# A manifesto for the future of laboratory medicine: what remains to be done?

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## ABSTRACT

The definition of the specific role of the laboratory medicine professionals (conventionally known as "laboratorists"), their specific areas of activity, and their relationships with all the potential stakeholders, are aspects that are still largely debated in the context of the modern healthcare. To this end, in recent years we have attempted to respond to various unresolved issues (through a "Manifesto of Laboratory Medicine"), by defining a precise identity of the laboratorist, and elaborating a set of ten themes (the content of the "Manifesto") focused on specific areas for improvement. Almost five years after its publication, some aspects highlighted in the Manifesto have benefited from a significant evolution, while others remain partially or largely unanswered, as will be analyzed and discussed in detail in this article.

***Key words:*** *Laboratory Medicine, manifesto, diagnostics*

## LABORATORY MEDICINE AND ITS MANIFESTO

According to a modern conception (1), Laboratory Medicine should be considered a science and/or clinical discipline, aimed at quantification or qualitative assessment, for both medical and research purposes, of any substance that can be assayed in any type of biological fluid, of any animal species, therefore including humans. The results of these measurements are then translated in clinical information useful for improving health and/or maintaining the state of well-being, both of an individual and of an entire population. This definition explicitly implies the use of a vast array of analytical techniques, in particular, but not exclusively limited to, colorimetric, enzymatic, turbidimetric, electrochemical, immunochemical, separative, cytochemical, coagulative, molecular, cytogenetic assays, or through the use of specific techniques such as nuclear magnetic resonance and flow cytometry. As anticipated, the results of laboratory tests can be used for screening, diagnosis, staging, prognostication and therapeutic monitoring of a broad spectrum of pathological conditions, as well as for defining the health status, physical fitness and individual predisposition towards specific activities or behaviors.

Since its inception, Laboratory Medicine has been integral to the clinical decision-making, embracing a concept that categorically transcends the general meaning of "test factory" (2). The result of each laboratory test, whether numerical or qualitative, becomes always a clinical information in the mental process of the stakeholder, more or less useful for the clinical reasoning in relation to the appropriateness with which is requested (3). To this end, laboratory professionals now play a decisive, broad and irreplaceable function. They not only are custodians of pre-analytic and analytic quality, but become cornerstone of the post-analytic and post-analytic phases, in the last of which the result is interpreted according to a clinical question and/or the patient's condition, triggering a diagnostic and clinical reasoning which includes a vast array of actionable decisions. Although it is not possible to define *a priori*

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to what extent Laboratory Medicine contributes to the clinical decision-making (using expressions such as "70% of clinical decisions depend on laboratory data" has no real basis according to the evidence-based medicine) (4), it is now undeniable, and the recent COVID-19 pandemic has contributed to reinforce this concept (5), that the clinical reasoning is now largely dependent on results of laboratory tests. Just imagine the diagnosis of NSTEMI (non-ST elevation myocardial infarction), which is virtually impossible without cardiac troponins I or T values (6), the diagnosis of bacterial infection, greatly supported by procalcitonin measurement (7), or the identification of genetic alterations, which is only possible using molecular biology techniques (8), just to name a few examples.

The recognition of the specific role of the laboratory medicine professional (also called "laboratorist"), the specific areas of activity, and the relationships with all the potential stakeholders are aspects that have been for long debated in the context of modern medicine. To this end, in recent years we have attempted to respond to various unresolved issues (through a "Manifesto of Laboratory Medicine") by defining a precise identity of the laboratorist, and elaborating a set of ten themes (the content of the "Manifesto") focused on specific areas for improvement (9), and summarized in Table 1. Almost five years after its publication, some aspects highlighted in the Manifesto have benefited from a considerable evolution, while others remain partially or largely unanswered, as will be analyzed in detail in the next parts of this article.

