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The adoption of good laboratory practice principles by Italian test facilities

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Summary. - The principles of good laboratory practice (GLP) can be considered as a code of general behaviour potentially applicable to all experimental studies, although they were first conceived for harmonizing the conduct and assessment of toxicological tests designed to evaluate the impact of chemical substances on human health and the environment. From a general standpoint, therefore, GLP criteria aim at generating credible, comparable and cost-effective experimental information that can in turn make the decision-making process easier and sounder. On the other hand, of equal importance at the global level is the availability of and access to the wealth of critically assessed, self-consistent chemical data thus produced. Under both respects a key role is played by the activities undertaken under the aegis of international bodies such as the Organisation for Economic Co-operation and Development (OECD), the Commission of the European Union (CEU) and the International Register of Potentially Toxic Chemicals of the United Nations Environment Programme (IRPTC-UNEP). This cultural and scientific humus has been incorporated into legal provisions by most industrial countries to regulate production and commercialization of chemical substances. As regards Italy, the act DLvo no. 120 of 27 January 1992 focuses on the adoption of GLP principles by national test facilities and covers all possible categories of chemicals, namely industrial substances, pharmaceuticals, cosmetics, pesticides, food additives and still others. Accordingly, the compliance status with GLP principles of a test facility is ascertained by inspections carried out by public officers following a detailed procedure which will eventually result in the above acknowledgement provided that no major deviations in the laboratory performance are detected. So far, twenty-four centres have been inspected by Italian authorities and found to be in compliance. This led to their inclusion in the CEU official list of test facilities abilitated to carry out GPL studies in the twelve member states.

Key words: good laboratory practice principles, test facilities, compliance status, inspections, physical-chemical tests, toxicological tests, ecotoxicological tests.

Riassunto *(Adozione dei principi di buona pratica di laboratorio da parte dei centri di saggio italiani).* - I principi di buona pratica di laboratorio (BPL) possono essere considerati un codice di comportamento generale potenzialmente applicabile ad ogni studio sperimentale, anche se in realtà sono stati per la prima volta concepiti per armonizzare l'esecuzione e l'interpretazione di saggi tossicologici destinati a valutare l'impatto delle sostanze chimiche sulla salute e sull'ambiente. Pertanto, da un punto di vista generale, i criteri di BPL mirano a generare informazioni sperimentali attendibili, confrontabili ed ottimizzate sotto ogni profilo che possano a loro volta rendere più semplice ed efficace il processo decisionale. D'altro canto, uguale importanza a livello globale è rivestita dalla disponibilità di dati chimici criticamente rivisti e coerenti tra loro che vengono ad essere così prodotti. Sotto entrambi i profili svolgono un ruolo fondamentale le attività intraprese a cura di strutture internazionali, quali l'Organizzazione per la Cooperazione e lo Sviluppo Economico (OCSE), la Commissione dell'Unione Europea (CUE) ed il Registro Internazionale delle Sostanze Potenzialmente Tossiche del Programma delle Nazioni Unite per l'ambiente (RISPT-PNUE). Tale humus culturale e scientifico è stato incorporato nei provvedimenti di legge della maggior parte dei paesi industrializzati per regolamentare la produzione e la commercializzazione delle sostanze chimiche. Per quanto riguarda l'Italia, il Decreto legislativo n. 120 del 27 gennaio 1992 disciplina l'adozione dei principi di BPL da parte dei centri di saggio nazionali e copre tutte le possibili categorie di sostanze, dai prodotti chimici industriali ai farmaci, ai cosmetici, agli antiparassitari, agli additivi alimentari ed altro ancora. In accordo a ciò, lo stato di adeguamento di un centro di saggio ai principi di BPL viene accertato tramite ispezioni condotte da funzionari pubblici secondo una procedura dettagliata e consolidata che può portare al riconoscimento suddetto qualora non vengano riscontrate inadempienze di rilievo. Ad oggi, ventiquattro centri sono già stati verificati dalle autorità italiane che li hanno riconosciuti come operanti in accordo con i principi di BPL. Questo ha portato alla loro inclusione nell'elenco ufficiale della CUE per i centri di saggio abilitati a condurre studi in regime di BPL nei dodici stati membri.

