SUPPORTING INFORMATION TO THE SUPPLIERS' CHARTER ON CLINICAL LABORATORIES SEEKING ACCREDITATION TO EN ISO 15189:2012

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This document has been prepared by the Accreditation Working Group of SIDIV, the French national IVD association in September 2013 and has been translated with the agreement of SIDIV.

PREAMBULE

"ISO 15189:2012 Standard" in context

According to the order of 13 January 2010 and Law n°2013-442 of 30 May 2013 on a general reform of medical biology, all French medical laboratories will have to be accredited in accordance with EN ISO 15189 standard in order to be able to carry out their activities.

EN ISO 15189 standard on "*Medical laboratories — Requirements for quality and competence",* internationally recognised since 2003 – acts as the accreditation reference for medical laboratories and specifies the quality and competence requirements that laboratories have to meet. It is intended to be used in all disciplines practiced by those laboratories.

It includes requirements concerning patient preparation and identification, collection, transportation, storage, processing and examination of clinical samples, together with subsequent validation and interpretation of results, release of examination results with corresponding counselling when ensuring safety of personnel and respect of ethical principles.

EN ISO 15189:2012 standard in one hand and EN ISO 9001 and EN ISO 13485 standards on the other hand

EN ISO 15189:2012 standard on *"Medical Laboratories - Requirements for quality and competence"* shares a number of similarities with the other quality system certification standards, in particular EN ISO 9001 on *"Quality Management Systems – Requirements"* and EN ISO 13485 on *"Medical Devices - Quality management systems - Requirements for regulatory purposes"*: quality policy, objectives, management review, training of the personnel, corrective and preventive actions, documentation controls, quality manual, internal audits, management of non-conformities, continuous improvement, etc.

Role of IVD suppliers

EN ISO 15189:2012 standard lays down the requirements for medical laboratories and is not applicable to suppliers of in vitro diagnostic (IVD) medical devices.

For many years, IVD suppliers have been implementing quality management systems (QMS) on a voluntarily basis. Following the publication of the IVD Directive 98/79/EC, they have been legally obliged to operate within the European regulatory framework. Meeting CE marking requirements is based on the solutions implemented to meet the essential requirements of the directive and provided by the European harmonized standard but also on the implementation of a QMS.

Today, due to the accreditation of medical laboratories in France, IVD suppliers are being called upon by laboratories for assistance with their accreditation procedure in accordance with EN ISO 15189:2012 standard.

Document objectives

This document is intended for IVD suppliers to provide an explanation of the requirements applicable to accredited medical laboratories. It enables them to assess the relevance of the questions received from laboratories and to consider, in a consensual way, the possible responses.

The chapters, paragraphs and clauses of the EN ISO 15189:2012 standard have been examined thoroughly by the Accreditation Working Group of SIDIV, the French IVD industry association. They have been assessed with regards to the regulatory requirements linked to CE marking and the associated harmonised standards, taking into account the requirements of the quality system certification standards, EN ISO 9001 and EN ISO 13485.

Explanations have been provided with considerations to the current knowledge and practices and to the applicable regulation.

Apart from this document, the EDMA Position Paper on Laboratory Accreditation (published in October 2007) gives an overview of the challenges associated with medical laboratories' accreditation and clarifies some of the ways in which the IVD industry can assist laboratories in achieving accreditation.

The work done here has made it possible to select the requirements of EN ISO 15189:2012 standard for which IVD suppliers can legitimately provide assistance to medical laboratories with their accreditation procedure.

For IVD suppliers

This document is a training tool intended to ensure that laboratories understand the application of EN ISO 15189:2012 standard. It also provides support in drawing up and substantiating the responses given to laboratories.

Each company will be able to transpose it into its own organisation.

For medical laboratories

This document explains to laboratories what contribution the suppliers can make to assist them with their procedure.

Suppliers meet quality and regulatory requirements on a daily basis. They can therefore share their experience with laboratories as they engage in the procedure.

For participants in the accreditation procedure

This document can be used to explain to those involved in the accreditation process (national accreditation bodies, auditors, etc.) which resources are available from IVD suppliers in terms of their specific regulations and quality practices; this will ultimately allow to take part in the harmonisation of the auditing practices.

This document is available for EDMA members with the agreement of SIDIV, the French IVD association.