**Table 1**
*Mean topics of the Manifesto for the future of Laboratory Medicine*

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|---|---|
| 1. | Improve test results interpretation |
| 2. | Contribute to reduce diagnostic errors |
| 3. | Implement clinical laboratory stewardship |
| 4. | Support the introduction of innovative technologies |
| 5. | Improve reference ranges and decision limits |
| 6. | Move clinical laboratory out of the silos |
| 7. | Support changes in the reimbursement model |
| 8. | Support innovation in teaching laboratory medicine |
| 9. | Enhance all professional tasks |
| 10. | Promote the value of the profession |

## WHAT REMAINS TO BE DONE?

### Improve test results interpretation

The interpretation of laboratory test results has a strong impact on the accuracy and appropriateness of the clinical decision-making. It is undeniable that the challenges in selecting and/or interpreting laboratory tests represent two of the leading problems, areas in which laboratorists could provide advice and support. Especially in the context of test result interpretation, the clinicians may miss some pre-analytical and analytical aspects, which to some extent could justify an unexpected result or even data that do not match with the clinical condition, as well as aspects related to the specific biological significance of an investigation, the clinical significances of which may be only partially acknowledged. In this area, much has been done in recent years, planning joint clinic-laboratory meetings or congress sessions, participating in drafting of shared recommendations or guidelines, offering direct laboratory counselling to clinical colleagues within the same healthcare facility (10). However, more could still be done, thanks to information technology (IT), (e.g., remote training, videoconferences, chats, etc.), recently cleared by COVID, which would greatly foster the interaction between laboratorists and stakeholders. Strengthening the creation of integrated care pathways (ICP, also known as clinical pathways) at a local, national or even international level is the key to guarantee the performance of the right test, for the right patient, within the right clinical setting (11). Another area that offers ample prospects for improvement is investing in creation and implementation of the so-called "interpretative comments", which help clinician in interpreting the test result within laboratory reports, and thus even without direct interaction with the laboratorist (12).

### Contribute to reduce diagnostic errors

An extensive dissertation on the problem of diagnostic errors would deserve an entire encyclopedia, in the awareness of the vastness of the phenomenon from either a causal or epidemiological perspective. Nonetheless, it is essential to make a synthesis of the heritage that the past has left us, together with an analysis of the possible areas for (further) improvement (13). Errors in Laboratory Medicine are unquestionably many, in absolute terms, because the *in vitro* tests that can be requested and performed are vast and variegated. Nonetheless, in relative terms, recent statistics indicates that the number of *in vitro* diagnostic errors is almost ten times lower than the number of radiological errors. The process seems, therefore, already under good control; it has become increasingly governed over recent years, but is still perfectible. The crucial question is what more and better can be done in this area (14). Any phenomenon requires to be monitored in order to be governed. This is exactly what quality indicators have been designed for (15). The current state of the implementation of these indicators is vastly heterogeneous, in that only a few laboratories constantly monitor all the most

important quality indicators and use them for developing improvement activities. However, if I don't know where (and why) I am mistaking, I will not be able to implement the necessary countermeasures for preventing from making the same mistake again or to solve the problem. It is hence necessary to raise the awareness of clinical laboratories that using process indicators is an essential activity within a program of total quality maintenance. At the same time, knowing that most errors occur in the pre-analytical phase, planning specific training courses (already part of the *curriculum studiorum*) for all the personnel with responsibility of biological samples collection, inside and outside the laboratory environment, is another essential aspect to reduce uncertainty (16). As it will be analyzed in detail in a following part of this article, implementing IT tools such as gating rules, biological plausibility cross-checks, software for systematic error recording, are additional aspects that have shown favorable impact on error prevention, control and management (17).

## Implement clinical laboratory stewardship

The mutual interaction between the clinic and the laboratory is an integral part of a healthcare system abreast of the times. This close connection will become even more important in the foreseeable future, due to progressive diffusion of the so-called "disruptive technologies" in areas such as genetics, epigenetics, genomics and proteomics, which represent the cornerstone of personalized medicine. Also here, as already discussed, the creation of multidisciplinary teams in which the laboratorist can bring an active contribution to the discussion of clinical cases (especially the more intricate), represents a promising enterprise (18). It is basically a process that is already implemented in many healthcare facilities, but that could be strengthened also with establishment of local and/or regional networks. A better awareness of the clinical significance of the large and varied panel of biomarkers that the clinical laboratory now offers, together with a larger use of health technology assessment (HTA), can then guarantee a significant advance in diagnostic efficiency, with potential savings in human and economic resources.