Parole chiave: principi di buona pratica di laboratorio, centri di saggio, saggi chimico-fisici, saggi tossicologi, saggi ecotossicologici, verifica di conformità, ispezioni.

The overall framework

The mounting evidence accrued in the late 1960's on the noxious consequences of an uncontrolled growth in production of chemical substances as well as of their largely unregulated and haphazard use fostered a number of international initiatives aimed at protecting human health and the environment in a more systematic and conscious fashion without hindering at the same time the necessary economic development and technical progress. The launch of the International Register of Potentially Toxic Chemicals (IRPTC) as a part of the United Nations Environment Programme soon after the 1972 Stockholm conference on the environment as well as the formation of *ad hoc* working groups in the Organisation for Economic Co-operation and Development to deal with the various facets of such problems are only two of the possible examples of approaches set up by scientific institutions to cope with the chemical challenge [1, 2].

Such undertakings are also illustrative of two closely interrelated components that are essential to promote and actuate a sound and cost-effective policy in this field, namely the achievement of a consolidated data network on chemical substances endowed with critically assessed, constantly updated information easily accessible to all interested users on the one hand, and the development of highly harmonized experimental approaches that allow this information to be generated in a credible and comparable way independent of any specific test centre on the other hand.

It goes without saying that these two aspects do complement each other in that the more successfully the latter is accomplished, the more feasible the former is. In the ultimate, their synergistic combination will lead to sounder risk-benefit assessments, which in turn will the design of innovative and adequate regulatory acts. In this context the set of permanently improving criteria known as the principles of good laboratory practice (GLP) can be regarded as a code of general behaviour applicable to all experimental studies. In connection with substantial activities undertaken over the past twenty years to harmonize production, commercialization and risk assessment of new chemicals, this body of rules has greatly paved the way to the correct conduct of investigations, thus allowing for the obtainment of more reliable and reproducible data. The rationale behind all this is a more effective policy for the protection of human health and the environment, which must incorporate strategies of global prevention of the possible and foreseeable adverse effects of the production and use (when not misuse and abuse) of chemical substances, rather than sticking to the curative approach.

What has been achieved through OECD from the late 1970's onward in this respect certainly played a crucial role on the development of the majority of ensuing national regulations [3-5]. In particular, as regards the European Union, the GLP principles worked out by OECD were incorporated in the Council directives 87/18/EEC (18 December 1986) and 88/320/EEC (9 June 1988), the latter focusing on the performance of inspections for the verification of compliance with the said principles of physical-chemical, toxicological and ecotoxicological tests. A third Council directive (90/18/EEC of 18 December 1989) further expanded the scope of the previous regulations by including not only industrial chemicals, but also all other possible categories of substances, from food additives to pesticides, from pharmaceuticals to cosmetics. These provisions are linked, both ideally and operatively, to the parent directive 79/831/EEC (18 September 1979), better known as the sixth amendment, later replaced by the seventh amendment (Council directive 92/32/EEC of 30 April 1992).

In Italy these directives were enforced by means of three acts, namely the DPR 927 of 24 November 1981, the DM of 26 June 1986 and the DLvo 120 of 27 January 1992. The Ministry of Health and the Istituto Superiore di Sanità (Italian National Health Institute, ISS) are responsible for two major aspects of all this activity, i.e. the evaluation of technical dossiers on the one hand and the inspection of test centres which apply for formal accreditation as laboratories adopting the GPL principles in their activities on the other hand. Once accredited, these laboratories are legally authorized to prepare experimental reports on the characteristics and physical-chemical, toxicological and ecotoxicological properties of substances before their commercialization on behalf of a producer wishing to market them in the territory of the European Union. Analogous systems are obviously in operation in all the twelve member states, so that a notifier can resort to whatever test centre in any of these countries with the guarantee that, after its definitive approval, the technical dossier is valid throughout the European Union.

In the ultimate, the overall machinery can be considered the materialization of the tenets concocted by OECD and set forth in a number of booklets publicly available [6-13]. How all this has been accomplished so far in Italy is illustrated in the following section.