Summary of standard & Chapter	SUPPLIERS SUPPORT
ESQ 1. Field of application	--
	EN ISO 15189:2012 standard is exclusively intended for medical laboratories; it does not specify any binding requirements for IVD suppliers.
	It specifies the requirements for the assessment of their competence and adherence to their quality management system.
ESQ 4.1. Organisation and management	
4.1.1	
4.1.1.3 b) & c) Conflicts of interest and financial relations with companies	Relations between suppliers and health professionals at large (doctor or pharmacist, technician, nurse, etc.) are regulated by national legislations relative to transparency on advantages granted by firms producing or marketing products with health-related purposes and intended for human being (e.g. in France, Sunshine Act 2013-414 of 21 May 2013) . The EDMA code of ethics provides a general framework for IVD companies in this regard.
4.1.1.3 e) protection of confidential information	Signatories to the Suppliers' Charter have a confidentiality policy, which is laid down in this charter (EDMA has adopted the Supplier's Charter which was originally developed by the French national association SIDIV. This document was found very useful for other countries by EDMA and was translated in English after the agreement with SIDIV to circulate it to all the EDMA members). This undertaking commitment is made either by adhering to the EDMA charter, or by means of signing a letter of commitment on confidentiality; for such purpose, SIDIV has made available a letter form.
4.1.1.4 c) staff training	Suppliers can offer device training courses to users. Courses may take place on user site and/or on the premises of the companies, once requirements for course participation have been drawn up. A certificate of attendance/training certificate will be issued to attendees/participants at the end of the training courses. If the training effectiveness is assessed, results can be communicated to the laboratory. These documents can be used for the qualification of the personnel. Personnel qualification remains under the sole responsibility of the laboratory.
4.1.1.4 e) Ensuring laboratories with a safe environment	The environmental conditions of use of the reagents and instruments are described in the documentation provided by the manufacturers (instructions for use (IFU), user manual, requirements for installation, etc.), safety data sheet (SDS), instrument decontamination procedures….) The need to separate incompatible activities is stated in the Instructions For Use.

4.1.1.4 h) Selecting and monitoring suppliers	Laboratories shall assess their suppliers. IVD suppliers are critical suppliers. Suppliers can supply to customers their quality manual intended which includes a description of the services they provide, and of the implementation of their quality system requirements. The maintenance charter stipulates that: - Suppliers having signed the charter undertake "to have maintenance carried out only by duly trained professionals approved by the manufacturer or the authorised distributor of the instrument". - Qualification of the maintenance personnel helps meeting the suppliers' quality certification requirements. - In case the after-sales services are subcontracted, suppliers are responsible for ensuring that the subcontractor fulfils the requirements listed above.
ESQ 4.3 Document management	
Procedures for managing documentation from internal and external sources	Laboratories are responsible for the control of their documentation. There are two types of documents: internal and external documents. The three types of external documentation from suppliers address their products (IVD), their organisation (Quality Management System: QMS) and their services : **1/ Product documentation** Documents provided with products comply with the IVD Directive 98/79/EC and therefore with the requirements of the harmonised standards and of the current regulations. These documents are approved upon by the suppliers' regulatory affairs services, so as to ensure that the specifications stated do correspond to the data in the CE marking dossier. The CE conformity marking affixed on the instruments, the packaging and the instructions for use is a proof of CE marking and therefore of their compliance with the requirements of the IVD Directive 98/79/EC. There is thus no reason for the manufacturer to provide declarations of EC conformity. **2/ Organisation** If necessary, suppliers may provide: • A copy of EN ISO 9001/EN ISO 13485 certificates, • A brief description of its QMS in the form of a "Quality Manual intended to customers", • The supplier evaluation questionnaire, which provides laboratories with essential information. **3/ Services provided and contracts** All records provided for by suppliers further to an intervention and or training, as well as contracts signed between the two parties must be kept by laboratories.
Retention period of records	Laboratories shall manage their records; some instruments provide solutions to do so. If not, laboratories shall draw up a specific procedure, such as generating printouts of all records related to with record keeping rules. These printouts will provide access to data in case the instrument is change.

ESQ 4.8. Resolution of Dealing with complaints	
Determination of the complaints management policy and procedures. Management of records and corrective actions	Laboratories shall draw up a complaint management policy. This includes the management of incidents with potential adverse consequences, which falls within the context of vigilance, a regulatory obligation common to both suppliers and laboratories. Laboratories are responsible for the management of all records.

