the two professions, a number of industrial companies that are members of the SFRL have drawn up and signed the supplier charter "Support for the accreditation approach", as an extension of their own quality commitment and in response to their customer needs.
The supplier charter specifies the existence of:
- French-language records of reagents, containing storage conditions and stability, expected performance, lifetimes, bibliographical references;
-instructions in French for the use of the instruments;
- safety data sheets in French for any reagent classified as hazardous;
- the metrological connection of the values of the standards, in relation to international references (materials or methods);
- methods of in vitro medical device vigilance.

The suppliers' charter specifies the elements of this support in terms of the management part of their contribution:
- demonstration of the existence of their quality management;
- recording and follow-up of complaints;
- provision of a supplier evaluation questionnaire;
- provision of a confidentiality undertaking.
The suppliers' charter specifies the elements of this contribution with regard to the technical requirements (chapter 5 of the ISO 15189 standard):
- detailed training program for laboratory operators;
- issue of training certificates or attendance certificates;
- provision of prerequisite documents for the installation of instruments;
- documented process for verification of installations;
- performance of appropriate checks to ensure operation after on-site maintenance;
- intervention report signed by the customer.

diagdirect.com: what's new

Diagdirect.com is an economic interest grouping (GIE), a portal that is now widely used to place orders in a dematerialised way, with the objectives of simplifying relations between laboratories and suppliers and thus reducing the number of disputes.

diagdirect.com's current services

Currently, 16 diagnostic companies offer their services on this portal, as well as 4 inventory management software companies. More than 500 customers are currently using it, mainly in private biology, either directly or through groupings of laboratories. diagdirect.com is also present in the hospital sector. For example, from January to November 2009, some 120,000 orders were placed through this channel. The online catalogue, access to negotiated prices, generation of dematerialised purchase orders, subscriptions, access to order history and shipping notices are all directly linked to the portal itself.
Laboratories equipped with a stock management software use the specific characteristics of this software, namely the preparation of supplies on the basis of different alert and order thresholds, optimal traceability of products and reagents from their arrival in the laboratory until the end of their use... When this software is coupled with the diagdirect.com portal, they benefit in addition from various facilities:
- Facilitation of order sending (the order form generated by the software is dematerialised, sent by internet);
- Facilitation of order reception traceability (the delivery note is also managed electronically, with all regulatory information - expiry date, batch number, etc. - It is no longer necessary to transcribe batch numbers and expiry dates into the stock management software, this information is automatically stored in its place in the stock management software and thus meets the regulatory requirements for traceability.

diagdirect.com future services

Projects are currently being developed for the management of invoices. Through dematerialisation,

List of manufacturers who have signed this charter*

Abbott	Argène	Beckman Coulter
Becton Dickinson	Bio Advance	Biomedical Diagnostics
Biomérieux	Bio-Rad	Bioservices Antilles
Biotest	Brahms	Cepheid
Cis Bio International	Diagast	Diagnostica Stago
Diasorin	Elitech Group	Elvetec Services
Eurobio	Fumouze Diagnostics	Horiba Medical
Hyphen Biomed	Immunodiagnostics Systems	Ingen
Innogenetics France	Institut de Biotechnologies Jacques Boy	Instrumentation Laboratory
Ipsogen	Menarini	Meridian Bioscience Ortho-Clinical Diagnostics
Oxoid	Perkin Elmer	Phadia
Roche Diagnostics	Sebia	Siemens
S-Inter	Sobioda	Sysmex
Thermo Fischer Scientific	Tosoh Bioscience	Ventana Medical Systems

* at November 2009

OPTION/BIO
L'ACTUALITE DU PRATICIEN BIOLOGISTE
62 RUE CAMILLE DESMOULINS
92442 ISSY LES MOULINEAUX CEDEX - 01 71 16 55 00

APR 19, 10
bimonthly

Approx. Surface (cm²): 1192
Page N°: 18-20

Access to information was facilitated for the ordering and stocking stages. The bet is the same for the invoicing part. The objectives are multiple: to reduce direct costs, increase productivity, optimize relations with laboratories, increase the quality and safety of exchanges. (It is currently considered that the cost of a paper invoice for the buyer - the laboratory - is about 14 € per invoice, compared to about 8 € for the same electronic invoice).
By doing away with paper wherever possible, it is hoped to optimize the processing of the remaining paper documents, increase the quality of the data to be entered into the accounting system, facilitate the reconciliation stages and thus reduce disputes too. The implementation of this project requires a significant amount of work in taking into account accounting and tax rules.

The use of biological samples

The need

Manufacturers of in vitro devices need blood samples, in particular for:
- develop formulations;
- testing performance in terms of specification, sensitivity, stability;
- multi-step controls;
- final batch release testing.

These needs create a daily problem of access to these blood samples which must:
- respect biological diversity, namely be normal (the sources are often the French blood establishments), but also be pathological or correspond to therapeutic follow-ups;
- be in sufficient numbers.

The interest for industrialists is therefore to have access to the "tube bottoms", in other words, to the biological samples when they become waste, as well as to the tube samples "in addition".
The existence of complex regulatory texts, since around 1940, means that manufacturers have only very limited access to these famous tube bottoms, and this can even lead to a reduction or even an end to collaboration between manufacturers and health care institutions in this area. The greatest risk is then the relocation of industrial companies.

The texts

The first international bioethics laws date back to 1946 under the Nuremberg Code.
- The World Medical Association, created in 1947 as the representative of doctors throughout the world, drew up the Declaration of Helsinki in June 1964 (regularly amended at the association's General Assemblies). It is a declaration of ethical principles, recommendations made to doctors and other participants in medical research involving human beings.
- In France, the Huriet-Sérusclat law dates from 1988 and has undergone various modifications since then.
- In 2001, the European directive on medicinal products was drawn up, in which biology is "assimilated". Its transposition into French law does not answer the specific questions of manufacturers regarding the availability of biological samples.
- Since 27 August, 2006, biomedical research on MD & IVDMDs is subject to the opinion of the Committees for the protection of persons and an authorization issued by the Afssaps.

All this led the SFRL, the Afssaps and the Directorate-General for health to carry out a certain number of works that resulted in May 2009 in a ministerial order dealing with biomedical research on IVDs: the notion of clinical trials then made it possible to clarify matters.
As far as there is no clinical consequence for the patient, no legal classification, there is no declarative obligation or request for authorization from the Afssaps (www.afssaps.fr, "Clinical trials" section).
There are however a certain number of obligations, in the form of a supply contract and bioethical compliance, namely:
- no need for the patient's authorization but the patient can exercise his right of refusal (orally, by poster...);
- anonymization is irreversible;
- the respect of virologic tests (HIV, HCV, HBV) is transferred to manufacturers, and this must be specified in the contract: biologists do not have to perform these tests (see Afssaps documentation on basic research).

This facilitates access to biological samples. It should be noted that, for example, it is possible to "re-collect" a patient in this context. In this case, written authorization from the patient is required.
These simple rules can be used by the in vitro diagnostic manufacturers, but are also accessible to any laboratory which needs to use biological samples for purposes other than strictly the results of the analyses for which these samples were taken.

ROSE-MARIE LEBLANC
Consultant Biologist, Bordeaux (33)
rmleblanc@style-info.com

Source

Communications from industrial members of the SFRL, during the Journées Internationales de Biologie, November 2009.