## Support the introduction of innovative technologies

Laboratory Medicine represents the branch of medicine where the technological progress is more incessant (19). We have learned from the pandemic that new assays can be developed and validated in a very short time, whose accuracy, precision and rapidity catalyze the progress of science and medicine. Halting progress because of the fear of change, no matter how "radical" it may appear, is not reasonable, nor even justifiable. Technological innovation also acts as a catalyst for research which, in laboratory medicine, finds almost boundless fields, thanks to the incessant development of new techniques and discovery of innovative biomarkers.

## Improve reference ranges and decision limits

The definition and use of reference intervals and diagnostic thresholds (also known as "cutoffs") are essential prerequisites for correct interpretation of laboratory test results, regardless of the skills of the user (not even the most expert laboratorist will ever be able to remember the reference values or diagnostic thresholds of all available tests). In recent times a considerable effort has been made for harmonizing (standardizing is not always possible in this area) the activities in all phases of the total testing process (pre-analytical, analytical and post-analytical) (20). This is not enough, however. The communication of results to the stakeholders can often surprise the recipient, for example when two laboratories use and report different diagnostic limits. This may be justifiable and understandable when the analytical techniques are completely different, but when there is a substantial analytical uniformity, the dialogue between laboratories becomes mandatory. Besides, the approach used by clinical laboratories for defining their own reference intervals or for adopting decision limits must also be standardized, for example by using already existing guidelines. Looking into the future, the adoption of personalized reference intervals represents a cornerstone of personalized medicine (21). It should also be widespread the principle according to which the reference intervals are not synonymous with normality, due to the inherent statistical limits underlying their calculation, exactly as a laboratory value lying outside a reference interval does not always reflect a pathological state.

## Move clinical laboratory out of the silos

The usual and now reasonably obsolete conception of medicine, relegates the different diagnostic branches within virtual containers (silos), independent and isolated from each other. However, advances in technology and in our understanding of the biological mechanisms of diseases have highlighted how the different diagnostic branches integrally contribute to the clinical decision-making process (18). Just to cite one example, the integrated path of diagnosis and treatment of malignant neoplastic diseases presumes an integration of radiological investigations, pathological anatomy, laboratory biomarkers, and genetics. To date, there are only few concrete examples in which all the information deriving from these logistically different areas (because they operate in different environments) are integrated into the same virtual repository. Concretely, this is what the electronic health record (EHR) should be, which can also be accompanied locally by an electronic health dossier (EHD), designed in a such way that the clinician can simultaneously accesses a vast spectrum of diagnostic information. The integration between the various branches of diagnostics represents now an inevitable target, towards which digitization acts as a great catalyst.

The development of hospital information system (HIS) capable of integrating information from different software programs [i.e. Laboratory Information System (LIS), Research Information System (RIS)] will allow the clinician to garner an overall picture that will facilitate the clinical reasoning.

### Support changes in the reimbursement model

Considering that healthcare expenditure represents almost always the second part of national expenditure, the sustainability of the healthcare system could only be sustained maintained if tariffs and related reimbursements to the healthcare facilities remain aligned with their costs. Given that the profitability of a healthcare facility as a whole is a desirable but not always necessary condition (a balanced budget is the prerogative of public healthcare facilities), a reimbursement model based on tests suffers from a large series of caveats, first of all the fact that basic analytical costs may be largely heterogeneous among various laboratory services (it may depend, for example, on the analytical technique or on the total number of tests performed). Replacing this model with another reflecting the concept of diagnosis-related group (DRG) is a working hypothesis (22). In brief, what should be paid (or reimbursed) is the clinical information delivered by test results, irrespective of the fact that it could be a single test or a panel. However, we are still a long way from this paradigm shift, thus making it necessary to continuously update the catalogs of tests and the relative tariffs, eliminating useless or obsolete tests that still widely populate the regional catalogs (which remain, however, one different from another, based on the Title V of the Italian Constitution).