ESQ 4.13. Quality records and technical records	
The laboratory is responsible for the management of all records.	
Retention period of records	Retention period of records Laboratories shall manage their records; there exist some tools to do so. If not, laboratories shall draw up a specific procedure, such as keeping printed version of all records of analyses conducted for a minimal period of 18 months. Such a procedure will be beneficial in the event of change of tools.
4.1.3 b) **Records of staff training**	Suppliers can offer training courses to users of their devices. Courses may take place on site and/or on the premises of the companies, once requirements for course participation have been drawn up. A certificate of attendance/training certificate will be issued at the end of the users' training courses. If suppliers assess the training course, results can be sent to laboratories and used in order to contribute towards rating those involved. Authorisations issues to staff remains under the sole responsibility of laboratories. Refer to 4.1.14 c) and 5.1.9.
4.13 e) **Lot documentation, certificates of supplies, package inserts, product documentation, notices**	**1/ Batch/Lot documentation** In accordance with the CE marking requirements, all products are checked and released once suppliers demonstrate conformity. Therefore, laboratories do not need to obtain batch release certificates. They are kept by manufacturers and presented to competent authorities in the event of an incident and upon request. The "CE" conformity marking affixed on packaging and instructions for use serve as proof. **2/ Stability studies** In the context of CE marking, stability studies are carried out in accordance with the requirements of EN ISO 13640 standard. Real-time and in-use stability studies including simulated transport conditions are used to determine: • the limits of product storage conditions and stability over time; • the limits of transport conditions for all devices, in particular for those to be stored at controlled temperature. Conclusions of the studies shall be reported in the instructions on conditions of transport, storage and use of the reagent.

	The raw data of the studies are included in the CE marking technical dossier and are, as such, confidential. Should an incident occur, the quality control results shall attest the device performance is maintained. The use of products beyond their expiry date is in breach of the regulations and manufacturers cannot be held liable. **3/ Circulation and updates: instructions for use, manuals, material safety data sheets** According to the MEDDEV 2.14/3 paper on "IVD Guidance: Supply of Instructions For Use (IFU) and other information for In-vitro Diagnostic (IVD) Medical Devices - A guide for manufacturers and notified bodies", Instructions For Use may be provided on a medium other than paper, e.g. in electronic format (CD, internet). Were IFUs are only supplied by electronic means, a contact number will be provided for free of charge access. Suppliers must have in place a system to inform client/customer of any significant change affecting the examination procedure and/or the performances (mail, sticker, e-mail, etc.). Availability of the valid version of the instructions for use is ensured by the suppliers all along the marketing period of the product batch. Laboratories are responsible for managing and archiving IFUs, manuals and material safety data sheets. Material safety data sheets as required for dangerous products are systematically made available to users. **4/ Bibliographical references** Relevant bibliographical references must be included in the Instructions For Use and user manuals (EN ISO 18113-2 7.19 or EN ISO 375 § 5.18). Copyrights restrict the transmission of publications by the suppliers.
4.13 i) Records of instrument maintenance, including records of internal and external calibration.	**1/ Maintenance** IVD suppliers must provide maintenance reports as a result of their maintenance activities. **2/ Calibration** ***a/ CE marked IVD instruments provided by the IVD industry:*** According to the French guide intended for laboratories ('Guide de métrologie à l'usage des laboratoires d'analyses de biologie médicale LABM'), instruments are considered as black "boxes". Manufacturers are responsible for ensuring the metrological quality of the internal elements of those instruments. Quality control procedures conducted by laboratories enable them to ensure the instrument is operating as expected or properly. ***b/ Calibration of the device*** Whenever an IVD is calibrated by the manufacturer, instructions on the calibration and readjustment are included in the suppliers' documentation and laboratories should follow recommendations. Laboratories should keep a record of these operations. ***c/ After-sales service technicians' measuring instruments*** Depending on their impact on the quality of the results, measuring instruments used by technicians shall undergo metrological control (verification/calibration) to meet the requirements of Chapter Clause 7.6 ("*Control of monitoring and measuring devices"*) of EN ISO 9001 standard. The metrology unit or the person in charge of metrology should implement the relevant actions (adjustment / repair / declassification /) further to a failing verification of measuring instruments subject to metrological follow-ups. The management of the equipment shall be checked during audits of the supplier's quality management system. Suppliers should provide an EN ISO 9001/EN ISO 13485 certificate as a proof of such