Procedural aspects

In the early days, when GLP philosophy and goals were being shaped and consequently it was more and more apparent which duties a country should comply with, Italian public authorities decided to carry out a survey of existing national centres likely to aspire to accreditation at the moment that regulations on this topic would be passed. A questionnaire was thus circulated to more than 1500 test facilities, which had to answer quite

a number of detailed questions ranging from specific fields of activity to instrumental equipment available, characteristics of staff personnel, adoption of safety measures and the like. The response was very encouraging in that approximately 160 replies were received, both from the public and private sector.

The information gathered at that time was probative of a widespread awareness of the rather revolutionary aspects that were being brought about by the new policy for chemicals [14]. It also clearly emerged that most centres declared themselves ready to perform physical-chemical assays (71% of replies), while short-term and long-term toxicity and ecotoxicity test were offered only by a minority (26 and 15%, respectively) of the laboratories. This was not surprising, as less time-consuming and relatively more well-established methods clearly attracted the interest of responders, whereas more complex and yet to be fully evaluated and harmonized procedures were obviously restricted to specialized teams.

A few years later, as both the cultural and scientific humus worked out by OECD and the legal framework set up by the European Communities had to be incorporated into national regulations, it was deemed appropriate to prepare an *ad hoc* manual for GPL officers containing all formal and practical information necessary for the conduct of harmonized and systematic inspections of the candidate test facilities in Italy [15]. Not necessarily to be always followed in each single aspect, this guidebook was rather meant to provide the first small groups of protoinspectors with a defined code of conduct as well as to give assistance in facing ambiguous situations. It also included an adapted version of the questionnaire mentioned above to be forwarded to test facilities, after their formal application for accreditation, with the purpose of collecting all basic data on the centre's organization and capabilities prior to the actual inspection, so as to better finalize this last. The questionnaire in its present form is given in "Annex 1".

Within the legal framework touched upon in the previous section, the main phases of the process presently leading to the acknowledgement to a centre of being in compliance with the GLP principles are those summarized in Table 1. As regards the transmittal of the formal application to the competent authority (namely, the Ministry of Health), this takes place when the management of a given test facility, not yet accredited, deems appropriate for future activities to obtain this acknowledgement. The main prompt in such a decision may well be the awareness that the laboratory can be excluded from a major share of the chemical production business with unforeseeable consequences even on its very survival in the long run. Sometimes, however, the attainment of this status is perceived as an emblem to be exhibited in demonstration of the laboratory performance, independent of whether there are practical reasons to make this necessary in the specific area of interest of the laboratory. It is the task of the competent authority to discriminate between applicants with a minimum set of formal and technical prerequisites and those below this threshold. No definitive rules can be set forth to this aim, although the decision is certainly facilitated by a careful evaluation of the data reported in the questionnaire of "Annex 1".

Table 1. - Principal aspects of a GLP inspection

1. Application of the candidate test facility to the Ministry of Health
2. Evaluation of the preliminary questionnaire with possible inclusion of the test facility in the list of those to be inspected
3. Actual performance of the inspection which includes:
   a) an opening session
   b) verification of the general organization of the centre
   c) check of the operative mode of the quality assurance unit
   d) control of experimental facilities and operative procedures
   e) study audit
   f) debate on the degree of GLP compliance of the inspected centre
4. Preparation of the final report and formal comments by the test facility
5. Decision on the acknowledgement of the compliance status

The receipt of the centre's request by the Ministry of Health, in fact, triggers the subsequent step of the entire itinerary, i.e. the compulsory compilation by the applicant of the survey forms before any conclusion is made on the need for an inspection to be carried out. In the case that the decision is affirmative, the test facility is entered on a chronological list and officially informed that the inspection will take place in due course, provided that a fee is paid beforehand. The charge is fixed by law and is proportional to the complexity of the inspection, primarily to the number of officers necessary to deal with the various scientific fields called for by the applicant. On the other hand, if the centre is not in a position to be visited, motives for the refusal are detailed, which may possibly lead to another, more successful application. When all develops properly, a date is communicated to the centre's management and the inspection can actually be carried out.

