International Guidelines on Good Governance Practice for Research Institutions

CIOMS Working Group report Draft

12 April 2023

This report was posted for comment on 12 April 2023 at:
https://cioms.ch/working_groups/principles-of-good-governance-for-research-institutions/

The CIOMS Working Group (WG) GGPRI (Good Governance Practice for Research Institutions) welcomes your input to the report, or any parts of it. A list of GGPRI WG members can be found at the end of the document.

Please note that the layout will be improved in the final version, and best efforts will be made to correct remaining typographical and/or grammatical errors, as well those pertaining to references.

Permissions are being sought to reproduce some of the illustrative materials included in this report. We welcome responses from organizations that own any of these materials and have not yet been contacted in this regard.

Please submit your comments using the form posted on the CIOMS website : https://cioms.ch/working_groups/principles-of-good-governance-for-research-institutions/. The timeline for submission of comments is 7 June 2023. Thank you.

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Suggested citation: International Guidelines on Good Governance Practice for Research Institutions. CIOMS Working Group report. Draft for comment, 12 April 2023. Geneva, Switzerland: Council for International Organizations of Medical Sciences (CIOMS), 2022.

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LIST OF FIGURES, TABLES AND BOXES

ABBREVIATIONS AND ACRONYMS

CRIS: Clinical Research Information System

DMP: Data Management Plan

DTA: Data Transfer Agreement

DMP: Data Management Plan

GCP: Good Clinical Practice

GGPRI: Good Governance Practice for Research Institutions

ICH-GCP: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) *Guideline for Good Clinical Practice* E6(R2). 2016

IPA: Intellectual Property Agreements

MTA: Material Transfer Agreement

IRB: Institutional Review Board

LIMS: Laboratory Information Management Systems

NRA: National Regulatory Authorities

PI: Principal Investigators

PPIE: Patient and Public Involvement and Engagement

REC: Research Ethics Committee

SOP: Standard Operating Procedure

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GLOSSARY

Health-related research: activities designed to develop or contribute to generalizable health knowledge within the more classic realm of research with humans, such as observational research, clinical trials, biobanking and epidemiological studies. Generalizable health knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based related to health, which can be corroborated by accepted scientific methods of observation and inference[1].

Governance: The manner in which institutions exercise their power in the management of the organizational, human and infrastructure resources, directly or indirectly, dedicated to research activities. Governance includes mechanisms (structures, standards, procedures, strategies, processes etc.), both formal and informal, designed for the exercise of this power.

Good governance: Principles guiding research institutions in the responsible and efficient exercise of its power in conducting research activities in a way that fulfils its obligations and goals, as described in this tool, toward all research stakeholders, in particular the human participants, the researchers and the population.

Good Governance Practice for Research Institutions: A methodological tool describing good governance with the goal of helping research institutions to assess and improve the way they provide support to research stakeholders depending on their needs and according to their available resources. The purpose of the GGPRI is that each research institution is aware both of the research activities carried on within its infrastructures – or in relation with them - and of its responsibilities on that behalf, and adopts the appropriate level of governance of research depending on its needs and resources.

Research institution: Any public or private entity or agency or healthcare or public health facility where health-related research is conducted. For the purpose of this recommendation, the notion of research institution covers all facilities were health-related research activities are carried on regardless of whether research is explicitly recognized as part of their mandate or core business and is not limited to facilities primarily dedicated to health-related research (e.g. clinical trial centers).

Research waste: research outcomes that cannot be used or with no societal benefits.

Resources means time, training, qualified staff, facilities, clinical and laboratories equipment, hardware and software, communication tools, data protection infrastructure, health databases and biobanks, ethical and legal counselling, etc. This is not only a matter of financial support but also a question of governance: what services and supports are available for the researchers to meet their responsibilities as imposed by research ethics and regulation.

Study data: health related research data, internal clinical and/or research databank and biobank.

terms to also define: Research participants / Research/ research project/ research infrastructure/ biobank/ repository

To be completed with key terms from 2022 CIOMS Cumulative Glossary and other documents of refences (TRREE)

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[1] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health-related research involving humans*. 2016

171 # FOREWORD

172 ## INTRODUCTION

173 Scientific research is essential for the protection and improvement of the health and well-being of
174 the populations around the world[2]. Researchers are at the front line to respond to major crisis,
175 such as the COVID-19 pandemic and the climate change, that impact everyone. More than ever,
176 the scientific community bears heavy responsibilities to face those unprecedented challenges.
177 COVID-19 vaccines development is a unique example of the success of its concerted actions in
178 the health sector.

179 Since the 60s, research activities involving human participants has grown steadily with a trend
180 toward globalization and industrialization. Health-related research has become highly complex
181 with a wide range of stakeholders active at the local, regional and international levels. To facilitate
182 and contain this process, numerous ethical, professional and industrial guiding documents have
183 been adopted and constitute a dense normative framework. One of the first and most cited of
184 those documents is the Declaration of Helsinki adopted in 1964[3] by the World Medical Association,
185 largely recognized as the "Constitution" of research ethics and to which all other documents make
186 references to, including the 2016 CIOMS International ethical guidelines for health-related
187 research involving humans[4].

188 Most ethical guidelines and laws focus on individual researchers' responsibilities to protect the
189 welfare, rights and dignity of research participants, Research Ethics Committees (REC) acting as
190 gatekeepers. The 2016 International Council for Harmonisation of Technical Requirements for
191 Pharmaceuticals for Human Use (ICH) *Guideline for Good Clinical Practice* E6(R2) (ICH GCP) is
192 a noticeable exception as it provides detailed guidance on the responsibilities of the sponsors,
193 covering governance, SOPs, quality-assurance and data management issues. Yet they are
194 designed for drug trials, and they do not address the role of other stakeholders, such as patients'
195 organizations and the community, and research institutions, even if they are often used as a
196 reference in other health-related studies than drug trials. Another interesting document of
197 reference is the 2011 WHO Standards and Operational Guidance for Ethics Review of Health-
198 Related Research with Human, but it mostly focuses on the responsibilities of entities establishing
199 RECs, which in many countries are not research institutions. The Association for the Accreditation
200 of Human Research Protection Programs (AAHRPP) should also be mentioned as an
201 independent, non-profit organization, helping institutions to strengthen their human research
202 protection programs through an accreditation process. Although it is mostly based on the US
203 regulation according to which RECs or Institutional Review Boards (IRBs) are established by
204 research institutions, numerous institutions are using them in 17 countries of which 10 in Asia.

205 In practice, it is rarely assessed to what extent researchers have the necessary resources in their
206 institution to fulfil their responsibilities. This assessment is done separately for each protocol in
207 absence of an agreed reference framework, with the consequence that there is often little
208 information on the research activities and the resources available in each organization, hospital
209 or healthcare facility to guarantee the protection of research participants and of their communities,
210 and the quality of research.

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[2] World Health Organization. *WHO Health Report: Research for universal health coverage.* 2013.
[3] World Medical Association (WMA) *Declaration of Helsinki – ethical principles for medical research involving human subjects.* 2013.
[4] Council for International Organizations of Medical Sciences (CIOMS) *International ethical guidelines for health-related research involving humans.* 2016.

211   In 2016, the World Medical Association included a section on governance in the Declaration of
212   Taipei on Ethical Considerations regarding Health Databases and Biobanks[5]. The 2016 CIOMS
213   Ethical Guidelines for Health-Related Research Involving Humans also addresses the issue of
214   governance for biobanks which is likewise included in the 2016 Council of Europe
215   Recommendation CM/Rec(2016)6 on research on biological materials of human origin[6]. This
216   illustrates a growing attention in research ethics on the necessary resources to conduct research
217   and on the governance of those resources.

218   Another key issue is the recognition of the diversity of communities with their specific needs and
219   identities which must be addressed in a more comprehensive way in health-related research. In
220   this perspective this is essential to acknowledge the intersectionality of potential disadvantage
221   based in particular on sex, race, ethnicity, gender identity, disability, migrant status, education or
222   class. In other words, that "all forms of inequality are mutually reinforcing and must therefore be
223   analysed and addressed simultaneously to prevent one form of inequality from reinforcing
224   another."[7]

225   Addressing the challenge of promoting health equity in research ethics, and in line with the
226   conceptual work on vulnerability in the 2016 CIOMS Ethical Guidelines, other important
227   documents of references have been adopted recently focusing on the equitable use of existing
228   resources, while promoting collaboration and participation of all stakeholders, such as the 2015
229   FAIR Guiding Principles for scientific data management and stewardship[8], the 2018 Global Code
230   of Conduct for Research in Resource Poor Settings[9] and the 2021 CIOMS Consensus on Clinical
231   research in resource-limited settings[10]. Moving away from the paternalistic vision that research
232   participants are primarily defined by their vulnerability and their need to be protected, those
233   documents are based on a more egalitarian perspective that research participants and their
234   communities should also be considered as – and treated like – co-creators of the research they
235   are involved in. This calls for a change in the way their participation is organized, and their opinion
236   be heard from the conception of research projects to the dissemination of their results.

237   This shift of paradigm creates an urgent need to better recognize the essential role of institutions
238   in which – or in relation with – research is conducted. The current guidelines are meant to fill up
239   the gap in the normative framework of health-related research involving human participants with
240   the aim to help research institutions by offering a proper environment for the researchers to meet
241   with their ethical and professional responsibilities. They are grounded on the vision that institutions
242   should not be ignoring or covering up unethical research activities but should rather stand for the

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[5] World Medical Association (WMA) *Declaration of Taipei – ethical considerations regarding health databases and biobanks*. 2016.

[6] Council of Europe (COE) *Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin.* 2016.

[7] https://www.intersectionaljustice.org/what-is-intersectionality (last consulted on April 6, 2023)

[8] Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, Blomberg N, Boiten JW, da Silva Santos LB, Bourne PE, Bouwman J, Brookes AJ, Clark T, Crosas M, Dillo I, Dumon O, Edmunds S, Evelo CT, Finkers R, Gonzalez-Beltran A, Gray AJ, Groth P, Goble C, Grethe JS, Heringa J, 't Hoen PA, Hooft R, Kuhn T, Kok R, Kok J, Lusher SJ, Martone ME, Mons A, Packer AL, Persson B, Rocca-Serra P, Roos M, van Schaik R, Sansone SA, Schultes E, Sengstag T, Slater T, Strawn G, Swertz MA, Thompson M, van der Lei J, van Mulligen E, Velterop J, Waagmeester A, Wittenburg P, Wolstencroft K, Zhao J, Mons B. *The FAIR Guiding Principles for scientific data management and stewardship*. Sci Data. 2019 Mar 19;6(1):6. PMID: 26978244; PMCID: PMC4792175.

[9] Schroeder, Doris & Chatfield, Kate & Cook, Julie & Wynberg, Rachel & Chennells, Roger & Cavallaro, Francesca & Niekerk, Jaci & Norton, David & Coles, David & Andanda, Pamela & Woodgate, Paul. (2018). *Global Code of Conduct for Research in Resource-Poor Settings.* 10.13140/RG.2.2.19106.27848.

[10] Council for International Organizations of Medical Sciences (CIOMS) Working Group report: *Clinical research in resource-limited settings*. 2021.

243 principles of research ethics as part of their social contract and implement the highest ethical,
244 legal, professional and scientific standards in the field of health-related research.

245 The aim of those guidelines is to help research institutions better fulfill their responsibilities in terms
246 of protecting human research participants and their communities, by involving and engaging them
247 in the research processes and by guaranteeing the pertinence and quality of research while
248 making best use of their available resources. Those guidelines offer research institutions a
249 detailed and specific guidance on how to implement the existing ethical and professional
250 standards. They are complementary to the provisions on governance that have been introduced
251 in the most recent documents of reference as well as in the ICH-GCP.

252 **None of the following chapters are creating new obligations for research institutions.** First,
253 the institutions' responsibilities are derived from their general obligation toward their patients and
254 the populations they care for, but also linked to the fact institutions may be employers of the
255 researchers or potential sponsor of their researchers as they are supporting and financing them,
256 knowingly or not. Second, they are defined by existing guidelines and regulations concerning
257 health-related research involving human participants at the local, national and international levels.
258 The current guidelines do not modify the liability of research institutions by setting new standards.
259 They only intend to clarify the existing rules and help institutions better cope with them.

260 Institutions contribute to health-related research for instance through the participation of their
261 patients, or their employees or both, in research, surveys or questionnaires on health-related
262 issues helping to develop or contribute to generalizable health knowledge, or by authorizing
263 sharing health data and biological material with researchers within or outside the institution.
264 Concerning the further use of health data and biological material for research purposes, it can be
265 done in any healthcare or public health facility collecting such data and material. In fact, many
266 studies are not carried on in dedicated research centers but in public or private healthcare centers,
267 hospitals, day care or home care facilities or in public health services.