	management. In both cases, no specific document or certificate has to be provided to justify metrological control of the measuring instruments.
ESQ 5.1. Staff	
5.1.2 & 5.1.9	
Personnel qualifications **Personnel records**	Suppliers can offer training courses to users of their devices. Courses may take place on site and/or on the premises of the companies, once requirements for course participation have been drawn up. A certificate of attendance/training certificate will be issued at the end of the users' training courses. If suppliers assess the training course, results can be sent to laboratories and used in order to contribute towards rating those involved. Authorisations issues to staff remains under the sole responsibility of laboratories.
ESQ 5.2. Premises and environmental conditions	
5.2.2	
5.2.2 c) Facilities and environment / Laboratories and offices.	**1/** Suppliers may indicate installation requirements and conditions of use of their devices. **2/** In order to protect the persons (other than users) who can be in contact with medical laboratory instruments (persons external to the laboratory: maintenance technicians, transportation personnel…) it is necessary and required to decontaminate the instrument and all the associated devices before intervention or handling, in accordance with the suppliers' recommendations. Heads of laboratories must identify the level of risk linked to their activity (HIV, mycobacteria, prions, etc.) and inform externs to their laboratory. Heads of laboratories must provide external persons with a document certifying that the decontamination was carried out by the laboratory staff before their intervention. - The declaration of decontamination must accompany the instruments and contain the following: name of the equipment and serial number; - protocol used; - Name of the person responsible for decontamination
5.2.3	
Storage facilities	The environmental conditions in which reagents and instruments are used, are described in the manufacturer's documentation (user's guides, notices and/or in the prerequisites for installation, etc.). The need to separate incompatible activities is stated in the Instructions For Use.

5.2.6	
Facility maintenance and environmental conditions	Please refer to 5.2.3: Storage facilities.
ESQ 5.3. Laboratory equipment	
5.3.1	
5.3.1.1 Holding equipment required for services laboratories provide. **Using equipment outside its constant control.** **Taking into account the environment when selecting equipment**	**1/ Installation** Upon installation, suppliers shall provide laboratories with a document certifying the qualification of the instrument in accordance with specifications and procedures on qualification, drawn up by supplier, as well as the corresponding records. **2/ Preventive maintenance** After preventive maintenance, suppliers shall provide laboratories with a document certifying the qualification of the instrument in accordance with specifications and procedures on qualification, drawn up by the supplier, as well as the corresponding records. **3/ Qualification after repair** Suppliers' staff shall assess the criticality of the malfunction observed and, depending on the importance of the maintenance operation to be undertaken, qualifies the system in accordance with the specifications and procedures on qualifications further to corrective maintenance operation drawn up by the manufacturer. The certificate and corresponding records to laboratories shall be provided to the laboratory.
5.3.1.2 Equipment acceptance testing	***Qualification* /Verification/Validation** The fundamental criteria describing the method are included in the CE marking technical dossier are determined by the manufacturer. If reagent kits and systems are strictly used under the conditions described by manufacturers in the Instructions For Use, the methods laying out how to use these kits and systems shall be considered "standardised" methods. In that case, laboratories shall only verify the implementation of the methods in their own environment in comparison with their own pre-established criteria and specifications. Suppliers or manufacturers shall indicate the performances of their methods in the Instructions For Use. **Note**: IVDs without CE marking or with CE marking but modified or developed by the laboratory must be validated by the laboratory. The qualification of an analytical system must be distinguished from its validation and verification. See Clause 5.5.1. When installing an analytical system, or further to a maintenance requiring such installation, the supplier shall ensure the qualification of the analytical system by verifying its performances and/or functioning against specifications previously drawn up. ***1/ Installation qualification:*** Upon installation, suppliers shall provide laboratories with a document certifying the qualification of the instrument in accordance with the specifications and installation qualification procedures drawn up by manufacturers, along with the corresponding records.