As already briefly mentioned above, an inspecting body is formed taking into account the disciplines for which the verification has been requested, so as to have a sufficient number of experts to impartially judge whether the test facility can be considered in compliance with the GLP criteria. The third phase is obviously the most crucial of the overall procedure. Once the inspection starts, it follows a pattern that comprises a number of formal sequential actions. It is the task of the inspectors to clarify the scope and goals of their visit at its very

inception by holding a meeting with representatives of the candidate centre. In this session the legal framework and modes of conduct of the verification are illustrated in detail to the managing staff, namely the legal responsible, the scientific director, the study directors and the head of the quality assurance unit (QAU) at least. Specific requests are then formulated in order to have a room for the confidential aspects of the visit at the disposal of the inspecting team, to obtain access to all places, documents and facilities relevant to the pending accreditation and to receive a concise yet exhaustive description of the centre's activities and organization. This opening session also permits the conformity of the application with the real intentions of the management to be checked. Particular attention is also given on this occasion to the existence of written standard operating procedures (SOPs) for all important aspects of the laboratory operations, such as receipt of substances, proper use of measuring apparatuses, quality assurance programme and the like. That such SOPs are available in all laboratory areas where necessary, that they are periodically revised and that historical files are maintained is to be checked during the inspection itself.

The aperture is then followed by a systematic examination of the procedures adopted to admit, record, store, subsample and assign substances under test, whereby the correctness, confidentiality and reliability of all single acts are carefully scrutinized. In addition to this and further to the *ad hoc* presentation made in the course of the opening session, the practical conduct of the duties pertaining to the QAU is tested step by step. From this standpoint, it may be not out of place to recall that quality control (QC) is only a component, although essential, of QAU: the former, in fact, aims at checking data exactness, while the latter takes into account the overall process through which experimental information has been gained. What the inspecting team has to ascertain in particular is whether the person responsible for the QAU is entirely independent from the study performance, how frequently and in which way study plans, raw data and final reports are audited and to what extent corrective actions are taken when malfunctions or unjustified variations are reported by QAU to the management. This means, among others, that evidence should be provided of free access of QAU to all GLP areas as well as of a prompt and adequate response of the management to the remarks made by QAU.

Subsequently, facilities are carefully evaluated to assess their suitability in terms of dimensions, location and design so as to guarantee appropriate conduct of experimental activities, e.g. by allowing total separation among different studies to be achieved and optimal conditions for animal housing to be attained. As regards instrumental equipments, materials, reagents and specimens, inspectors should reach reasonable certainty about the proper functioning of all apparatuses with adequate records of maintenance, unequivocal labelling and proper storage of chemical products, and identification of samples, each in dependence of its specific origin as well as on the existence of meaningful procedures for the handling and control of test systems necessary for the conduct of the study, be they physical, chemical or biological. An almost endless series of aspects should be listed in this connection, which become of a certain complexity especially when biological test systems are taken into account with the ensuing needs for care, housing, containment and disposal.

Systems in use for safe storage, retention and retrieval of records, reports, plans and specimens are then examined, mainly with the purpose of ascertaining the univocal traceability of all materials back to the corresponding study and their availability for a specified period or, in the case of samples and specimens, as long as preparation quality still makes sense. The detailed information gained up to this stage by the inspectors allow them to proceed to the next step, namely study audits, i.e. an exhaustive review of studies still ongoing or already completed aiming at reconstructing a study from its original design through the relevant SOPs, raw data and stored material. This process may well require to evaluate whether a given study could actually be carried out under the terms formally declared by the management, including time constraints, work assignments and training and experience of personnel, from the study director to technicians.

This phase is generally followed by a meeting restricted solely to the inspectors, in the course of which views are exchanged on the faults and merits of the GLP system in operation at the test facility. This discussion may eventually lead to the identification of a number of more or less serious items capable of impairing the centre's ability to fully comply with GLP requirements. In the ultimate a decision is taken on whether deviations are of minor nature, such as to permit the status of compliance to be granted, or the encountered discrepancies call for a deep revision of the centre's organization before it can be accredited. In the first instance, however, the management should commit to modify faulty structures or procedures as recommended. The centre's representatives are then admitted to the closing session to be informed on the outcome of the inspection, with particular reference to unsatisfactory facets. As a rule, according to the experience of Italian authorities, criticisms and remarks formulated by the inspectors are understood and accepted by the management and an agreement is reached on actions necessary to overcome existing problems. As mentioned above, under such circumstances full guarantee is given by the test facility that all errors will be amended in the shortest possible time. Nor should it be overlooked that in the most serious cases the status of compliance will not be acknowledged and the interested centre will have to thoroughly rethink procedures adopted up to that moment before applying again.