268 Having research carried on in - or in relation with - an institution involves some degree of
269 responsibilities for that institution even when an external sponsor is driving the study. Public or
270 private entities or institutions are legally and ethically responsible and accountable for the health-
271 related research they conduct or sponsor, for fulfilling their obligations and responsibilities not only
272 towards their own mission, and also for the human participants, researchers, population at large
273 and any other research stakeholders. This includes protecting the welfare, rights and dignity of
274 the participants, but also their employees' rights and scientific freedom, in a sustained way and
275 with respect for the environment. Even when research activities remain at a low level, they raise
276 issues in terms of research ethics, public health and scientific integrity. Yet, this is neither
277 necessary nor desirable to create clinical research centers in most institutions. What is essential
278 is that each research institution is aware of the activities carried on within – or in relation with – its
279 infrastructures and adopts the appropriate level of governance depending on its needs and
280 resources.

281 In many institutions in which – or in relation with – research is conducted, there is limited attention
282 paid to research by the management. The first reason is obviously that research is simply not part
283 of their mission. Yet, for physicians and healthcare professionals, research is essential to address
284 the needs of their patients and is, therefore, an ethical and professional obligation. For physicians
285 and other healthcare providers it can also have an important impact on their careers and academic
286 recognition. Those guidelines can thus also be used by researchers themselves to engage in a
287 dialog with their institutions while addressing broader issues in terms of governance, quality-
288 assurance and control or patients' safety and involvement. Commercial sponsors and funding
289 agencies could also consider referring to them when implementing their research projects at the
290 institutional level.

291 By raising the awareness of research institutions to the above-mentioned issues, the aim is to
292 provide them with a tool to better benefit from research activities while limiting the diversion of
293 resources needed for healthcare and public health interventions. Implementing those guidelines
294 requires first and foremost (1) to identify the current and planned research activities being
295 conducted within – or in relation with - it and evaluating the main issues at stake. Based on this
296 assessment, (2) the next step is to map the existing resources used for research and how they
297 are integrated in the primary mission of the institution. Having completed this mapping or while
298 doing it, (3) a strategy could be designed to improve coordination of research activities for the
299 benefit of the institution's overall activities. In most instances, research strategy should not be
300 defined in isolation but in relation with broader strategies related to improving the efficiency of the
301 institution, quality-assurance and quality control as well as patients' safety and involvement. (4)
302 This can be done in a participatory process with all the professionals in the institutions, the patients
303 and the population. There is a direct link between research, quality of care and the capacity of
304 institutions to respond to the health needs of the population[11]. Including research activities in the
305 management of the institution's resources is therefore beneficial for all the other activities of the
306 concerned institutions.

307 ## **BACKGROUND**

308 The Council for International Organizations of Medical Sciences (CIOMS) is an international, non-
309 governmental, non-profit organization established jointly by WHO and UNESCO in 1949. CIOMS
310 mission is to advance public health through guidance on health research including ethics, medical
311 product development and safety.

312 CIOMS reports are in-depth guidance documents which serve as worldwide references and
313 guidance for specific subject matters. In addition to the revised 2016 CIOMS International Ethical
314 Guidelines for Health-Related Research Involving Humans, CIOMS Working Groups have
315 published in 2021 a Consensus Report on Clinical research in resource-limited settings[12] and a
316 2022 Report on Patient involvement in the development, regulation and safe use of medicines.[13]

317 As a unique global and scientific organization, CIOMS is well positioned to develop a multi-
318 stakeholders' international guidelines on the good governance practice for research institutions. A
319 Working Group was mandated by CIOMS Executive board to address the issue building on
320 existing ethical and professional guiding documents as well as the current regulation at the
321 national, regional and international levels. The main task is to target institutions which do not
322 consider research as part of their primary mission in order to improve their capacities in the field
323 by offering an appropriate environment for their researchers to conduct their activities according
324 to the high standards in research ethics and regulation.

325 The starting point of CIOMS Working Group in charge of drafting those guidelines on Good
326 Governance Practice for Research Institutions has been to identify the various resources needed
327 to realize research projects. "Resources" here means time, training, qualified staff, facilities,
328 clinical and laboratories equipment, hardware and software, communication tools, data protection
329 infrastructure, health databases and biobanks, ethical and legal counselling, etc. It is not only a
330 matter of financial support but more of a governance question, in other words, what services and
331 supports are necessary for researchers to meet their responsibilities as imposed by research
332 ethics and regulation.

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[11] World Health Organization. *WHO Health Report: Research for universal health coverage*. 2013.

[12] Council for International Organizations of Medical Sciences (CIOMS) Working Group report: *Clinical research in resource-limited settings*. 2021.

[13] Council for International Organizations of Medical Sciences (CIOMS) Working Group report: *Patient involvement in the development, regulation and safe use of medicines*. 2021.

STRUCTURE AND CONTENT

To facilitate their understanding and use, those guidelines have been divided in twelve domains into which institutions should pay attention, namely:

- o Management
- o Ethics
- o Law
- o Research integrity & Conflict of interests
- o Scientific standards
- o Collection, storage and use of data and biological materials:
  - ▪ Biobanks & Registries
  - ▪ Data Handling & Information Technology (IT)
- o Budget & Financing
- o Collaboration
- o Communication
- o Education & Training
- o Institutional research oversight

Each domain encompasses various resources that can be subdivided in terms of infrastructures, human resources and organizational resources. Those resources should already be available in all research institutions, especially concerning the infrastructure and human resources being used for research, but not necessarily under the explicit control and supervision of the institutions themselves. Improving the good governance of research in each domain is an efficient way of making a better use of those resources. Each domain is equally important depending on the circumstances.

Figure 1: *Main Domains to Consider in the Good Governance Practice of Research Institutions*
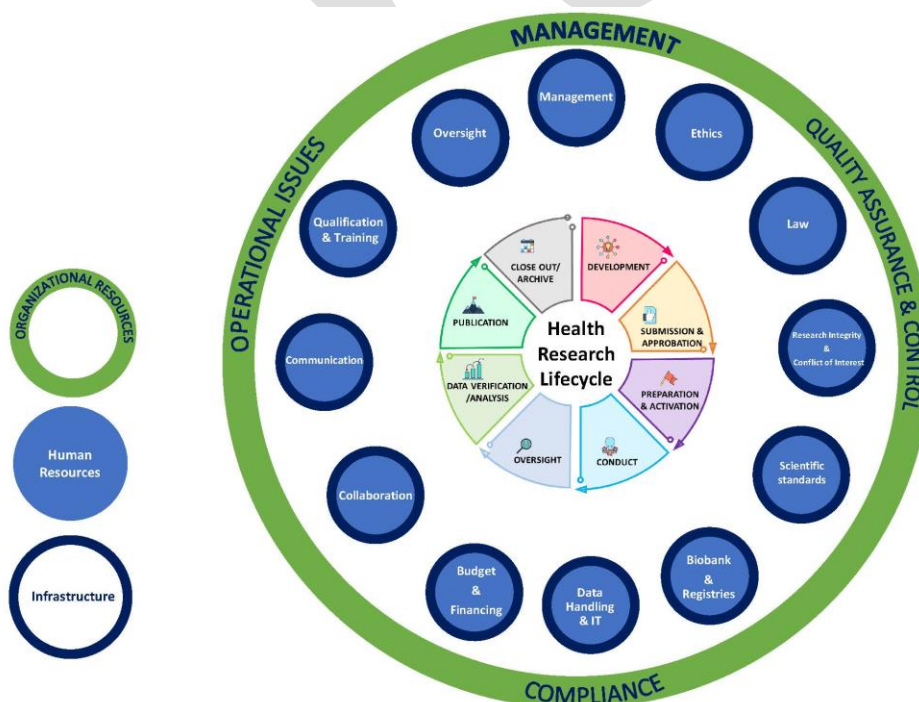
361 In general, there is one chapter per domain, but some domains have been merged in a single
362 chapter as they are treated so closely in practice that researchers are used to deal with them
363 together. Each chapter should be interpreted and read at the light of the others, and not in
364 isolation.

365 Research involving human beings is a highly complex activity operating under numerous
366 constraints and a detailed regulatory framework. This explains why some chapters are more
367 detailed and technical than others, as this is only reflecting the domain it addresses such as IT or
368 biobanking. This technicality cannot be ignored. This is especially true in the field of drug trials
369 since many tend to consider them as the gold standard in biomedical research with human
370 participants. Although the importance of the ICH-GCP in research practice cannot be diminished,
371 it is also true that in many research fields, such as behavioral research, observational studies or
372 qualitative studies, they are not adapted/appropriate. In some instances, their implementation
373 could even be detrimental to both the protection of research participants and the quality of
374 research.

375 Each chapter includes a list of key words, the background and the applicable principles, as well
376 as the main points to consider in the given domain and how to address them. There is also a list
377 of documents of references creating the link with the existing normative framework of research
378 involving human participants. The points to consider are also listed in annex as a tool for the
379 research institutions to map research activities and available resources but also as a tool to follow
380 up the progress being made to reinforce the good governance practice of research in the
381 institutions.

382

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Chapter 1: Research Institution Management

Key words

Accountability – Compliance – Corporate communications – Corrective actions and preventive actions – Delegation – Dimensions of management – Discrimination – Harassment – Integrity – Knowledge management – Leadership – Learning organization – Matrix management – Mission, Organizational culture – Organizational structure – Quality management – Risk management – Social responsibility – Sustainability – Transparency – Trust – Value – Vision – Whistle-blowing

Background and Principles

Research institutions, like any other enterprises and organizations, exist for a specific social purpose. The three "**dimensions of management**" for any organization are:

- defining the specific purpose and mission of the organization;
- making work productive and the workers achieving;
- managing social impacts and social responsibilities.

Good governance for research institutions – that relies on corporate ethics, compliance, transparency and public accountability – should be built on four core management elements including:

- defined research scope, mission, vision and values;
- effective organizational structure, leadership and culture;
- robust knowledge management, quality management and risk management;
- corporate communications.

Points to consider and how to address them

1. Research Scope, Mission, Vision and Values

Research institutions are of a wide diversity in their business scopes. While some may be academic research institutions engaging in a full spectrum of research areas ranging from interventional clinical trials on novel medicinal products to non-interventional health-related studies (e.g. university hospitals, clinical trial centers), others may have their main business in areas other than research (e.g. hospitals and healthcare facilities providing clinical services) and some may also allocate part of their time and resources to support health-related research projects with particular interest (e.g. patients-oriented outcomes research, pediatrics research). Each research institution should therefore, considering its core business, direction and corporate social responsibility, define its research mission, vision and values in alignment with its scope of research. Clear research scope, mission, vision and values are of paramount importance to a research institution as they set the ground for:

- formulating its organizational structure, personnel composition, resource plans and development strategies;
- designing its facilities and infrastructures, operational workflow and technology applications;
- attracting qualified professionals and guiding their professional conduct and behaviors.

2. Organizational Structure, Leadership and Culture

Health-related research is knowledge-based, multidisciplinary, dynamic, forward-looking whilst practical. To respond to its needs in research based on its available resources, a research institution should build up an organizational and human infrastructure with:

- leaders interested in research and empowered to undertake ethical leadership in driving the management and development of the research institution;
- a suitable mix of diversified professionals that together cover the research institution's scope of research, with well-defined roles and relationships which facilitate effective teamwork among the members and support efficient delivery of research outputs;
- an ethical culture that facilitates the productive execution of the institution's research activities – both at organizational and individual levels – and supports the accomplishment of the institution's social responsibilities and social impacts.

Understanding of health-related research adds value to research institution leadership. However, the motivation and vision for accomplishing an institution's mission and social responsibility via research may be of even higher importance to effective leadership. A research institution leader should therefore be motivated to appreciate research ethics and compliance standards, and should possess professional management skills, in particular in attracting, retaining and growing suitable professionals, facilitating teamwork and resolving conflicts and dilemmas. With due respect to the importance of science, leaders of research institutions do not necessarily need to be top scientists.

Effective teamwork starts from clear delegation of job roles, definition of lines of reporting/collaboration and allocation of responsibilities, which should be illustrated on a clear organizational chart and outlined on the corresponding written job descriptions. Modern organizations in dynamic industries, such as research institutions, may adopt a "**matrix management**" approach where a functional specialist may report to a functional team leader and to several project team leaders at the same time in order to enhance open and efficient cross-functional communication necessary for multidisciplinary collaboration.