### Support innovation in teaching laboratory medicine

Laboratory Medicine, perhaps more than other medical branches, suffers from a shortage of vocations (23). The causes are several and multifaceted, making it impossible to address all of them in this Opinion paper. However, what seems to emerge strongly after more than three years of pandemic is that the situation, instead of improving, has further worsened, at least at a national level. Ministry sources reveal that the percentage of new enrolled in the Specialty of Clinical Pathology and Clinical Biochemistry only reach 37% of potential enrollments, a reality that places our discipline in the second place for number of unassigned positions, preceded only by Microbiology and Virology, a “sister” discipline. Therefore, the question now is no longer how to support innovation in teaching laboratory medicine, but rather how to convey an attractive image of Laboratory Medicine to the students. It is clear that the current teaching model fails (or works poorly). In the awareness that there is no simple answer to the question, some solutions could be hypothesized, mostly deriving from what has been discussed in the previous parts of this article, and finalized at conveying more effectively the role of the laboratorists in the context of modern medicine. Changing the teaching model means transmitting to the students a message of laboratorists centrality, of their value as consultants during all phases (pre-analytical, analytical and post-analytical) of the total testing process, and of their essential role in clinical governance. Discussing interactive clinical cases, were the role of the laboratorists within the clinical decision-making clearly emerges, could be a valid support.

### Enhance all professional tasks

The role and activities of laboratorists have progressed in parallel with the socio-cultural and economic evolution. Over time, especially clinical laboratory managers needed to complement their skills with a wide range of administrative tasks, which include the management of tests catalogs, personnel training and management, budgeting and tendering processes, the introduction of new techniques and technologies, regular professional education. Most of these activities are often overlooked, because the intellectual resources (and time) required are underestimated. In practice, the modern laboratorists spends 30-60% of time on bureaucratic activities (digitization is not always helpful) designed to ensure the economic-administrative functioning of the reality in which he/she works. It is therefore necessary, but very little has been done in recent years, that these “submerged” activities are officially recognized, also by means of an adequate remuneration. There is no clear evidence now that the discussion of all these issues occurs in the context of union bargaining, as laboratorists often represent a minority of the trade union to which they belong. Creating a single, strong and representative laboratorist trade union (and perhaps also just a single Scientific Society of Laboratory Medicine), which bears the discussion of all professional disputes in the most suitable forums is an almost obligatory step.

## PROMOTE THE VALUE OF THE PROFESSION - CONCLUSIONS

This last aspect is nothing more than the sum/synthesis of all those previously discussed, representing their ideal conclusion. It is necessary to transcend the concept of the laboratorist as simple producer of data transmitted unchanged and unchangeable to the clinical colleagues. The professionalism of the modern laboratorist is assayed in terms of manager of clinical information, catalyst of knowledge, team leader, guardian of quality and administrator of public goods, but also of expert patient counsellor. In the last five years the situation does not seem to have changed so much. The real pivotal point, therefore, is how these real “values” that the laboratory professional now possess can be communicated and promoted at all levels of civil society (patients, clinicians, administrators, politicians). The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has sanctioned the annual celebration of the “week of laboratory professionals” (in 2023 it was held from 23 to 29 April), aimed at highlighting the role and activities of the laboratory professionals with the clinical reasoning and decision-making.