Inspection in itself may be considered concluded with this closing session and inspectors have to prepare, immediately afterwards a written report summarizing what has been ascertained and whether a compliance declaration can be released. Copies of this report go both to the GLP monitoring authorities and to the candidate centre, which, in turn, may lay down counter-remarks (if any) and, most of all, state the willingness to conform with suggestions formulated by the inspectors. In other words, the conclusions of the closing discussion are laid down in a permanent form by both counterparts. In the present legal framework a declaration is finally issued to acknowledge the compliance status of the test facility. This can be thus included in the official list of centres to which a sponsor can resort to have studies done in a GLP regime. Before the entry into force of the DLvo no. 120, on the other hand, accreditation was granted through a ministerial decree published in the official journal of the Italian Republic. Test facilities authorized according to the previous regulation are considered accredited also under the new one. In both instances it is foreseen that further verifications of a continuing compliance should be planned at a frequency of two-three years. Any serious deviations at any level of the centre from the GLP performance have as a consequence the withdrawal of the authorization. This may also happen whenever significant variations from the situation inspected actually occur (e.g. the appointment of a new responsible for the QAU) that have not been duly notified to the GLP monitoring authority and accepted by this last.

The machinery described above resulted so far in the accreditation of the test facilities reported in Table 2, while for others it is still pending. The list also includes test facilities accredited on the basis of the previous good manufacturing practice (GMP) criteria for the production of pharmaceuticals, now covered by the same DLvo no. 120, as all other chemicals.

Table 2. - Italian test facilities to which the GLP compliance status has been acknowledged by the GLP monitoring authority

Denomination of the test facility	Address	Field of validity	Date of the first authorization
Antoine Marxer RBM (SpA)	Via Ribes,1 Colleretto Giocosa (TO)	Toxicological and ecotoxicological tests	7 January 1988
Enichem Synthesis (SpA)	Via Maritano, 26 San Donato Milanese (MI)	Physical-chemical tests	20 July 1988
G. Natta, Himont Italia	P.le Privato, 12 "G. Donegani" Ferrara	Physical-chemical tests	20 July 1988
Cyanamid Italia (SpA)	XV Strada, Zona Industriale Catania	Toxicological tests	7 October 1988
Farmitalia Carlo Erba	Via Carlo Imbonati, 24 Milano	Physical-chemical and toxicological tests	1 March 1989
Stazione Sperimentale per le Industrie degli Oli e Grassi	Via Giuseppe Colombo, 79 Milano	Physical-chemical and toxicological tests	1 March 1989
Life Science Research, Rome Toxicology Centre (SpA)	Pomezia (Roma)	Toxicological tests	20 May 1989
ISF	Via Leonardo da Vinci, 1 Trezzano sul Naviglio (MI)	Physical-chemical, toxicological and ecotoxicological tests	11 January 1990
G. Donegani (SpA)	Via Fauser, 4 Novara	Physical-chemical tests	12 July 1990
Studio Laboratorio ASA	Viale Brigate Marche, 12 F Treviso	Physical-chemical tests	17 May 1991
Stazione Sperimentale per i Combustibili	Via Alcide De Gasperi, 3 San Donato Milanese (MI)	Physical-chemical tests	17 May 1991