Table 1: *Example of matrix management*
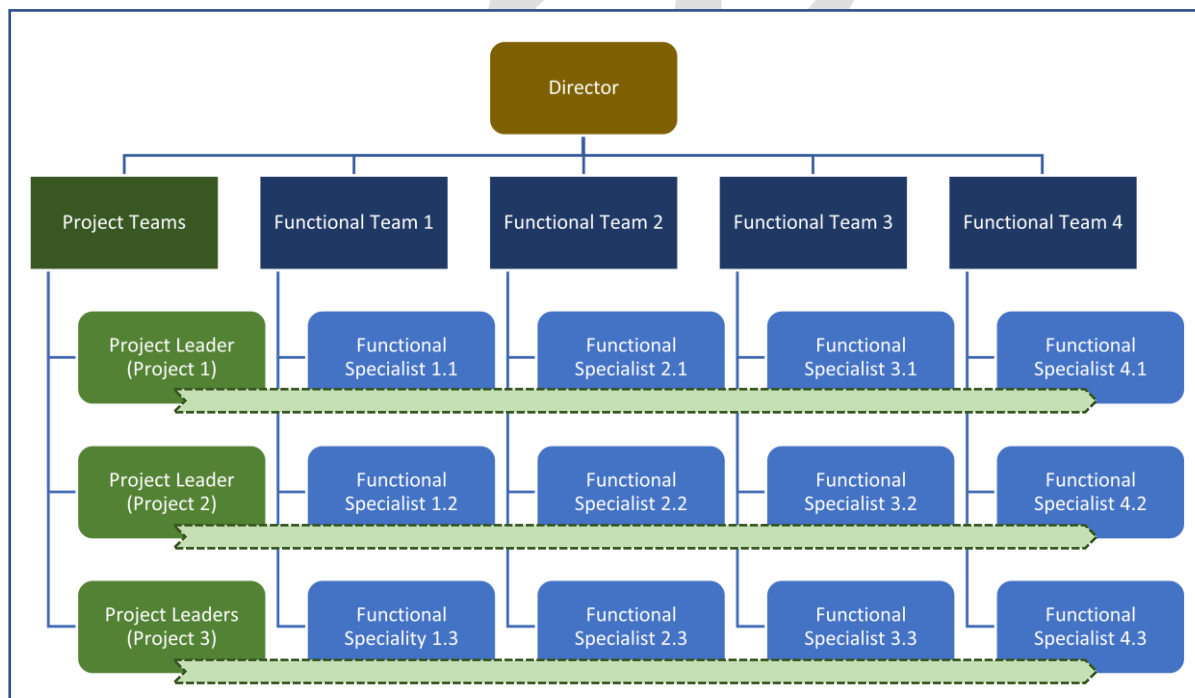
Organizational culture refers to a set of shared assumptions and norms that guide the behavior of an organization's members. An ethical culture in workplace is the base for effective management and teamwork for sustainable organization. Research institutions should therefore strive to build an ethical culture by securing the core ethical principles at work through developing and enforcing relevant codes of conduct, on:

456 • social value and social accountability;

457 • ethical, legal and quality compliance;

458 • transparency, integrity and whistle-blowing;

459 • equal opportunity (including but not limited to cultural diversity and pluralism, non-
460 discrimination of minorities and vulnerable groups, and intolerance of sexual or other types
461 of harassment);

462 • maintaining an inclusive and unbiased approach to staffing, and appoints research staff
463 keeping gender balance in mind;

464 • promoting, and supporting the principle of gender inclusivity and equity throughout the
465 research cycle;

466 • respect, open mindedness, open communication and collaboration;

467 • continuous learning;

468 • occupational health and safety.

469   *3. Knowledge Management, Quality Management and Risk Management*

470 A research institution could only achieve its objectives through continuous accumulation of
471 knowledge and experience – which may take times. This means that a research institution should
472 facilitate not only contemporaneous collaboration among staff members working together at the
473 same time but also cross-generational collaboration for members who worked for the institution at
474 different time. Robust "**knowledge management**", "**quality management**" and "**risk
475 management**" are therefore the key for sustainable research institutions.

476 Knowledge management is the way to collect, organize and retain information and knowledge in
477 a retrievable and usable manner. Good knowledge management supports the efficient and
478 effective acquisition, accumulation, organization, processing, utilization and sharing of
479 professional knowledge and experience – among staff members and over time – and facilitates
480 innovation and development of a research institution as a "**learning organization**" able to evolve
481 continuously to meet its changing research needs and operate with long-term sustainability.
482 Knowledge management may be powered by an adaptive information technology system, but
483 should more importantly be built on a learning culture signified by open exchange, sharing and
484 proactive learning, as well as continuous improvement with the support of a robust quality
485 management system.

486 Quality is a cornerstone of health-related research. A quality management system is a continuous
487 cycle consisting of four components including:

488 • **quality planning and standard
489 establishment**: identifying or defining
490 applicable quality standards and
491 establishing suitable policies and
492 standards operating procedures (SOPs)
493 (e.g. establishing institutional policies
494 mandating research ethics and scientific
495 oversight by a research ethics committee
496 appointed by the research institution);

497 • **execution of quality standards**: training
498 of staff and continuing monitoring of
499 performance (e.g. providing training on
500 updated concepts and requirements on
501 health-related research);

502 • **quality evaluation**: regular and
503 systematic evaluation of performance

Table 2: *The quality management cycle*
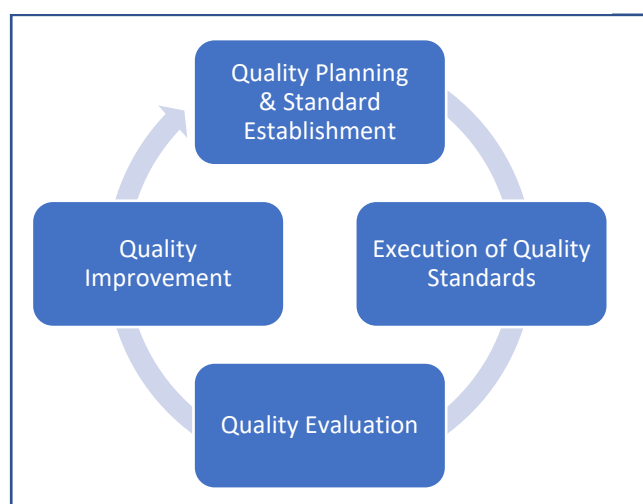
504   (e.g. establishing a quality control mechanism and performing quality control regularly and
505   as needed);
506   • **quality improvement**: undertaking corrective actions and preventive actions in response
507   to any quality issues identified, including escalation to senior management and research
508   ethics committee, and adjusting quality standards and quality plans to support continuous
509   improvement (e.g. classifying quality issues based on the nature and level of impact and
510   prescribing appropriate corrective and preventive actions).

511 Any research institution aiming at continuing involvement in health-related research is
512 recommended to establish an operable quality management system meeting its research needs.
513 Robust quality management also helps an institution to control its risk and attain long-term
514 sustainability.

515 Research is a process of discovering new knowledge. This unavoidably involves uncertainty and
516 hence some risks. Health-related research relies on the willingness of research participants and
517 the public, involves utilization of scarce (public and private) research resources, and is subject to
518 stringent compliance requirements. Any research institution therefore should consider at least
519 three main areas of risk including:

520   • **participant risk**: risk on protecting the rights, safety and well-being of research
521   participants and the related communities;
522   • **compliance risk**: risk on ethical, legal and quality compliance;
523   • **resource risk**: risk on appropriate acquisition and utilization of research resources.

524 Research institutions should not be afraid of risks provided that those risks are well known and
525 are under control. Whilst risks may not be fully eliminated, they could be effectively managed by
526 applying the "**6As risk management strategy**" as outlined in Table 3 below.

527 **Table 3:** 6As risk management strategy for research institutions

Risk Management Strategy		Examples of Risk Management Measures
Alert	Identifying risks and communicating with the relevant stakeholders	• Identifying risks through scientific and ethical review • Communicating risks with research participants via informed consent
Abate	Minimizing the likelihood (probability) of risk occurrence	• Implementing public involvement in research design and arrangements • Enhancing research competence of research personnel via training and learning • Implementing a robust quality management system
Alleviate	Minimizing the consequence (harm) of risk occurrence	• Implementing continuing oversight of research activities to facilitate early detection of risk occurrence (e.g. establishing safety monitoring committees for research projects of higher safety risk) • Implementing a complaint management mechanism and a contingency management mechanism to facilitate prompt handling of risk occurrence
Assign	Transferring risks to third parties	• Transferring risks by insurance/indemnity to insurers/indemnifiers • Allocating risks appropriately by written contracts among collaborating parties
Accept	Accepting identified risks	• Accepting identified and controlled risks by allocating sufficient resources and implementing an appropriate risk management mechanism

Abandon	Giving up research activities with unacceptable risks	• Giving up research activities with unacceptable risk • Making substantial modifications to research projects to bring their risk to an acceptable level

528

4. Corporate Communications

530 Health-related research is people-oriented, since it is performed by people (e.g. researchers,
531 research institution personnel and sponsors), with people (i.e. research participants) and for
532 people (i.e. patients and public). Research institutions are therefore accountable to the public, in
533 particular the key stakeholders, and has the responsibility to properly communicate their research
534 activities, results and outputs to them in a timely manner.

535 Corporate communications refer to the way an organization communicate with its internal and
536 external stakeholders. With respect to a research institution, key stakeholders include (but not
537 limited to):

538 • research participants;
539 • patient groups;
540 • the general public and media;
541 • research ethics committees and regulatory agencies;
542 • professional scientific associations/organizations/networks;
543 • research project sponsors;
544 • funding bodies; and
545 • researchers, research personnel and supporting staff.

546 Corporate communications are not only about disclosure of research results. They should be taken
547 as a part of a research institution's organizational strategy and bring important value including:

548 • **social responsibility and social impacts**: fulfilling an institution's social responsibility of
549 research transparency and accountability and communicating the social impacts;
550 • **public awareness and trust**: increasing public awareness and trust, and their support on
551 health-related research;
552 • **patient/public focus**: aligning research focus with the needs of patients/public and
553 improving research design through patient/public participation;
554 • **research participants involvement**: involving the participants in research projects and
555 activities;
556 • **scientific exchange**: accelerating research by sharing of research methods and results
557 via publication and public disclosure;
558 • **research collaboration**: encouraging research collaboration among research institutions;
559 • **funding**: attracting research funding and resources;
560 • **staff commitment**: promoting staff's commitment to the institution's mission, vision and
561 values and improving the institution's performance, sustainability and long-term success.

562

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580

Chapter 2: Ethics, Law and Scientific Integrity

581

Key words

582

583 *Obligations – Rights – Responsibilities – Scientific freedom – Scientific integrity – Social license –*
584 *Scientific culture*

Introduction

585

586 Health-related research raises a wide range of ethical and legal challenges. In this chapter we will
587 describe the responsibility of institutions to create an environment where people adhere to the
588 principles described below. If national laws use a description of biomedical research that narrows
589 research to drug clinical trials, we urge the institutions performing research to follow the broader
590 definition of health-related research used in this guideline, in the 2013 Declaration of Helsinki, the
591 2016 Declaration of Taipei and the 2016 CIOMS International ethical guidelines.

592 First, there are issues related to the **protection of research participants**: respect for autonomy
593 of participants and for their dignity, fair inclusion of populations, protection of vulnerable
594 populations, respect of privacy and confidentiality, informed consent, favorable balance between
595 the risks and the benefits, choice of comparators, compensation in case of research related
596 damages, etc.

597 Second, the **rights of the researchers and scientific freedom must be respected**. This
598 includes having access to the necessary resources, having limited barriers to publish and share
599 research data and results, being protected from negative external pressures (financial,
600 professional and academic), etc.

601 Third, the **scientific integrity of research activities must be guaranteed**. This not only requires
602 managing conflicts of interests, preventing and addressing the occurrence of scientific
603 misconducts but it also creates a culture in which more emphasis on the social value of research
604 can flourish.

605 Fourth, regardless of their statutes and whether research is part of their mandate or core business,
606 **research institutions are accountable to research participants and populations** whose trust
607 is indispensable/essential to ensure participation in - and support for - research. This implies
608 working in transparency, co-creation in research, communicating about research activities and
609 thus earning the trust and social license to operate from patients, communities and the public in
610 order to be able to continue scientific research.

611 In many research institutions, the task to cope with all those complex ethical and legal issues lies
612 on the shoulders of the individual researchers. Yet, the research institutions have their own
613 responsibilities - first towards research participants who also are patients or key stakeholders in
614 those institutions, and then/second, towards the researchers themselves as their employees or
615 service providers/consultants. At least, their responsibilities should be carefully assessed to
616 manage liability risks if something goes wrong in a research project.

Points to consider and how to address them

617

5. *Responsibilities towards research participants*

618

619 Research institutions are responsible to ensure that research participants rights are respected
620 because these institutions function either as employers of the researchers or as research sponsors
621 when there is no external sponsor (funding agencies, foundations, industry). In most countries,
622 institutions are not allowed to waive their responsibilities. This means they should implement
623 oversight mechanisms over research activities conducted by their employees or within their
624 infrastructure – or in relation with them – , ensuring that researchers act according to the applicable

ethical, legal, professional and scientific standards and that the welfare, rights and dignity of the participants are guaranteed. The level of scrutiny depends on the nature and the intensity of research activities and the level of risks for the participants, the community and society at large. The more intense the research activities are and the higher the risks are for the participants, the higher is the interest in research institutions to set up the necessary mechanisms to fulfill their obligations to limit the risks and manage the consequences or research induced damages (see Chapter 9: Institutional Research Oversight).