	2/ Qualification after intervention: Suppliers' staff members shall assess the criticality of the malfunction observed and, depending on the importance of the maintenance operation to be carried out, rate the system in accordance with the specifications and practices of the Functional validation Rating procedures – drawn up by manufacturers – to be carried out further to a corrective maintenance. Suppliers shall then provide laboratories with a certificate and the corresponding records. ***3/ Qualification after update:*** Suppliers shall provide information on the operations performed when updating systems (instruments and software) describing the updating procedures and any potential impacts.
5.3.1.3 **Equipment / Instructions For Use**	IVD suppliers shall provide their clients with an up-to-date documentation (Instructions For Use, user manual, notices, etc.). A new version, a corrected version of or an addendum to (information, post, etc.) the user's guide shall be made available to the user further to any major modification of a system, which can have impacts on the user-machine interface and/or on the application of new maintenance instructions. Additional documents to consult: Material safety data sheet / Decontamination procedures. See Clause 5.2.3 Installation requirements. SIDIV has prepared a form for a letter setting out transport and storage conditions.
5.3.1.4 **Equipment calibration and metrological traceability**	Regarding quantitative methods, the metrological traceability of the value assigned to the standard is mandatory according to the requirements set out in the IVD Directive 98/79/EC. Reference methods or materials selected by manufacturers are provided in the Instruction For Use. There is no metrological traceability need for the value assigned to internal quality controls, as these are not intended to directly assess the accuracy of the results (comparison group). Such exemption is described in the scope of application of EN ISO 17511 standard *("In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and control materials."*), and the values assigned to control materials are for information only. In fact, traceability of results of this type of internal quality control, effectively obtained in the laboratory, is the same as that of the patients' results. Laboratories shall determine their calibration and maintenance policy, taking into account manufacturers' recommendations. **1/ CE marked IVDs** The validation (CE marking) carried out by IVD manufacturers which have been selected by laboratories, ensures that device performances are in line with laboratories' needs. As regards to metrological characterisation, the metrology guide for the use of laboratories – published by the *Collège Français de Metrologie* (French Metrology Body) – considers that measurements made by automatic analysers can be guaranteed by quality management measures, such as internal and external quality control (use of witnesses, inter-laboratory comparisons, etc.). Note: reagents/techniques developed in laboratories must be validated in full by their users. **2/ After-sales service technicians' measuring instruments** Depending on their impact on the quality of results, the technicians' measuring instruments shall undergo metrological confirmation (verification/calibration) to meet the requirements set out in Chapter 7.6 (Control of Monitoring and Measuring Equipment) of EN ISO 9001/ EN ISO 13485 standards. The metrology unit or the head of metrology shall take the relevant measures (adjustment / repair / declassification / modification) further to

	a defective verification of measuring instruments having undergone a metrological follow-up. Control procedures shall be checked during audits of suppliers' quality management systems. EN ISO 9001/ EN ISO 13485 standards' certificates provide proof of this control. In both cases, no specific document or certificate is required to justify metrological checks carried out on instruments. For further information, please refer to clause 4.13 i) 'Records of instrument maintenance, including records of internal and external calibration'**.**
5.3.1.5 Equipment maintenance and repair	**1/Preventive maintenance** The objective of preventive maintenance is to ensure that equipment retain their optimal reliability. Maintenance must be carried out with a frequency determined by manufacturers, within a defined interval [indicating maintenance intervals (e.g. + or – 1 month), is preferable to set dates.]. • Maintenance programme: shall define the maintenance programme based on the system design, and possibly on feedback on experience gained. • List of maintenance tasks to be performed by operators and after sales services: the distribution of maintenance tasks between users, laboratory operators and suppliers shall be defined by manufacturers, in relation to the system design and possibly, to feedback on experience gained. • Suppliers shall provide laboratories with a document certifying the functional validation rating of instruments in accordance with the functional validation rating specifications and procedures, further to a preventive maintenance drawn up by manufacturers, in conformity with manufacturers' data and corresponding records (checklist of what has been done, signed by both the technician and the client). **2/ Equipment safety** For systems: CE marking implies compliance with all the applicable safety directives and regulations. For reagents: suppliers shall make available the material safety data sheets for products containing hazardous substances, the decontamination procedure and the user maintenance procedures. **3/ Managing contamination risks of defective equipment** To guarantee the safety of all people working on medical laboratory systems (e.g. external participants, maintenance technicians, biomedical engineers, transporter …), laboratories must decontaminate instruments before use or manipulation, in accordance with suppliers' recommendations. Heads of laboratories must identify the level of risk linked to their activity (HIV, mycobacteria, prions, etc.) and inform externs to their laboratory of it. Heads of laboratories must provide external participants with a document certifying that the decontamination was carried out by the laboratory staff before their arrival. - A declaration of decontamination must be provided with instruments and contain the following: name of the equipment and serial number; - used protocol; - Name of the managing authority responsible for decontamination The decontamination certificate must be duly dated and signed. **4/ Management of equipment repaired or serviced outside the laboratory** After each intervention (preventive or corrective maintenance), suppliers' staff members shall carry out the tests as prescribed by manufacturers (adapted to the type of the intervention). Suppliers shall demonstrate that the results of these tests are within