Table 2. - *(continued)*

Denomination of the test facility	Address	Field of validity	Date of the first authorization
Biolab SGS	Via Buozzi, 2 Vimodrome (MI)	Physical-chemical and toxicological tests	4 June 1991
Istituto di Ricerche e Collaudi "M. Masini" (Srl)	Via Moscova, 11 Rho (MI)	Physical-chemical tests	29 October 1991
Centro Ricerche Fitofarmaci Isagro (Srl)	Via Fauser, 4 Novara	Physical-chemical tests	16 November 1993
Bioresearch	Via Europa, 35 Muggiò (MI)	Other studies	1 March 1992
Boehringer Mannheim	Viale Libertà km 0,750 Monza (MI)	Toxicological tests	1 May 1992
Bracco	Via E. Folli, 50 Milano	Toxicological tests	1 November 1991
Chiesi Farmaceutici	Via Palermo, 26/A Parma	Toxicological tests	1 December 1991
Crinos	Piazza XX Settembre, 2 Villa Guardia (CO)	Toxicological tests	1 July 1991
Cyanamid Italia (SpA)	Zona Industriale Via F. Gorgone Catania	Toxicological tests	1 January 1992
Dompé	Via S. Martino, 12 Milano	Toxicological tests	1 October 1991
Farmitalia Carlo Erba Istituto di Ricerca Cesare Serono	Via Giovanni XXII, 23 Nerviano (MI)	Toxicological tests	1 March 1991
Glaxo	Via Fleming, 2 Verona	Toxicological tests	1 May 1991
Istituto Gentili	Via Mazzini, 112 Pisa	Toxicological tests	1 December 1991
IRCS	Via del Mare Pomezia (Roma)	Toxicological tests	1 March 1992
Laboratori farmaceutici CT	Via D. Alighieri, 69-71 Sanremo (IM)	Toxicological tests	1 April 1992
Lepetit	Via R. Lepetit Gerenzano (MI)	Analytical, chemical and toxicological tests	1 February 1992
Magis-Mitin	Via Cacciameli, 34 Zona Industriale Brescia	Toxicological tests	1 October 1992
Mediolanum Farmaceutici	Via S.G. Cottolengo, 15-31 Milano	Toxicological tests	1 October 1991
Poli Industria Chimica	Via Volturno, 48 Quinto de' Stampi (MI)	Toxicological tests	1 January 1991
Polifarma	Via Tor Sapienza, 138 Roma	Toxicological tests	1 May 1991
Sigma Tau	Via Pontina, km 30 Pomezia (Roma)	Toxicological tests	1 May 1991

Table 3. - The Community reference laboratories of the European Commission

Denomination	Chemicals category
Rijkinstituut voor de Volksgezondheid en Milieuhygiene, Bilthoven, The Netherlands	Stilbene, stilbene derivatives, their salts and esters; thyrostatic substances estrogenic, androgenic and gestagenic substances *(a)*
Laboratoires des MèdicamentsVeterinaires, CNEVA, Fougères, France	Antibiotics and similar antimicrobial substances
Bundesgesundheitsamt, Berlin, Germany	Chloroamphenicol, β-agonists and sulfamides
Istituto Superiore di Sanità, Rome, Italy	Contaminants present in feeding stuffs and contaminants present in the environment

(a) Substances in accordance with article 4 of directive 81/602/EEC and article 2 of directive 88/649/EEC are also included.

An expanding horizon

The need for harmonization and standardization at the root of the GLP criteria is presently emerging in a variety of fields that can only benefit from the adoption, legally enforced, of similar principles. Although these should obviously be tailored to each specific sector in dependence of its characteristics, it is undeniable that the basic approach remains the same. Food production technology and clinical chemistry, just to mention two cases as diverse as possible among those for which this exigency is keenly felt, do aim at one common goal, i.e. credibility and comparability of experimental data through an uninterrupted chain of verifiable events. Nowadays this is becoming more and more an irreversible process in which it is worth investing to adequately protect human health while also maintaining commercial competitiveness. It is not by chance in this context that the European Commission has recently established four Community reference laboratories (CRLs) for residues in foodstuff and the environment, as shown in Table 3, with the mandate of achieving the highest possible harmonization throughout the twelve member states in such a delicate matter [16]. No crystal ball is therefore necessary to forecast that the mental attitude of scientists and decision-makers as well will be ever more oriented toward this kind of solutions to adequately cope with the defying challenges posed by present times.