Special attention should be given to:

- Assuring that employees, collaborators and partners involved in research as investigators or member of research teams have the required education, training and expertise according to the applicable standards and law;
- Ensuring that researchers and research team members are gender balanced and belong to diverse ethnic groups that are representative of the research populations under study;
- Ensuring that research projects are submitted to the competent research ethics committee (REC) and competent authorities for review and that no project starts without prior approval/positive opinion of the competent REC and competent authorities when required by law. For that purpose, establishing a register of research proposals with their status (submitted, approved, on-going, ended) and tracking this at a central level is important;
- When there are more than one REC operating within the research institution or in relation with it, providing clear guidance to researchers to which REC they must submit any given project and preventing any form of "forum shopping";
- When by law a project should not be reviewed not only by the competent and relevant REC, but also by other committees such as biosafety board or resource management committee, ensuring that researchers are informed about their obligation and providing them with clear guidance on the procedure to follow;
- Ensuring that all required contracts and agreements (e.g. Material Transfer Agreements, Data Sharing Agreements or Intellectual Property Agreements) are adequate and signed to protect the participants as well as the interests of the researchers and the institution;
- Ensuring that any documents including contracts:
  - o Are compliant with the information and consent form;
  - o Provide for care for participants' health needs while participating in research in accordance with applicable law (cf. 2016 CIOMS International ethical guidelines, Guideline 6[14]);
  - o Provide for participants access to medical care and compensation in case of damages suffered while participating to research, in accordance with applicable law;
  - o Do not limit the communication of any new information of interest to participants.
- Following up in case of complaints about research misconduct.
- Ensuring that personal data and biological material are handled with respect to the applicable principles, including privacy, confidentiality, and global justice. Making sure that the institution provides substantial support to the researchers to assess the required level of data safety as well as ethical and legal counsel to meet those requirements (see Chapter 4: Collection, storage, and use of data and/or biological materials in health-related research).

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[14] Council of Europe (COE) *Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin.* 2016.

669 ### *6. Responsibilities towards researchers and research team members*

670 The first responsibility of institutions towards researchers and research teams' members is to
671 provide them the necessary support so they can fulfill their responsibilities towards research
672 participants and respecting the quality standards of research. Therefore, all measures aiming at
673 respecting the rights of research participants should be considered as protecting and supporting
674 the researchers and the research teams' members as well. However, researchers also need
675 specific support to protect their interests in terms of scientific freedom and integrity. These
676 responsibilities are also reflected in the 2017 UNESCO recommendation on science and
677 scientific researchers[15]

678 Special attention should be given to:

679 - Defending scientific freedom in the negotiation and conclusion of research agreements
680 and all other contracts related to research activities. This includes warranting that
681 researchers, in the respect of participant's rights, keep control over the design of their
682 projects, over the collected data and biological material, over the research analysis and
683 the publication. Any limitation to the right to publish results, either positive or negative
684 depending on the research primary and secondary outcomes, should be carefully
685 assessed to guarantee that it is limited in time and that all results could be published within
686 a reasonable time.
687 - Providing ethical or legal support and counselling to researchers for issues that may raise
688 in the drafting, evaluation, conduct, analysis and publication of research projects. This
689 could take the form of giving access to the institution's ethical and legal resources, by
690 offering resources to seek legal counselling on specific issues, such as liability, and by
691 providing some legal support in relation with the conclusion of the various agreements
692 related to the conduct of research projects, for instance by making agreements templates
693 available.
694 - Create conditions for meaningful engagement and participation in the full cycle of a
695 research project, as well as capacity building and contributions towards research outputs.
696 Research participants, patients and local communities should be included throughout the
697 research process from planning through post-study feedback and evaluation.
698 - In research partnerships where researchers are operating in limited-resources settings,
699 additional care should be granted to guarantee that the local researchers benefit from the
700 same freedom and protection as their colleagues from high income settings, for instance
701 by securing their rights in research agreements and research funding agreements.
702 - Institutions are encouraged to provide research management, financial risk management
703 and forecasting as well as administrative and legal support.
704 - Assessing research agreements. This at least implies:
705 o Advising researchers on their capacity to sign or not to sign an agreement on behalf
706 of the institution.
707 o Assessing whether those contracts respect the applicable laws in terms of
708 protecting the participants and the interests of the researchers and the institution.
709 o Developing templates for agreements (or using existing ones at the local,
710 professional or national levels) and signing umbrella agreements with partner
711 institutions and stakeholders with whom there are regular collaborations in terms
712 of research activities and exchanges of personal data and biological material.

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[15] United Nations Educational, Scientific and Cultural Organization (UNESCO), *Recommendation on Science and Scientific Researchers*. 2017.

7. Institutional culture to enhance working with scientific integrity

714 In a lot of scientific environments there still is a culture which can be described as 'publish or
715 perish'. That culture has put scientific integrity under stress and has let the scientific community
716 to produce a lot of research waste (Lancet series 2014) (see Chapter 3: Scientific standards),
717 which has produced results that are hard to replicate and brings hardly any social value. In such
718 a culture of 'publish or perish' the likelihood of scientific misconduct increases with detrimental
719 consequences.
720

721 The countermovement is visible under different headings (e.g. Open Science, Responsible
722 Research and Involvement, Science in transition) and puts much more emphasis on the quality,
723 usability and social value of research and less emphasis on H-index and on Citation Indexes of
724 journals. It should be noted that Open Science does not only mean publishing in Open Access
725 journals, but also means open to society during all research phases.

726 Another aspect of scientific culture centers around hierarchy. Although clear communication lines
727 are beneficial for an efficient conduct of a research project (see Chapter 1: Research Institution
728 Management), it must be underlined that a strict hierarchy may contribute to an atmosphere in
729 which conflicts of interest could flourish and scientific misconduct could occur. It is essential for
730 researchers to operate from a stance that the other person could be right; to allow
731 counterarguments; to acknowledge that reigning paradigms may be wrong and that new creative
732 ideas help to bring a field forward. Hence it is important to create a safe atmosphere in institutions
733 that perform research in which scientific creativity can flourish.

734 Scientific knowledge is a source of hope and of dispute in times of uncertainties. It requires trust
735 from the public but also within the scientific community at the local, national and international
736 levels. Research institutions have a responsibility in maintaining and fostering that trust as they
737 are directly affected when it is questioned or lost, and also because it impacts trust in the larger
738 scientific enterprise. A breach of scientific integrity, either by a researcher or by the research
739 institution, can affect the participants' welfare, rights and dignity but also the capacity of research
740 institutions to fulfil their mission beyond the research field.

741 According to the 2016 CIOMS International ethical guidelines (Guideline 25[16]) research
742 institutions, researchers and research ethics committees should take the following steps:

743 - Research institutions should develop and implement policies and procedures to mitigate
744   conflicts of interest and educate their staff about such conflicts;
745 - Researchers should ensure that the materials submitted to a research ethics committee
746   include a disclosure of interests that may affect the research;
747 - Research ethics committees should evaluate each study in light of any disclosed interests
748   and ensure that appropriate means of mitigation are taken in case of a conflict of interest;
749   and
750 - Research ethics committees should require their members to disclose their own interests
751   to the committee and take appropriate means of mitigation in case of a conflict of interest.

752 Special attention should be given to:

753 - Setting up internal procedures or guidelines addressing conflicts of interests and scientific
754   misconducts and protecting whistleblowers;

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[16] Council of Europe (COE). *Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin.* 2016.

755   -   Ensuring access to training on those issues at all levels, starting with undergraduate
756   education institutions and including all personnel potentially involved in research activities
757   (see also UNESCO 2017[17]) including Research Ethics Committee members[18];
758   -   Adhering to anti-bribery laws;
759   -   Offering researchers the necessary legal support especially for research with external
760   partners.

761

8. *Accountability, transparency and participation*

763 Research institutions rely on the potential participants and the population to conduct research
764 activities. This requires a high level of trust that can only be achieved when acting in an
765 accountable and transparent way including some level of participation of all stakeholders,
766 especially the research participants, patients, and the population.

767 Special attention should be given to:

768   -   assuring that research activities are included in the annual report and subject to question
769   by the competent organs/units/committees of the institution and the general public.
770   -   Reporting to clinical trial registries or similar research registries (where applicable) and/or
771   making information available on the website of the institution (where available), so that
772   information about research can become available also in ICTRP
773   (https://www.who.int/clinical-trials-registry-platform).
774   -   Defining procedures that allow patients, research participants and the general public to be
775   involved in defining research priorities and in the drafting of research strategies or research
776   projects.
777   -   Including patients, participants or their representatives in the organs/units/committees of
778   the institution, if possible, with decision power.

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[17] United Nations Educational, Scientific and Cultural Organization (UNESCO), *Recommendation on Science and Scientific Researchers*. 2017.
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793 and governing dual-use research https://www.who.int/publications/i/item/9789240056107

794 WHO *Standards and Operational Guidance for Ethics Review of Health-Related Research with*
795 *Human*. 2011

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797 *research involving human subjects*. 2013

798 World Medical Association (WMA) *Declaration of Taipei – ethical considerations regarding*
799 *health databases and biobanks*. 2016

800 Other international laws such as EU regulations and directives

801 National laws

802 - Human rights
803 - Patients' rights
804 - Labor law (protection of the researchers as workers/employees)
805 - Contract law
806 - Liability law
807 - Data protection law
808 - Intellectual property law (authorship, patent …)
809 - Public health law
810 - Therapeutic products law (medicinal products, medical devices, human cells, tissues and
811   organs …)
812 - Biological safety, fight against epidemics
813 - Education and research law
814 - Scientific integrity (conflict of interest, scientific misconduct …)
815 - Anti-bribery law
816 - Human research law
817 - Biobanking law

818

Chapter 3: Scientific standards

Key words

Expertise – Feasibility – Methodology – Scientific review – Study conduct – Study design – Rigor – Resources

Background and Principles

The primary goals of health-related research are to understand human health and well-being, the causes, development and effects of diseases, and to identify or improve preventive, diagnostic and therapeutic interventions to maintain or restore health and improve quality of life. There are many useful approaches to health-related research, including clinical trials, observational studies, natural history studies, epidemiological studies, social science studies, and research using existing human biological material and data. Not necessarily depending on the approach, research involving human participants can be based on quantitative methods, qualitative ones or a mix of both. For all approaches, and regardless of the envisioned risks to the research participants, scientific rationale and methodological rigor are considered *sine qua non* ethical and scientific requirements. Attention to scientific quality, rigor and feasibility in the research objectives, design and methods is essential in order to assure the usefulness and quality of the data, avoid waste, and justify asking humans to participate while protecting their rights, safety, and well-being.

Studies also show that research produces blind knowledge by not including sex and gender differences in the design and not reporting sex or gender of participants in their results. This reduces reproducibility, resulting in a waste of resources, being a missed opportunity for innovation, causing harm and contributing to health inequity[19]. It is the responsibility of research institutions to ensure that researchers consider and account for sex and gender throughout the entire research process, including the conceptualization and design of research and the publication of results. The inclusion of sex and gender is not solely a matter of including men and women in trials, but rather it necessitates the collection and reporting of data that is disaggregated by sex, as well as meaningful sex- and gender-based analyses. In fact, a growing number of medicals journals and funding agencies are requesting today a gender-sensitive approach and/or gender equality plan.

In order to avoid as much as possible research waste, it is important to improve health related research workflow. The term "research waste" can been defined as research outcomes that cannot be used or with no societal benefits. That waste could be potentially avoided if the development of health-related research preceded by a systematic assessment of the existing evidence. In addition, the institution should encourage their researchers to perform health related research focused more on producing replicable results with social value instead of their own visibility through an H-index or on citations indexes[20].

Much of the responsibility for scientific quality and integrity lies with the researchers. Yet, institutions that host research are responsible for making sure their researchers and research teams have the appropriate guidance, training, and support to conduct quality research and that there is sufficient review and oversight of the science and the research plans. To fulfill these

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[19] Building back better: towards a gender-responsive international instrument for pandemic prevention, preparedness, and response, Consensus Statement. 2020. Available at: https://www.gendro.org/consensus-statement

[20] Chalmers I, Bracken M, Djulbegovic B, et al. *How to increase value and reduce waste when research priorities are set.* Lancet 2014; 383: 156–65.

858 obligations, institutions should ensure the quality, integrity, and rigor of the science and the
859 scientific standards employed in their research. Research that is not scientifically sound and that
860 cannot achieve its stated objectives is not considered ethical[21].

861 ## **Points to consider and how to address them**

862 ### *9. Awareness and coordination of proposed and ongoing research*

863 Quality research requires knowledge and skills, planning, coordination, caring and resources.
864 Institutional attention to the significance of the research, the details of research design and
865 conduct, and the feasibility of successfully completing the research are essential to protect
866 participants and to generate useful and reliable knowledge, as well as compliance with regulations
867 and efficient use of institutional and research resources.

868 Specific attention should be given to:

869 • Identifying applicable policies and guidelines for researchers or, when need be,
870 establishing policies and adopting guidelines for them to understand requirements for
871 protecting human participants, sharing of data, the mission and research scope of the
872 institution, available support resources, and procedures for review and approval of the
873 research proposals;
874 • Assuring compliance with applicable laws, regulations and institutional policies on human
875 research and protection of personal information;
876 • Designating responsible individual(s) or, when need be, establishing a central office to
877 assure awareness of research being conducted in the institution and that these studies are
878 performed with high quality standard and aligned with institutional policies;
879 • Ensuring that institutional policies are inclusive and pay attention to removing biases in
880 recruitment, and promotions and are gender sensitive;
881 • Ensuring that all involved services and committees within the institution are gender
882 balanced and representative of the populations in which research is conducted;
883 • Ensuring that researchers are duly informed of the mission and research scope of the
884 institution, the support resources available, and the procedures for review and approval of
885 the research proposals;
886 • For institutions that are primarily intended for the provision of services define their research
887 goals and approaches considering their legal and social mandate towards the served
888 population and capability to assure compliance with quality standards of health research
889 with the existing infrastructure and human resources;
890 • Depending on the intensity of research activities, developing and implementing standard
891 operating procedures (SOPs) for interactions between investigators and the institution´s
892 research coordinating individuals or entities. The SOP should specify requirements for
893 researchers including research staff during the planning and review of their research
894 proposals, and then during the implementation and conduct of the approved studies;
895 • Assuring that the research plan is feasible and that the institution and the researchers have
896 the necessary resources to fulfill their obligations derived from the implementation of the
897 study, for example the retention of source documents and regulatory files for eventual
898 inspections and/or need of re-contacting the participants after the closing of the study;
899 • Assuring that the data collection is well standardized in the institution and follow the
900 ALCOA+ principles as detailed in Chapter 4: Collection, storage, and use of data and/or
901 biological materials in health-related research;

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[21] Council for International Organizations of Medical Sciences (CIOMS) *International ethical guidelines for health-related research involving humans*. 2016.