	manufacturers' acceptance limits. Laboratories shall keep evidence of the conformity of these tests. Laboratories shall follow their usual re-starting procedures.
5.3.1.6 Report on adverse events	Laboratories shall establish a complaints management policy. This includes the management of incidents with potential adverse consequences, which falls within the context of vigilance, a regulatory obligation common to both suppliers and laboratories. Laboratories are responsible for managing all records.
5.3.1.7. Records of equipment	Laboratories are responsible for managing all records. After each intervention (preventive or corrective maintenance), suppliers' staff members shall carry out the tests as prescribed by manufacturers (adapted to the type of the intervention). Suppliers shall demonstrate that the results of these tests are within manufacturers' acceptance limits. Laboratories shall keep evidence of the conformity of these tests. Laboratories shall follow their usual re-starting procedures. When interventions are carried out by telephone, suppliers shall be responsible for providing clients with the technical assistance necessary for the proper use of IVDs in laboratories. However, suppliers will not be able to check that the recommended actions have been properly carried out by laboratories' staff. In order to comply with good practices, suppliers and clients shall each keep their own records. They may be compared if necessary. Laboratories shall validate the implementation of corrective actions and ensure that they are recorded. The importance of validation will depend on the criticality of the intervention (risk analysis). There are two cases of remote maintenance: • Simple consultation • Remote intervention. In any case, suppliers shall abide by the ethical rules on confidentiality and must obtain laboratories' agreement. Traceability, for remote interventions, is needed and reports must be sent to laboratories. Should an incident occur following a remote maintenance operation/intervention, manufacturers must be able to indicate which actions were taken during the operation/intervention.
5.3.1.7 i) Undertaken or programmed maintenance	Once the equipment has been installed, and after each intervention (preventive or corrective maintenance), suppliers' staff members shall carry out the tests drawn up by manufacturers (adapted to the type of the intervention). Suppliers shall demonstrate that the results of these tests are within manufacturers' acceptance limits. Laboratories shall keep evidence of the conformity of these tests. Laboratories shall follow their usual re-starting procedures.
5.3.1.7 j) Equipment performance records confirming that equipment is fit for purpose	Records should also include documents concerning functional validation of systems upon installation, upon validation/verification, when being put into service and when used on a routine basis (quality control) and concerning functional validation further to a preventive and corrective maintenance activities/intervention.

k) any damage to, or malfunction, modification or repair of, the equipment	Same as i).
5.3.2 Reagents and consumables	
5.3.2.1 Inventory Stocks and records management **5.3.2.5 Reagents and consumables – Instructions For Use**	Each device shall bear a batch number / serial number and an expiry date, if applicable. Within the scope of CE marking, suppliers shall ensure the traceability of the devices until they are delivered to laboratories. Stability studies: Within the scope of CE marking, stability studies are carried out in accordance with the requirements of EN ISO 13640 standard. Stability studies on real-time use of reagents and on simulated transport conditions are used to determine: • the limits of product storage and stability conditions over time, • the limits of transport conditions for all devices, in particular those which need to be stored at controlled temperature. Conclusions reached in these studies shall be reflected in the instructions regarding the conditions of transport, storage and use of the reagent. The raw results of these studies are included in the CE marking technical dossier and are, as such, confidential. Should an incident occur, the quality control results will confirm that the device performances have been maintained. The use of products beyond their expiry date is contrary to the regulations and manufacturers cannot be held liable.
ESQ 5.4 Pre-examination analysis procedures	
5.4.4.2. Specific instructions for the proper collection on taking and handling of samples	IVD manufacturers shall indicate in the Instructions For Use: - the nature of the biological environments for which the technique has been validated, - if appropriate, specific handling and storage conditions of samples to be examined. Such information has to be looked at in conjunction with the instructions provided by the suppliers' of the collection devices.
5.4.7	
Pre-examination handling, preparation and storage	For some parameters and under defined conditions, IVD manufacturers may indicate, in the device Instructions For Use, specific sample handling conditions for the purpose of retest.
ESQ 5.5 Examination Analytical procedures	