This initiative certainly represents a good means to promote the value of the profession, but more can be done. For example, and besides what has already been previously discussed, scheduling periodic meetings and round tables with the "decision makers" (politicians, hospital administrators) would help increase their awareness of our value and of the contribution that in the past, now and especially in the future, Laboratory Medicine will continue to deliver to science and medicine

## CONFLICT OF INTEREST

None

## REFERENCES


1. Lippi G, Plebani M. A modern and pragmatic definition of Laboratory Medicine. Clin Chem Lab Med 2020;58:1171.
2. Plebani M. Clinical laboratories: production industry or medical services? Clin Chem Lab Med 2015;53:995-1004.
3. Lippi G, Bovo C, Ciaccio M. Inappropriateness in laboratory medicine: an elephant in the room? Ann Transl Med 2017;5:82.
4. Hallworth MJ. The '70% claim': what is the evidence base? Ann Clin Biochem 2011;48:487-8.
5. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med 2020;58:1063-9.
6. Cervellin G, Lippi G. Of MIs and men--a historical perspective on the diagnostics of acute myocardial infarction. Semin Thromb Hemost 2014;40:535-43.
7. Cervellin G, Schuetz P, Lippi G. Toward a holistic approach for diagnosing sepsis in the emergency department. Adv Clin Chem 2019;92:201-16.
8. Mannello F, Plebani M. Current Issues, Challenges, and Future Perspectives in Clinical Laboratory Medicine. J Clin Med 2022;11:634.
9. Plebani M, Laposata M, Lippi G. A manifesto for the future of laboratory medicine professionals. Clin Chim Acta 2019;489:49-52.
10. Kahn SE, Jones PM, Chin AC, Christenson RH . Defining the path forward: guidance for laboratory medicine guidelines. EJIFCC 2015;26:158-67.
11. Plebani M, Aita A, Sciacovelli L. Patient Safety in Laboratory Medicine. 2020 Dec 15. In: Donaldson L, Ricciardi W, Sheridan S, Tartaglia R, editors. Textbook of Patient Safety and Clinical Risk Management [Internet]. Cham (CH): Springer; 2021. Chapter 24.
12. Buoro S, Da Rin G, Fanelli A, Lippi G. Harmonization of interpretative comments in laboratory hematology reporting: the recommendations of the Working Group on Diagnostic Hematology of the Italian Society of Clinical Chemistry and Clinical Molecular Biology (WGDH-SIBioC). Clin Chem Lab Med 2018;57:66-77.
13. Lippi G, Plebani M. A Six-Sigma approach for comparing diagnostic errors in healthcare-where does laboratory medicine stand? Ann Transl Med 2018;6:180.
14. Lippi G, Mattiuzzi C, Bovo C. Are we getting better at the preanalytical phase or just better at measuring it? J Lab Precis Med 2018;3:11.
15. Sciacovelli L, Lippi G, Sumarac Z, West J, Garcia Del Pino Castro I, Furtado Vieira K et al. Quality Indicators in Laboratory Medicine: the status of the progress of IFCC Working Group "Laboratory Errors and Patient Safety" project. Clin Chem Lab Med 2017;55:348-57.
16. Lippi G, Chance JJ, Church S, Dazzi P, Fontana R, Giavarina D et al. Preanalytical quality improvement: from dream to reality. Clin Chem Lab Med 2011;49:1113-26.
17. Lippi G, Sciacovelli L, Simundic AM, Plebani M. Innovative software for recording preanalytical errors in accord with the IFCC quality indicators. Clin Chem Lab Med 2017;55:e51-3.
18. Lippi G, Plebani M. Integrated diagnostics: the future of laboratory medicine? Biochem Med (Zagreb) 2020;30:010501.
19. Lippi G, Mattiuzzi C. Project management in laboratory medicine. J Med Biochem 2019;38:401-6.
20. Zaninotto M, Graziani MS, Plebani M. The harmonization issue in laboratory medicine: the commitment of CCLM. Clin Chem Lab Med 2022;61:721-31.
21. Coşkun A, Sandberg S, Unsal I, Cavusoglu C, Serteser M, Kilercik M et al. Personalized reference intervals in laboratory medicine: a new model based on within-subject biological variation. Clin Chem 2021;67:374-84.
22. Plebani M. Clinical laboratories: production industry or medical services? Clin Chem Lab Med 2015;53:995-1004.
23. Guidi GC, Lippi G. Laboratory medicine in the 2000s: programmed death or rebirth? Clin Chem Lab Med 2006;44:913-7.