902 • Evaluating and mitigating the potential impact of diverting institutional human or material
903 resources from healthcare activities towards research activities.

904

905 *10. Scientific value and appropriate research plan*

906 The goal of health-related research is to generate or contribute to generalizable knowledge about
907 health and illness. This applies to both quantitative, qualitative and mixed methods research. An
908 appropriate and rigorous design and careful conduct of research helps protect participant safety
909 and the generation of reliable evidence.

910 A rigorous research proposal requires knowledge of particular areas of science and related
911 research, reasons for the specific approach to answering the research question(s) and attention
912 to whether the approach is feasible. A written research proposal or protocol should describe the
913 study's justification, objective(s), design, methodology, statistical considerations and organization,
914 qualifications of the research team, and other information to ensure the safety of participants and
915 the quality and the integrity of the data collected.

916 Specific attention should be given to:

917 • Assuring clear and concise written research proposals or protocols that describe the
918 study's justification, objective(s), design, outcomes, methodology, statistical
919 considerations and organization, and other information;
920 • Considering adoption of a standard template for writing research protocols, based on
921 existing country-specific or study topic-specific templates. Although the component parts
922 of a given research proposal may differ for a variety of reasons, every research proposal
923 should clearly state what the research question is, why it is important, how it improves
924 upon what is already known, and how the design, methods, and procedures will be used
925 to answer the question and determine the primary outcome (s);
926 • Even though ICH-GCP recommendation are intended to conduct interventional trials with
927 drugs, compliance with ICH-GCP for all health-related research could be considered, when
928 applicable, to ensure public assurance that the rights, safety and well-being of participants
929 are protected;
930 • Assuring that the study design is consistent with accepted scientific principles, appropriate
931 for answering the research question, and ethically acceptable. There should also be a
932 feasible and clear plan for how data will be collected, analyzed, and reported in a
933 scientifically appropriate manner;
934 • Assuring that the research protocols are attentive to sex and gender and inclusive of race,
935 ethnicity, age, and other relevant considerations;
936 • Assuring that sex and gender considerations are taken into account during data collection,
937 and analysis, that sample sizes allow for disaggregated data analysis based on sex and
938 gender considerations and other relevant variables, or providing justification when they do
939 not;
940 • Ensuring that the research is feasible and that the institution has the necessary resources
941 and infrastructures to successfully complete the proposed research in order to avoid as
942 must as possible research waste;
943 • Considering implementing Sager guidelines "sex and gender equity" if relevant for the
944 research;
945 • Considering including participants or their representative (Patient and Public Involvement
946 and Engagement, PPIE) and/or health care users in the process of the study design in
947 order to avoid mismatch between what researchers want to do and what patients and local
948 communities need and then improve social value of the study.

949

11. Scientific rigor—review and training

Planning and conduct of quality health related research require thorough and up-to-date knowledge of the study-specific topic, and / but also expertise in matters of scientific methodology, statistics, bioethics or research ethics, quality management, and legal and regulatory issues applicable to human research, patients' rights, and protection of personal information.

Institutions should have and support mechanisms for reviewing, evaluating, and providing oversight of health-related research. Such mechanisms are important to ensure scientific quality, reduce possible biases and waste, fulfill ethical standards, comply with regulations and laws, protect participants and other stakeholders, and maintain public trust. Some national laws allow for exceptions, but ethical guidelines and regulations require review by a research ethics committee (REC) before a health-related study begins. In addition, assessment of the scientific quality of the proposed research is necessary as "Bad science is Bad Ethics", and wastes resources.

Special attention should be given to:

- Assuring appropriate review of the science and scientific rigor of a proposed research design and plan. Scientific review should be provided by the competent REC/IRB or the appropriately constituted one. Alternatively, independent scientific review by a scientific review committee or designated individual(s), a peer review group, or some other mechanism is recommended, and should include individuals who have the expertise to evaluate the scientific questions and the methods proposed;
- Assuring that investigators and research team members have the proper skills and knowledge to conduct the proposed research. This may include knowledge and skills in the scientific and professional area as well as in appropriate and rigorous research methodologies;
- Considering referring to or providing initial and ongoing training on ethical standards, good practice and local and international regulations applicable to human research, and on scientific methodology, biostatistics, and scientific writing;
- Providing resources, whenever possible, such as methodologists, statisticians, research coordinators, and others who are experienced with the kinds of research being conducted in the institution and can support the investigators and research teams, or be part of the research team;
- Establishing a culture committed to the responsible conduct of science (see scientific integrity);
- Establishing a mechanism to monitor data and participant well-being throughout a research study (Chapter 9: Institutional Research Oversight).

Table 4: Summary checklist for research institutions to assure scientific standards

Infrastructure	Expertise & Training
• Coordinating designated institutional research official(s) or establishing a research office • Institutional policy and SOPs for researchers and other staff involved in research (support) activities	• Access to expertise in methodology, research design, statistics, etc. • Training for researchers and research teams, and other key-staff involved in research (support) activities
Tools	**Review & Monitoring**
• Standard templates for written research proposals/protocols	• Process for scientific and ethics review of the rigor in the design and conduct of research • Plans for monitoring data

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Chapter 4: Collection, storage, and use of data and/or biological materials in health-related research

Key word

Biological materials – Biobank – Data – Databank - Participants' rights – Good custodianship – Data protection – Data integrity and validation – Database – Informed consent – Source data

Background and Principles

Collections of data and biological materials are important tools for health-related research which contributes to a better understanding of diseases, health, health behaviors and the relationships between the various factors that influence them. This guideline covers all collections of data and/or biological materials, including those where the data and material are not stored but directly used for a specific research project, as well as biobanks and databanks that involve secondary uses. Of note, the term "use" of data and biological materials covers collection, analysis, storage, archiving, sharing, exporting, reporting and destruction.

As stated in 2016 CIOMS International ethical guidelines (Guideline 11)[22]: "When data and biological materials are collected and stored, institutions must have a governance system to obtain authorization for use and future use of these data and biological materials in research. Researchers must not adversely affect the rights and welfare of individuals from whom the data and materials were collected".

As a general rule, proper governance and good custodianship should protect the rights and interests of individuals and promote quality research including data integrity. The governance mechanisms should be comprehensive and correspond to the research institution's scope and intensity of research activities. The governance measures enable promises to be kept to participants, researchers, authorities, and other stakeholders in health-related research and foster trustworthiness. Any activity, operation or procedure carried out or established during the life cycle of collection and use should follow the principles of transparency, accountability, and inclusion of interested persons in compliance with country's applicable national and international ethical and professional standards and legal requirements.

Institutions collect data and/or biological materials for different purposes including routine diagnostic and clinical activities and research, but data collection is a more widespread practice than biological material collection. Institutions must respect data protection principles and ensure data integrity, quality, privacy and security.

Data handling in the context of health-related research raises two major concerns. First, a key component to conduct research is that the institution should provide adequate support/tools to record source data. Indeed, the original medical records or patients' files (and/or certified copies of original records) are the first place where some or all data relevant for a study are recorded, representing the source documents/data of the research study (for instance according to ICH-GCP 1.51 & 1.52 for clinical research). Secondly, the data flow in health-related research, meaning the transcription of the source data into a study database and then their analyses should be well planned, in compliance with applicable quality and regulatory standards, and ensure data integrity, quality, privacy and security. High quality of data (source data as well as study data[23], data

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[22] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health related research involving humans.* 2016
[23] Study data is referring to clinical research data, internal clinical and/or research databank and biobank.

1062 collected in a databank and/or biobank) generated is a crucial condition for the validity of the
1063 outcomes of research projects.

1064 In order to comply with the standards of good data handling, it is strongly recommended for the
1065 institution to have some basic tools in place to conduct health-related research, such as a Clinical
1066 Research Information System (CRIS).

1067

1068 **Points to consider and how to address them**

1069 *12. Responsibilities towards the participants*

1070 Participants who accept to provide data and biological materials for health-related research have
1071 rights and interests that must be protected throughout the life cycle of a project or a collection and
1072 (re)use. The starting point is broad informed consent and confidentiality measures. These
1073 mechanisms alone are not sufficient to protect the rights of participants; other transparent
1074 measures and procedures must also be put in place. The participation of individuals depends on
1075 their trust in the institution, which is why it is also important to include participants in the
1076 development and execution of governance procedures whenever possible (see 2016 WMA
1077 Declaration of Taipei, paragraph 20). The status of the broad informed consent (positive, negative
1078 and withdrawal) and the terms of the agreement should be checked on an ongoing basis during
1079 the collection of data and materials and during use or further use.

1080 Special attention should be given to:

1081 - Providing a template for the information and consent form. The informed consent could be
1082 specific for a known project or broad informed if a further use is planned. Templates for
1083 both forms should be available. Different information and consent forms should be
1084 available for legally competent or incompetent adults and for children. Broad informed
1085 consent may be a good solution for biobanks and databanks aiming for a data and
1086 biological materials storage for further use. For further requirements on informed consent:
1087 2016 WMA Declaration of Taipei, paragraphs 11-16, 2016 CIOMS International ethical
1088 guidelines, Commentaries on guidelines 11 and 12 [24];
1089 - Ensuring a procedure for withdrawal of consent (how to contact, whom, where) and its
1090 consequences is in place. The way of handling and/or destruction of data and biological
1091 materials after withdrawal of consent should be specified;
1092 - Ensuring the follow-up of the consent decision (positive, negative and withdrawal) over the
1093 time in order to make sure that the collected data and biological materials will not be used
1094 for research purposes if participants refused or decided to withdraw their consent.
1095 - Ensuring a general procedure for re-contacting the participants, if needed;
1096 - Ensuring that the researchers are mindful of and pay special attention to including gender
1097 diverse populations as well as including minority and other vulnerable populations in
1098 various aspects of the research project;
1099 - Ensuring the confidentiality of the participants' data and biological material. For the data,
1100 see point 5 "Data lifecycle". The coding of the samples should be the rule. Only a limited
1101 number of qualified personnel should be able to link the code to the name of the source
1102 person (i.e., have access to the key). The roles and responsibilities of team members, their
1103 privileges and access rights should be defined and documented. For further requirements

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[24] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health-related research involving humans.* 2016

on confidentiality: 2016 WMA Declaration of Taipei, paragraph 10 and 21, 2016 CIOMS International ethical guidelines, Commentaries on guidelines 11 and 12[25];

- Ensuring that a procedure is in place to inform research participants and the general public about the ongoing research and research outcomes. This communication could be done through the general communication channels (such as the public website of the institution) and/or be included in the annual report available to the public;

- Assuring that a procedure on return of results and disclosure of (un)solicited/incidental findings is in place. Particular attention should be paid to results that have an influence on the health of the participants. The procedure should explain which findings will be communicated to the participants, how and by whom. The participants however may refuse to be informed of these results. For further requirements on return of results and disclosure of (un)solicited/incidental findings: 2016 CIOMS International ethical guidelines, Commentaries on guidelines 11 and 12[26].

13. Access and transfer of data and biological materials

The use of stored data and biological materials implies first that researchers should have access to them. Rules of access and transfer, meaning who can request data and biological materials and how, should be put in place, in the respect of the limits of the informed consent and the principle of fairness as set out in the Global code of conduct for research in resource-poor settings, 2018 (articles 1 to 7).

Special attention should be given to:

- Ensuring that the rules for transfer of data and/or biological materials are clarified. A legal agreement (such as Material Transfer Agreement (MTA) and/or Data Transfer Agreement (DTA)) should be used for the transfer of data and biological materials for research. Such agreement may also be included in the research protocol. This allows research institutions and researchers to protect the rights of the participants and to keep promises made through informed consent. If needed, templates of these documents should be made available to researchers. Research institutions should provide guidelines and/or designate dedicated experts to support researchers in adapting those templates to the settings of their research;

- Providing guidelines on the rules for sharing collected data and/or biological materials with different types of users – such as researchers from the same institution or other institutions, or those coming from the academic sector, the commercial industry or governmental bodies;

- Ensuring a procedure for handling requests for access to stored data and/or biological materials. If needed, a resource management committee could be set up to manage these requests. This committee could assess the scientific relevance of projects before sharing resources and check that projects have the authorization of the relevant REC. This committee could include members representing different groups such as the management of the institution (e.g., departmental or institutional level), researchers, healthcare professionals and persons representing the participants and communities contributing to the biobank or databank. If data and biological materials come from participants in multiple countries, representatives from these countries could also be included in the committee.