5.5.1	
5.5.1. Selection, validation and verification of analytical examination procedures	Validation procedures must be as thorough as necessary, bearing in mind the scope of accreditation. • **Flexible Scope A**: implementation of methods regarding the use of CE marked IVDs and based on technical competence previously demonstrated by laboratories. NB: laboratories can change suppliers within this context. • **Flexible Scope B**: adaptation (modification) or development of methods regarding the use of CE marked IVDs. Both scopes of method may be found in the same laboratory. IVDs that comply with the requirements of the IVD Directive 98/79/EC (CE marking) shall be considered "standardised"; the validation having been carried out by manufacturers, the user shall verify the performances of the devices. Documents provided with the products should comply with IVD Directive 98/79/EC and therefore with the requirements of the harmonised standards. These documents shall be approved upon by the suppliers' regulatory affairs services, so as to ensure that the stated specifications do correspond to the data in the CE marking dossier. For CE marked devices, laboratories shall carry out a mere verification in their own environment. 1/ Laboratories shall first read the information provided by manufacturers (Instructions For Use, bibliographical references…) and assess it in the light of: • Recommendations or regulatory texts, • Performance criteria drawn up by professional associations, • Expectations of persons prescribing IVD examination. 2/ in a second step, the verification itself shall then be carried out in laboratories. As laboratories use CE marked IVDs, the performance criteria of these devices shall have been determined by manufacturers (e.g. in line with the Common technical specifications for the products in Annex II, list A of the IVD Directive 98/79/EC). Laboratories shall therefore only check the implementation in their own environment by making sure that the acceptable performance criteria they have set, in order to meet the needs of their clients, are fulfilled. 3/ Finally, this verification shall continue through quality control. IVDs without CE marking or with CE marking but modified or developed in laboratories, shall be validated by laboratories. In any case, laboratories are responsible for verification/validation.
5.5.1.4 Measurements uncertainties and measured variables	Laboratories are responsible for determining the measurement uncertainty of results (quantity values). The aim of such an assessment is to determine uncertainties specific to laboratories, so that the latter can judge how appropriate are the chosen measuring methods with regards to clinical requirements on the one hand, and to their implementation *in situ* (in their natural or original position or place) on the other hand. There is currently a consensus in Europe on how to determine measurement uncertainty in medical laboratories, which is set out in the EDMA position paper on Estimation of Uncertainty of Measurement in Medical Laboratories, published in September 2006, and included in that of SIDIV in 2010. In this respect, uncertainties regarding the calibration value of a quantitative method shall be provided upon request.

5.5.2	
Reviewing biological reference intervals	Manufacturers shall provide their biological reference intervals along with the reference population used to establish them. Laboratories shall check the relevance of the application of these biological reference intervals to the laboratory's patients.
5.5.3	
Documentation on of analytical examination procedures	Documents provided with products should comply with IVD Directive 98/79/EC and therefore essentially with harmonised standards' and current regulations' requirements. These documents shall be approved upon by the suppliers' regulatory affairs services, so as to ensure that the specifications stated do correspond to the data in the CE marking dossier.
Calibration procedures modes (metrological traceability)	Regarding quantitative methods, the metrological traceability for the calibration reference value is mandatory according to the requirements set out in the IVD Directive 98/79/EC. Reference methods or materials selected by manufacturers shall be provided in the Instruction For Use. The measurement uncertainty of the standard of value may be provided upon request. The uncertainty regarding the calibration value is provided upon request.
ESQ 5.6 **Ensuring the quality of examination analytical procedures**	
There are two sources of internal quality control (according to the COFRAC definitions): - **Kit QC (QC material)**: internal quality control material developed and manufactured for the specific assessment of an in-vitro diagnostic kit and usually provided with it. - **Independent QC (QC material)**: Internal quality control material developed and manufactured independently of any in-vitro diagnostic kit and supplied separately. - **Internal quality control (internal quality assessment or IQA):** procedure carried out in laboratories, along with measurement of patient specimens, to assess whether the analytical system is working properly, within the predetermined tolerance limits. The internal quality control materials are those used in this context. - **External quality control (external quality assessment or EQA):** laboratory performance assessment procedure involving an inter-laboratory comparison carried out by a third-party organisation. The external quality control materials are those used in this context.	
5.6.2	
The QMS shall include internal quality control and participation in inter-laboratory comparisons.	Quality control: Clinical biologists shall bear sole responsibility for choosing and drafting (internal and external) analytical quality control protocols. However, should manufacturers indicate a frequency within which these quality control operations should be carried out, the given frequency will constitute a minimum requirement. When implementing these operations, it is important to clearly identify: • The protocols aimed at ensuring that the analytical performances of the system remain within their range of natural variability. This is usually done by following up the average and the standard deviation actually obtained in laboratories, in order to identify any loss of control in the system (drift, etc.); • The protocols aimed at ensuring that specific analytical objectives are achieved for the given examinations, such as follow-ups on standard deviation and total error as compared to predetermined objectives (e.g. Ricos, SFBC, etc.),