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Annex 1

Questionnaire for the collection of essential information on test facilities prior to inspection as established by the decree D.L.vo no. 120, 27 January 1992 (adoption of directives nos. 88/320/EEC and 90/18/EEC dealing with inspecting procedures and verification of good laboratory practice).

1. Main data on the test facility

1.1. Name of the laboratory

1.2. Address, phone, telex and fax number

1.3. Type of institution (tick as appropriate)
- a) government
- b) university
- c) semipublic body
- d) local organization
- e) private association
- f) industry
- g) hospital laboratory
- h) other (please describe)

1.4. Main work areas
- a) physics and chemistry
- b) microbiology
- c) toxicology
- d) pharmacology
- e) ecotoxicology
- f) pharmacokinetics (chemobiokinectics)
- g) biotechnologies
- h) other (please describe)

1.5. Name of the scientific manager

1.6. Name of the legal manager

Signature of the legal manager

2. Organization and personnel of the test facility

2.1. Staff members

a) Ph.D. members, (scientific disciplines)	no.	.....
b) Graduates and laboratory technicians	no.	.....
c) Auxiliary personnel	no.	.....

CV's of the scientific manager, veterinarians, staff members and technicians should be enclosed, with clear indication of the highest academic degree possessed, the year when this was granted, all post-doctoral titles attained and list of scientific publications. Date of employment for each staff member and type of activities (whether total or part time) should be indicated.

2.2. Detailed description of the laboratory organization and scientific structure with mention of key individuals (e.g. persons responsible for the various departments and technical services, such as maintenance, archives, etc.)

2.3. List of personnel assigned to each section.

2.4. Qualification programmes, training courses and health monitoring programmes.

2.5. Brief illustration of the type of tests performed in each activity sector with mention of relevant research lines.

3. Quality assurance unit

3.1. Programme of quality assurance.

3.2 List of standard operative procedures (SOPs) at the disposal of the quality assurance unit as well as of the other SOPs available with explanation of the identification codes used and the date of their most recent revision approval.

4. Facilities

4.1. Urban or non-urban site.

4.2. 1:100 map of the entire establishment, laboratories and animal housing included.

4.2.1. Maps should indicate the progressive number of each room, what activities are performed therein, where experiment animals are housed, which species are available and the maximum number of animals that can be hosted.

4.2.2. Isolated areas should be highlighted.

4.2.3. Pathways of individuals, animals and materials should be marked in different colours.

4.2.4. Safety measures should be reported, in particular as regards unauthorized access to archives and animal housing, systems for electric power and the like.

4.3. The uses and pretreatment of water supplied to the centre should be detailed.

4.4. Procedures adopted to dispose of solid and liquid wastes should be described and copy of the contract with the waste management company should be attached. Removal and incineration of animal carcasses and of all toxic and noxious wastes should be illustrated.

4.5. The characteristics of fire-extinguishing systems should be reported, with particular reference to animal housing, archives and EDP setups. If Halon is used, latency time for gas release should be given.

4.6. Characteristics of the air-conditioning system should be described, with particular reference to animal housing and archives. Moreover, mention should be made of:

a) the frequency of total replacement, temperature and humidity as well as monitoring, recording of relevant paramaters;
b) light-darkness cycles and lux number;
c) noise (only for animal housing).

5. Equipment

5.1. Main instruments available for each section.

5.2. Maintenance programmes (both regular and according to needs) of equipment, with indication of the cases when the service is provided by an external contractor.

6. Test systems

6.1. Test systems in use and name of suppliers.

6.2. Foodstuff type, bedding type and name of manufacturers and suppliers.

6.3. Water type and precautions taken before it can be destined to drinking system (automatic devices or bottles).

6.4. Copy of the authorization for animal testing and of its renewal, if applicable.

6.5. Systems for environmental confinement of microorganisms and/or genetically modified cell lines.

7. EDP system

7.1. The characteristics of the EDP system should be detailed, in particular as regards:

a) hardware scheme;
b) list of software sets and their use;
c) layout of the validation programme.

8. Archives

8.1. Archiving procedures should be given for:

a) paper records;
b) residues of test systems;
c) magnetic tape-supported data.

9. Other information

9.1. Connection with data banks.

9.2. Any other useful information.