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[25] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health-related research involving humans*. 2016

[26] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health-related research involving humans*. 2016

1147   ### *14. Biobank & Databank*

1148   The minimum requirements for setting up a biobank and a databank include the designation of
1149   persons responsible for its management, the preparation of documentation outlining its structure
1150   and activities, and the availability of resources necessary to achieve its purpose. Resources
1151   correspond to funding, qualified staff, infrastructure, a governance framework including PPI, and
1152   equipment, all of which must be planned for the long term. The institution has the responsibility to
1153   support researchers in their efforts to formalize their activities and assist with resource allocation
1154   or ensure that researchers have sufficient resources. A biobank and databank can only be
1155   qualified as an organized research setup if these minimal requirements are met, and a proper
1156   governance is in place.

1157   **Figure 2:** Biobank & Databank

1158
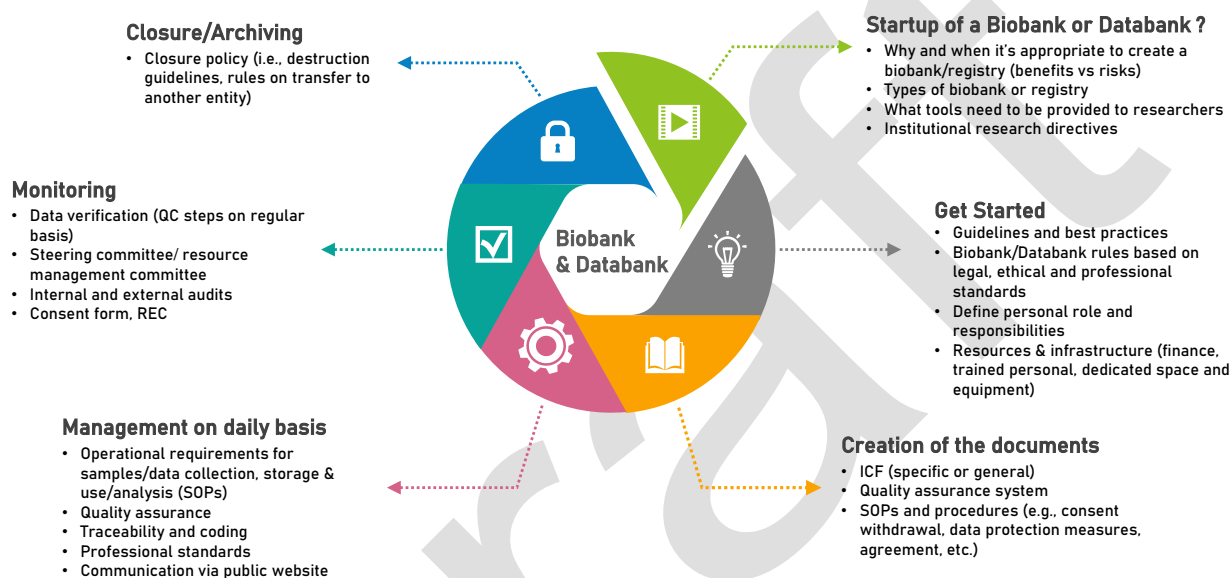
1159   Special attention should be given to:

1160   -   Ensuring that the researchers have access to the guidelines and best practices available
1161   in the field (such as those listed in the references to these guidelines). Knowledge of these
1162   standards can be the first step in formalizing the types of biobanks or databanks (i.e.,
1163   including biobank accreditation: ISO or other labels);
1164   -   Providing or identifying a template of document that describes the biobank or databank
1165   and its procedures, structures, and rules (a Regulation) in accordance with the applicable
1166   rules (see 2016 WMA Declaration of Taipei, paragraph 21 and 2016 CIOMS International
1167   ethical guidelines, Commentaries on guidelines 11 and 12[27]). The regulation should
1168   include the description of the biobank and/or databank and present the governance
1169   mechanisms. Guidelines could be made available to support researchers in adapting the
1170   template to the settings of their biobanks or databanks. The institution should consider
1171   having internal dedicated experts for advice and support to ensure that the information
1172   described in the regulation correspond to the real practice, that the structures are in place
1173   and that the rules and procedures correspond to daily management;
1174   -   Ensuring that the person(s) responsible of a biobank or databank is (are) designated with
1175   his/her (their) clear roles and responsibilities;
1176   -   Offering opportunities for participants and their communities or their representatives
1177   (PPIE) to be involved in the structures of the biobank or databank and/or in the

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[27] Council for International Organizations of Medical Sciences (CIOMS). *International ethical guidelines for health related research involving humans.* 2016

1178 creation/revision of the governance documents including but not limited to informed
1179 consent forms;
1180 - Ensuring the availability of financial, personal, and material resources necessary to
1181 achieve the purposes. The first step is to define the objectives of the biobank or databank
1182 and identify the resources needed to achieve them. Then it is necessary to identify the
1183 resources currently available to the institution or directly to researchers and to find a
1184 balance between the available resources and the planned objectives. Resources
1185 considered should include financial support (i.e. a clear and transparent financial concept),
1186 qualified staff (i.e. enough persons with appropriate qualifications and training) and
1187 infrastructure/equipment (i.e. including a procedure for the acquisition and maintenance of
1188 the equipment and space);
1189 - Ensuring a procedure in case of the end of activities or change of ownership.

1190

15. *Operational requirements for the collection, storage and use of data and biological materials*

1191
1192

1193 The operational measures must ensure the quality, security, integrity and privacy of the data and
1194 biological materials throughout the collection, storage, and use. For this purpose, a system for
1195 traceability should be setup and a basic quality management system (basic quality documents)
1196 should be available to the researchers. Traceability is also important to enable participants to
1197 exercise some of their rights (e.g. withdrawal of consent and its consequences). For specific
1198 requirement regarding data, see "Data lifecycle".

1199 Special attention should be given to:

1200 - Ensuring that the collection of source data and study data (electronic system and/or paper
1201 based) follow the ALCOA+ principles, namely: data should be **a**ttributable, **l**egible,
1202 **c**ontemporaneous, **o**riginal, **a**ccurate, **c**omplete, **c**onsistent, **e**nduring and **a**vailable;
1203 - Ensuring that standard operating procedures (SOPs) are available and operable,
1204 describing how technical and/or administrative activities are conducted, including detailed
1205 process addressing what, who, where and how these are to be performed.

1206 Specifically for biobanks, special attention should be given to:

1207 - Ensuring that the biobank facilities and equipment are aligned with the overall missions /
1208 objectives of the biobank. In particular, the biobank room must meet the requirements to
1209 provide safe space for the staff and biological materials stored, with controlled access;
1210 - Assuring that guidelines regarding biosafety measures related to work in laboratory are in
1211 place;
1212 - Ensuring that appropriate records and/or laboratory information management systems (i.e.
1213 LIMS or others) are in place to track the movement of biological materials (i.e. from
1214 collection to storage, retrieval and return);
1215 - Assuring to have a procedure regarding medical waste that can be used for disposal and
1216 destruction of biological materials.

16. *Data lifecycle*

1217

1218 Data management or data lifecycle is the process of collection, cleaning, and management of data
1219 in compliance with regulatory standards. The primary objective of the data management process
1220 is to ensure data accuracy, integrity, quality, privacy, and security. The tools available for
1221 researchers in the institution should comply with a data life cycle in order to improve the quality of
1222 the primary data collection but also to facilitate the conduct and support the data quality control of
1223 the study.

1224

Figure 3: Data lifecycle
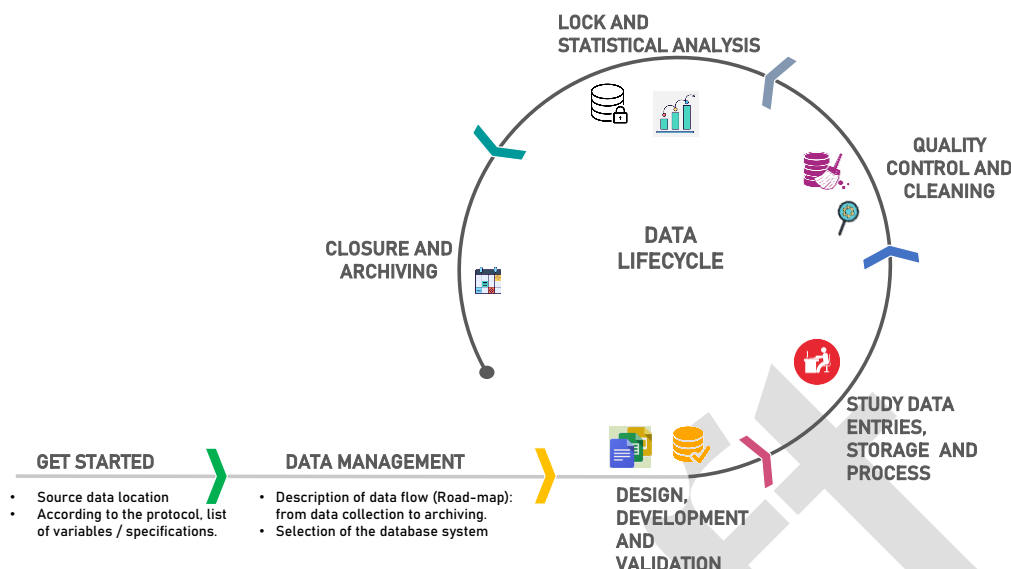
Special attention should be given to:

- Assuring to have in place a template of document (such as a Data Management Plan, DMP) that describes the procedures to be followed in the preparation and documentation of the collection of the data (e.g. electronic database). This document should describe all the steps to handle data from collection to archiving as illustrated by **Figure *3*:** Data lifecycle;

- Assuring that the database system available in the institution used to support a study, clinical and research databank and biobank is designed to prevent errors in data collection, modification, maintenance, archiving, retrieval or transmission. If electronic database cannot be used in the institution for any reasons, the data flow must be well documented;

- Assuring simplified guidelines are in place and/or dedicated experts are available to support the researchers in the different process of database design and development and data validation;

- Assuring that study data can be stored in such a way that backup copies can be easily and frequently made. In principle, paper documents should be scanned, stored, and archived electronically, they will be either included with the backup with other study files or stand-alone;

- Assuring the availability of a physically secure room with controlled access available to the researchers to archive all the study paper documents and electronic dedicated spaces on secure servers to archive all electronic the study data;

- Database servers should be physically secured with controlled access. Direct access to database servers should be restricted to individuals who are responsible for system monitoring and data backup;

- Assuring that your institution has a process in place to perform quality control and cleaning of the data either electronically or manually (see Chapter 9: Institutional Research Oversight);

- Assuring that the institution has a process in place to make the research databank openly available for reuse by the community after the data publication process, in accordance with FAIR Data principles/Open access, whenever applicable.

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1259
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1286

Chapter 5: Financial Management and Budgeting

Key words

Alternative institutional resource – Anti-bribery – Budget – Budget structure – Cashflow – Conflicts of interest – Cost recovery – Direct cost – Fair market value – Financial audit – Financial statement – Fixed cost – Indirect cost – Line item cost – Payment schedule – Per volunteer cost – Recurring institutional resource – Transparency

Background and Principles

Comparing with common areas such as research ethics, research participants protection, regulatory and legal compliance, management, data disclosure and publication, discussions on budgeting and financial management are relatively limited in the domain of health-related research. This may be attributable to the wide diversity of financial objectives, funding sources, funding structures and financial management policies among research institutions and research teams involved in different types of health-related research, leading to the difficulty in recommending generalizable budget structure and financial management policies applicable to all research institutions.

Good quality does not come without cost, but poor quality may induce even higher cost to research institutions. Inappropriate or inefficient financial planning and management could jeopardize the management of research institutions and their research projects. It may hamper the institutions' success and sustainability and their research projects' quality, and even compromise their primary mission as well as the interest of research participants and the public.

Whilst recognizing the diversity in financial objectives, policies and practice among research institutions, this chapter outlines four key areas in financial management for consideration by research institutions, including:

- institutional resources planning;
- project budgeting;
- financial administration; and
- financial compliance.

Points to consider and how to address them

17. Institutional Resources Planning

Setting up good governance practice for a research institution is a substantial and long-term commitment, which requires:

- investment on initial setup;
- allocation of resources for the institution's continuous operation; and
- availability of resources for individual research projects.

Manpower and facilities/equipment are the major resources required by any research institution, but viable institutions need more than these. Depending on the targeted scopes and volume of research, research institutions may have their specific cost structures and therefore different sets of cost items. A list of common cost types and cost items are highlighted in **Table 5:** Common cost types and cost items for research institutions below for reference.