	depending on the use of parameters, their biological variability or state of the art. These objectives are usually determined when the method is verified. Clinical biologists shall bear sole responsibility for choosing the type of internal quality control. Should an investigation proved necessary, controls recommended by manufacturers will be used to demonstrate anomalies. Control materials shall be representative of patients samples with regards to the composition (matrix) and the measuring interval that need to be considered. Clinical biologists shall bear sole responsibility for choosing the type of control. There is no obligation made to suppliers to provide an internal quality control with IVDs. Should laboratories have several analytical instruments or analytical methods for the same test, they shall provide evidence via their internal quality control programmes that the results provided by these various instruments or methods are comparable, if appropriate, at several levels.
5.6.3	
Obligation to take part in inter-laboratory comparisons	EN ISO 15189 Standard requires participation in inter-laboratory comparisons (ad hoc external controls or inter-laboratory comparisons of internal quality control data).Laboratories shall have the quality of medical biology test results they carry out, checked by external quality assessment bodies. Those bodies shall send to the AFSSAPS an annual report, the content of which will be determined by a decree (not yet published) issued by the ministry of health, at the proposal of the director general of the AFSSAPS. The AFSSAPS shall publish an annual summary of these reports. Laboratories concerned and external quality assessment bodies shall immediately report to the National Competent Authority any anomalies detected during the control process, if likely to cause serious risks for patient health (risks not yet defined). The frequency of participation and the intervals of acceptability of the results shall be defined by decree (not yet published), and based on professional associations' recommendations. The national quality control undertaken by the AFSSAPS is also mandatory.
5.6.3	
Comparability of examination results	Laboratories shall assess the comparability of the results obtained for the same measure and used on different analysers, with different procedures or on different sites. Measurement results, which are metrologically traceable to a same reference, shall be considered comparable.
ESQ 5.7 Post- examination procedures	
5.7.2	
Samples storage	For certain parameters and under certain conditions, IVD manufacturers may indicate, in the Instructions For Use, specific sample storage conditions for the preparations' (re-)dosage.
5.10 Laboratory Information management	
5.10.1	

General considerations	Signatories to the Suppliers' Charter have a confidentiality policy, which is laid down in this charter. This commitment is either made by adhering to the EDMA charter, or by means of submitting a letter of commitment on confidentiality; for such purpose, SIDIV has made available a letter form.
5.10.2	
Authorities and responsibilities	Some systems can offer solutions using hierarchies of access levels, for which passwords are required. If this is not the case, laboratories shall draw up authorisation policies.
5.10.3	
Management	Software programs installed on IVDs shall be validated by manufacturers, under the CE marking conditions. Manufacturers shall ensure the integrity of the results produced by the systems' computers. Some systems can offer solutions using hierarchies of access levels, for which passwords are required. If this is not the case, laboratories shall draw up authorisation policies.
5.10.3 a) Validation	The validation (CE marking) carried out by IVD manufacturers which have been selected by laboratories, will help ensure that device performances are in line with laboratories' needs. Device performances shall remain in line with laboratories' needs whenever there is a change in software. Suppliers shall mention the extent of the CE marking on IVD analysers.
5.10.3 b) Documentation	Documents provided with products should comply with IVD Directive 98/79/EC and therefore essentially with harmonised standards' and current regulations' requirements. These documents shall be approved upon by the suppliers' regulatory affairs services, so as to ensure that the specifications stated do correspond to the data in the CE marking dossier. IVD suppliers shall provide their clients with an up-to-date documentation (Instructions For Use, user manual, notices, etc.). A new version, a corrected version of or an addendum to (information, post, etc.) the user's guide shall be made available to the user further to any major modification of a system, which can have impacts on the user-machine interface and/or on the application of new maintenance instructions.
5.10.3 e)	The environmental conditions, in which reagents and instruments are used, are described in the manufacturers' documentation (user guides, Instructions For Use and/or requirements for installation, etc.).