1327 **Table 5:** Common cost types and cost items for research institutions

Cost Type / Cost Category	Initial Setup Costs	Recurring Costs	Project Costs
Facilities & Equipment			
Spaces, fixtures & fittings	Renovation, furniture	Repairing & maintenance	Project-specific facilities
Equipment	Office equipment, research equipment	Repairing & maintenance	Project-specific equipment
Staffing			
Salaries & benefits		Management staff, research/technical staff, supporting staff	Project-based staff
Training & development		Training courses, conferences, meetings	Project-specific training & meetings
Information Technology			
Hardware	Servers, computers, handheld devices, accessories	Repairing & maintenance	Project-specific hardware
Software subscription	Software licence subscription	Software licence renewal	Project-specific software subscription & renewal
Application development	Tailored application development	Application maintenance, debugging & upgrading	Project-specific application development & maintenance
IT services		Data hosting, cloud services, information security services	Project-specific IT services
Compliance & Risk Management			
Licences	Initial licence applications	Licence renewal	Project-specific licences/permissions
Accreditation	Initial accreditation applications	Participation in accreditation programmes	Project-specific accreditation application & maintenance
Business insurance		Medical malpractice, professional indemnity, public liability, property risk	Project-specific insurance
Operating Expenses			
Utilities		Electricity, gas, water	Project consumption
Consumables		Office consumables, research consumables	Project-specific consumables
Telecommunication, postage & courier		Phone/fax lines, international courier	Communication with collaborators & research participants

Cost Type / Cost Category	Cost Item Examples		
	Initial Setup Costs	Recurring Costs	Project Costs
Travelling & accommodation		Local transportation, overseas trips	Attending project meetings
Communications & marketing		Marketing materials, marketing events, newsletters, websites, social media	Project promotion, research volunteer recruitment
Outsourced services		Housekeeping, warehouse	Project-specific services

1328

1329 Individual research projects should in general be funded by project-specific resources such as
1330 research grants and industry sponsorship. Researchers are responsible for soliciting the required
1331 grants/sponsorship by leveraging their research merits which address scientific, social and public
1332 health needs. Establishment and maintenance of a research institution's human, facility and
1333 system infrastructure, however, should be financed by a combination of "**recurring institutional**
1334 **resources**" and "**alternative institutional resources**" as outlined in **Table *6*:** Recurring and
1335 alternative resources available to research institutions below.

1336 **Table 6:** Recurring and alternative resources available to research institutions

Examples of Recurring Institutional Resources	Examples of Alternative Institutional Resources
• Research institution's regular funding • Research institution's regular business incomes • Indirect/overhead fees generated from research projects	• Non-recurring government funding • Charity funding • Donations • Special grants • Research institution's reserve funds

1337

1338 Initial step toward good governance practice of a research institution could be financed by one-off
1339 alternative resources, depending on the type and scale of establishment. Continuing maintenance
1340 and operation of a research institution should be funded by recurring resources to ensure long-
1341 term sustainability. Dedicated research institutions are regularly engaged in many research
1342 projects and may generate sufficient resources by charging indirect/overhead fees out of the
1343 budgets for their research projects. Non-dedicated research institutions, however, may not have
1344 a stable and sufficient number of research projects to achieve a sustainable level of income.
1345 Hence, commitment by institutional management to continuously allocate necessary resources
1346 from their recurring institutional budgets is necessary. This is important to note that commitment
1347 of recurring resources does not necessarily imply perpetual allocation of substantial budgets. A
1348 research institution with a small number of research projects may easily kick-start its research
1349 establishment by a small budget covering only basic costs (e.g. minimal staff and facility costs). If
1350 and when research activities start to rise, contributions from indirect/overhead fees will increase
1351 in parallel and gradually become the major financial resources for supporting the research
1352 institution's continuing operation.

1353 ### 18. Project Budgeting

1354 Most research institutions, in particular public institutions or charities, do not aim to earn profits
1355 out of their research projects. However, they should at least secure the principle of "**cost**
1356 **recovery**" to ensure sufficient resources are made available for proper performance of their
1357 projects in accordance with all ethical, legal and quality standards.

1358 Different funding bodies may have different requirements on budget structures and presentation,
1359 and different research institutions may have different financial management policies. This section
1360 primarily gives a general guidance to research institutions and their researchers on preparing their
1361 research budget proposals from three key perspectives including:

1362 • cost types and cost items;
1363 • budget structure; and
1364 • payment terms and schedules.

1365 **Direct and Indirect Costs**: A project budget usually comprises "**direct costs**" and "**indirect**
1366 **costs**". Direct costs are costs and expenses which are directly incurred from project activities,
1367 whilst indirect costs are costs that do not directly arise from a project but are apportioned from an
1368 institution's general overhead costs and expenses such as office facility and administrative costs.
1369 The following table gives some examples of direct and indirect costs applicable to a research
1370 project:

1371 **Table 7:** Direct and indirect costs for research projects

Project Cost Types		Examples of Project Cost Items
Direct Costs	Staff Costs of Research Personnel	• Salaries of research staff specifically employed for research project • Apportioned manpower costs of existing research staff
	Equipment and Supplies	• Project-specific equipment • Project-specific software • Research evaluation tool licences • Project-specific consumables (e.g. laboratory, drugs etc.)
	Data Communication	• Wide area network (WAN) setup specifically to meet the requirements of a research project
Indirect Costs		• Licence fee of general software • Maintenance fee of general equipment • Rental of research institution's regular offices • Salaries of regular administrative staff

1372

1373 Since it is not straight-forward to objectively apportion indirect costs to individual projects, research
1374 institutions usually apply a standard overhead charge as a percentage (e.g. usually in the range
1375 of 15 to 30%) of the direct costs for the convenience of budgeting and administration. A research
1376 institution should consider its funding structure and set a reasonable overhead charge rate which
1377 aligns with the principle of cost recovery and at the same time allows sufficient resources allocated
1378 to cover the direct project costs.

1379 **Budget Structure**: A budget structure may be directed by funding bodies, but the principles of
1380 budget estimation remain valid. For instance, the budget structure requested by governmental
1381 funding bodies may adopt a modular concept, i.e. budget presented as a lump-sum for each area
1382 of activities (e.g. protocol development, statistical analysis). For commercial driven studies,
1383 however, commercial sponsors normally request detailed presentation of itemized costs in form
1384 of a budget spreadsheet under three major categories, including:

1385 • fixed costs (i.e. basic costs that are incurred for setting up a project irrespective of the
1386 actual number of research participants recruited in the project or research activities
1387 performed);
1388 • per participant costs (i.e. costs that are incurred from the participation of each research
1389 participant); and

1390 • line item costs (i.e. costs that are incurred only if a certain activity is performed).

1391 **Table 8:** Budget structural categories and corresponding cost items for research
1392 projects

Budget Structural Categories	Examples of Cost Items
Fixed Costs	• Professional indemnity and insurance, research ethics committee fee, participants recruitment, regulatory submission fee, pharmacy setup cost, laboratory tests setup cost, drug cost
Per Participant Costs	• A summation of cost of performing study procedures per each study visit (per visit cost) during the entire study for each participant. Example of cost items for study procedure: conducting informed consent, checking eligibility criteria, performing physical examination, data collection, performing internal quality check, drug dispensing, subsidy to volunteer
Line Item Costs	• Laboratory tests or imaging assessments that will only be performed if needed

1393

1394 **Payment Terms and Schedules**: In addition to the total amount under a budget, "**cashflow**" is
1395 also very important. Despite the variation of budget structures, research institutions should pay
1396 attention to the payment terms and schedules to ensure that sufficient funding is received for
1397 covering the expenses during different stages of a research project. For example, if the first
1398 payment under a budget will only be received by the research institution upon recruitment of 100
1399 volunteers, the institution and the researcher may not have resources to set up the project and
1400 perform the works before recruitment completion and the project could end up a failure. Close
1401 monitoring of project progress and regular processing of payments (e.g. quarterly) during the
1402 project period are therefore highly recommended to maintain a healthy cashflow for supporting
1403 the success of a research project.

1404 ### 19. Financial Administration

1405 Researchers are experts in health and science but, in general, may not be so skillful in finance
1406 and accounting. Nonetheless, proper administration of financial transactions and maintenance of
1407 financial records, from commencement until completion of a research project, are essential for
1408 assurance of financial compliance and facilitation of financial audits irrespective of the nature of
1409 funding received. Research institutions therefore should assist researchers in managing financial
1410 transactions, maintaining accounting records and preparing financial statements through:

1411 • providing routine consultancy services to researchers via its research administration office
1412 or finance department;
1413 • organizing regular training workshops in relation to research financial administration and
1414 compliance;
1415 • developing financial statement templates specific for health-related research for reference
1416 by researchers; and
1417 • supporting internal/external financial audits.

1418 Institutions dedicated to research, and with a high and regular volume of research projects, may
1419 also consider to establish a central research office to undertake the aforesaid financial
1420 administrative duties in collaboration with their researchers.

1421

1422   *20. Financial Compliance*

1423 Financial compliance is crucial in health-related research projects, whether for those supported
1424 by public or private resources. In particular, research institutions should establish appropriate
1425 guidance and mechanism to avoid conflicts of interest and bribery/corruptive actions.

1426 Without prejudice to other chapters discussing the importance of declaration of conflicts of interest,
1427 research institutions and researchers are strongly recommended to undertake the following
1428 measures to avoid any "perceived" or even "real" conflicts of interest from the perspective of
1429 financial management:

1430 •   Upholding Transparency of Research Budget: Budgets should be open for independent
1431   audits and inspections by internal quality departments and regulatory agencies;
1432 •   Proper Documentation: Budget table with detailed cost items and breakdown to assure
1433   there are no hidden cost items. If possible, more than two quotations should be collected
1434   from different vendors for items to be procured to avoid procurement bias.

1435 Research institutions should, and should procure that their researchers, observe all applicable
1436 local and international laws and regulations in relation to anti-bribery and anti-corruption (e.g. US
1437 FCPA, UK Bribery Act[28]).

1438 When a research project is supported by a third party, the research budget must be prepared
1439 based on the actual procedures and requirements defined in the study protocol without taking into
1440 account any other business relationships. It is also recommended that a research budget should
1441 be compiled according to the principle of "fair-market-value," which could be demonstrated by
1442 documented market information and consistency across research projects. If an agreement is
1443 executed between a funding body and a research institution, it should specify that all the payments
1444 by the funding body under the agreement should be made only to the research institution but not
1445 directly to the researcher or any individual person to avoid any possibility or suspicion of bribery.

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Chapter 6: Collaboration

Key words

Accountability – Collaboration agreement – Data protection – Data rights and ownership – Data sharing – Fair partnership – Intellectual property rights – Public disclosure – Research interest – Samples sharing – Transparency

Background and Principles

Each research institution, like any other organizations, exists for a specific social purpose (see Chapter 1: Research Institution Management). With the rapid advancement in health sciences, increasing awareness of diversity (whether socio-economical, ethnic, cultural, gender or otherwise), and increasingly stringent ethical, regulatory and quality requirements worldwide, health-related research is becoming more challenging. Challenges can be even greater for those organizations that carry out research outside their core mandate (such as some NGOs and some international organizations). Research institutions may therefore encounter constraints that limit the extent of achievement of their research objectives on their own. Collaboration between research institutions and/or with other partners could be considered as opportunities to help overcome such constraints.

Collaboration is the act of two or more parties working together within a mutually agreed scope to achieve certain goals that bring shared benefits/outcomes. A collaboration could be established for a particular project or event (e.g. a research project, a joint research seminar, etc.), or for a strategic purpose covering a certain scope or series of projects or activities (e.g. a research program consisting of a number of research projects around a certain discipline, a long-term research personnel development program involving exchange and placement of staff, etc.). A successful collaboration may, in addition to achieving the defined collaboration goals, also bring extended long-term benefits to the concerned institutions, the researchers and the research community at large, by:

- supporting the achievement of the research institutions' organizational missions;
- supporting the development of new research and research-supportive skills and capacities;
- supporting the upgrade of the research institutions' infrastructure and skills;
- creating and/or supporting long-lasting collaboration among the researchers;
- encouraging and facilitating exchange of good research and governance practices;
- developing a larger network of like-minded institutions;
- contributing to the continuing improvement of the local, national and/or international research environments.

In the domain of health-related research, collaborations are usually driven by researchers with common research interests. It would be very important that research institutions – in line with their research scopes and missions – offer necessary and appropriate supports to their researchers and exercise good governance over their collaborative projects and activities.

Collaboration is not a purpose by itself, but it is a useful way of facilitating the achievement of the research purposes of research institutions and their researchers. To work out a meaningful and fair collaboration that create value for all collaborating parties, it is highly recommended that research institutions and researchers, prior to the start of the collaboration:

- identify suitable collaborators;
- formulate a collaboration plan and define the way of execution;
- stipulate the agreed terms and conditions in a collaboration agreement (or equivalent).

1513 It is also highly recommended that research institutions continue to oversee the performance of
1514 collaborative activities throughout the entire period of collaboration (see Chapter 9: Institutional
1515 Research Oversight) and evaluate the immediate outcomes upon conclusion of the collaboration
1516 and, when applicable, the long-term outcomes at defined time after its formal conclusion.

1517 **Points to consider and how to address them**

1518 *21. Identification of Suitable Collaborators*

1519 Identifying suitable, like-minded collaborators is the pre-requisite for a successful collaboration.
1520 Depending on the subject domain and context, a research institution may collaborate with entities
1521 such as:

1522 • other public/private health research institutions;
1523 • non-health research institutions (for instance, in the field of economics and other social
1524   sciences);
1525 • industry/commercial corporations;
1526 • professional associations;
1527 • governmental bodies;
1528 • international organizations;
1529 • non-governmental organizations or charity organizations;
1530 • patient associations;
1531 • specialized bodies (e.g. reference diagnostic laboratories);
1532 • funding bodies.

1533 Solid collaboration among collaborators is founded on three fundamental elements including:

1534 • common research interests;
1535 • shared values and common goals of collaboration;
1536 • complementary qualities/elements that justify the collaboration.

1537 No research institutions will ever be the same, but in order to work together it is important that
1538 they share certain common research interests, common values and common goals. Furthermore,
1539 it is desirable that collaborators carry complementary qualities/elements – whether in terms of
1540 expertise, capacity, financial resources, human resources, facilities, time, regulatory environment,
1541 access to research population, local culture or otherwise – that supplement the limitations of the
1542 other collaborators and/or enhance the synergistic outputs out of the collaboration.

1543 *For example,* university epidemiologists, university social scientists and elderly homes in a city
1544 may all be interested in exploring the pattern of spread of an infectious disease in the elderly
1545 population, and have the common goal of protecting the health of the elderly by preventing disease
1546 transmission within confined nursing facilities using an evidence-based approach. On these
1547 common grounds, they could jointly organize a collaborative research project on the subject matter
1548 utilizing their complementary strengths, under which the university, epidemiologists and social
1549 scientists offer their research personnel and research expertise, and the elderly homes offer their
1550 expertise in elderly care and provide access to their nursing facilities and potential research
1551 participants.

1552 In spite of the wide diversity of research institutions, it seems critical that special attention is paid
1553 to the principle of "**fair partnership**" which consists of three domains including:

1554 • **fairness of opportunity**: which refers to the fair opportunity to contribute to the
1555   collaboration (e.g. in terms of defining the collaborative scope, goals, methodologies,
1556   management mechanism, roles, financing and contractual arrangements, etc.);

1557 • **fair process**: which refers to the fair management and operation of a collaboration (e.g.
1558 data use and ownership, transfer and future use of biological materials, centralized versus
1559 decentralized processes, etc.);

1560 • **fair sharing of benefits/outcomes and costs/liabilities**: which refers to the fair sharing
1561 of collaborative benefits/outcomes corresponding to each party's inputs and contributions,
1562 both at research institution's and researcher's level (e.g. authorship policies, intellectual
1563 property rights, technology transfer, training opportunities, etc.); and the undertaking of
1564 costs/liabilities corresponding to each party's responsibilities and shared
1565 benefits/outcomes (e.g. insurance, indemnity, etc.).

1566 ### *22. Collaboration Plan and Concerted Execution*

1567 Each research institution may have different practices and follow different standards applicable to
1568 its own scope of activities. To ensure all collaborating parties will work towards the common goals
1569 and deliver the expected outputs under a collaboration, it is very important that they jointly
1570 formulate a collaboration plan and define the way of execution.

1571 A collaboration plan generally consists of essential components including but not limited to:

1572 • **the context of collaboration**: detailing the objectives, rationales, arrangements,
1573 deliverables and expected outcomes of collaboration (and in case of a collaborative
1574 research project, including the research protocol);

1575 • **a duties allocation plan**: defining the delegated roles and responsibilities of each
1576 collaborating party;

1577 • **a time plan**: defining the key milestones and estimated time schedule;

1578 • **a financial plan**: setting out the budget, funding sources and cash flow (see Chapter 5:
1579 Financial Management and Budgeting);

1580 • **a compliance, quality and risk management plan**: listing the ethics, regulatory and
1581 quality standards to be followed (see Chapter 2: Ethics, Law and Scientific Integrity), the
1582 measures to be applied to monitor compliance (see Chapter 9: Institutional Research
1583 Oversight), and the measures to be taken to prevent and control risks (see Chapter 1:
1584 Research Institution Management).

1585 It is important to note that, even if the specific formulation of the plan will depend on the kind of
1586 research, these five recommendations are applicable across all research disciplines. *For instance*,
1587 the specific measures to be applied to monitor compliance will be different across clinical trials,
1588 epidemiological studies, pharmacoeconomic studies and behavioral studies, but monitoring
1589 compliance is equally important in all these studies.

1590 Effective execution of a collaboration plan relies on the concerted efforts of all collaborating
1591 parties. It is therefore recommended that research institutions and researchers pay attention to:

1592 • **governance**: by jointly establishing and authorizing a steering committee (or equivalent)
1593 governing the collaboration (with documented terms of reference and key-decisions
1594 made);

1595 • **sharing of responsibilities**: by fairly allocating responsibilities among the collaborating
1596 parties, with special attention to avoid asymmetries of power;

1597 • **delegation of project team**: by delegating their representatives (e.g. project managers,
1598 coordinators, data managers, field data collectors, etc.) to perform communication,
1599 management and operation of the collaboration;

1600 • **communication and execution**: by defining the way of communication (e.g. by regular
1601 meetings, progress reports) and aligning the practical arrangements for exercising their
1602 duties (e.g. how data are collected, analyzed, interpreted, stored, accessed, transferred,
1603 published and disseminated, etc.).

1604 ### *23. Collaboration Agreements*

1605 To ensure that a collaboration is fully transparent to all the collaborating parties and for the
1606 avoidance of misunderstanding and dispute, it is highly recommended that the detailed terms and
1607 conditions of collaboration (in particular each party's rights, responsibilities and liabilities) are
1608 clearly stipulated in a collaboration agreement (or equivalent) among the collaborating research
1609 institutions. Such agreement terms and conditions are desirably written in such a way that reflects
1610 the core principles of:

1611 • **fair partnership**: as outlined in point to consider 221 above;
1612 • **ethical and legal conduct**: all the parties sharing the responsibility of complying with the
1613 applicable ethical and legal requirements in performing their responsibilities under the
1614 collaboration;
1615 • **transparency and accountability**: public disclosure of collaborative activities and results
1616 being warranted and planned for any health-related research, irrespective of research
1617 disciplines and contexts.

1618 In this connection, it is recommended to pay special attention to the contractual provisions relating
1619 but not limited to:

1620 • applicable (national and international) ethical and legal standards;
1621 • data and sample rights and ownership;
1622 • intellectual property rights and ownership;
1623 • publication and public disclosure of results;
1624 • data protection;
1625 • right of termination;
1626 • liabilities, indemnity and insurance.

1627 Last, it is very important that all legal professionals, researchers and management executives
1628 familiar with the context and operation of the collaboration are timely involved in developing the
1629 agreement to ensure that all legal, scientific and operational perspectives are well considered and
1630 the agreement is practically operable. The agreement will be entered in the capacity of the
1631 collaborating institutions and executed by their authorized representatives to ensure
1632 enforceability. The responsible researchers and/or key personnel may also be required to provide
1633 their written acknowledgement on the agreement to confirm their understanding and consent to
1634 the terms and conditions.

1635 For the avoidance of doubt, the existence of a collaboration agreement does not replace the need
1636 for other specific contracts or agreements (e.g. material transfer agreements, data sharing
1637 agreement, etc.).

1638

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1660

Chapter 7: Communication

Accountability – Community engagement – Communication – Ethics – Honesty - Integrity – Intranet – Media – Policy makers – Publication – Research dissemination – Social Media – Stakeholder engagement – Transparency – Website

<u>Background and Principles</u>

Each research institution has a specific mandate and social purpose. With the rapid advancement in health sciences, the availability of multiple ways of communicating within and outside the scientific community, and the increasing societal awareness of the need of accountability and transparency, both research institutions and individual researchers face increasing challenges in adequately communicating on the research undertakings and findings. Nonetheless, transparent communication is essential for ensuring internal and public accountability and thus for realizing the social and scientific value of health-related research.

It is recommended that a communication plan is articulated at various levels:

- Internally – Within the research organization or consortium (see also Chapter 1: Research Institution Management and Chapter 7: Communication).
- Externally – Toward peers within the scientific community;
- Externally – Toward institutions that oversee research (see also Chapter 2: Ethics, Law and Scientific Integrity);
- Externally – Toward the research community;
- Externally – Toward the mainstream and social media;
- Externally – Toward policy-makers in health systems.

A well-thought internal communication plan may ensure that everybody in the organization and in the research consortium have clear and easy access to policies, procedures, decisions made etc. In addition, it will contribute to creating a climate of transparency, mutual learning and trust, and to the continuing improvement of their research policies and practices.

In order to achieve effective internal communication, it is desirable that a research organization acts both at project level, i.e. by communicating on plans, policies and achievements about a specific research project, and at a broader institutional level, i.e. by communicating on scientific, ethics and legal policies and regulations that govern research and research supporting activities.

A well-though external communication plan may in first place support organizational and individual compliance with research ethics and integrity principles. In addition, it will contribute to building a solid scientific reputation for the institution and for the individual researchers; and to the continuing improvement of the local, national and/or international research environments.

In order to achieve effective external communication, it is recommended that a research organization acts both at project level, and at institutional level. At project level, it is desirable to develop a communication plan that articulates who will initiate communication and be responsible for it; what information will be communicated; to whom (e.g. scientific community, policy-makers, lay public…); how (i.e. using which communication tools or modality); and when (i.e. at what time points before, during and after completion of the research). At institutional level (see Chapter 1: Research Institution Management), it is desirable to develop institutional policies that facilitate researchers to integrate transparency and integrity in research communication. For instance, there should be institutional guidance on accurately and comprehensively communicating on any research findings, whether positive, negative or inconclusive; and the researchers' evaluation criteria should not only be focusing on bibliometric criteria, in order to prevent a 'publish or perish' institutional culture (see Chapter 2: Ethics, Law and Scientific Integrity).

<u>Points to consider and how to address them</u>

24. Internal communication

Internal communication within a research institution or consortium is important to nurturing an evidence-based and ethical research culture, upholding the research standard, and staff engagement. An institution/consortium may consider to delegate a unit or team (e.g. communication unit or officer, research office, or others) to coordinate internal communication activities – including but not limited to the dissemination of institutional research policies and guidelines, updating of research project status and results, receiving inquiries from research personnel – via suitable communication channels. Intranet pages where the staff can easily access research policies, procedures and regulations, reference guidelines, organigrams, etc. have proven to be useful for effective internal communication. Other communication channels/methods that may be considered include but not limited to periodical newsletters, internal emails that informs about new policies or procedures, internal seminars for reflection on topics of common interests, and different types of meetings.

For specific research projects, internal communication is normally led by principal investigators, and may be supported by delegated team members (e.g. study coordinators). It is desirable that it is executed by ways of regular and ad hoc project progress meetings, seminars, update reports or otherwise. Communication on project progress, funding utilization, quality and compliance issues, and specific challenges are common focuses.

In all cases, it is important that internal communication is designed and implemented in an interactive rather than unidirectional way, planning spaces and tools for listening to staff and research participants experiences and concerns, and preparing to act upon them.

25. External Communication Plan

The responsibility to define and periodically revise the Communication Plan generally depends on the size and governance of a research project or program (e.g. single-center or multi-country, involving a single institution or a research consortium, etc.). For instance, it can be the task of the principal investigator (PI), or of the study coordinator, or of the Steering Committee, or of other(s).

Once the communication plan has been defined and agreed in written, it is useful that the execution of the different tasks is delegated to the concerned function(s) in the research group. For instance, the PI and/or Steering Committee will likely be leading the communication toward the scientific community (point 3 below) and the policy-makers (point 7), while the study coordinator and field researchers will be likely leading the communication toward research communities (point 5). When possible, it is preferable that the communication via mainstream and social media (point 6) is led by professionals of communication. While this will be possible for bigger research institutions which usually have a Communication Unit or Department, small research institutions may choose to seek the advice of communication experts when possible.

1. Communication toward peers within the scientific community

As reminded by the 2016 CIOMS International ethical guidelines (Guideline 24) [29], "public accountability is necessary for realizing the social and scientific value of health-related research. Therefore, researchers, sponsors, […] have an obligation to comply with recognized publication ethics for research and its results. Researchers should prospectively register their studies, publish the results and share the data on which these results are based in a timely manner. Negative and inconclusive as well as positive results of all studies should be published or otherwise be made publicly available". Therefore, it would be important that a Communication Plan includes:

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[29] Council for International Organizations of Medical Sciences (CIOMS) *International ethical guidelines for health-related research involving humans*. 2016

- The registration of the protocol in a registry recognized by the World Health Organization (International Clinical Trials Registry Platform (ICTRP) (who.int)) - only for clinical trials and other prospective research in humans that fall under the policy of the International Committee of Medical Journal Editors (ICMJE);

- Clear criteria and modalities for sharing deidentified research data (and samples) from the research. It is generally preferable to frame them in a general institutional policy for data (and samples) sharing (see Chapter 3: Scientific standards);

- Plans for the dissemination of research findings (including interim results when applicable) through presentations at scientific conferences, (possibly) pre-prints[30], and publications in peer-reviewed journals. It is recommended that communications at conferences and pre-prints are rapidly followed by submission to a peer-reviewed journal; and that for peer-reviewed publications, preference is given to open-access journals, and care is taken to avoid "predatory journals" with poor marketing and peer-review practices.

2. *Communication toward institutions that oversee research*

Any health-related research projects are overseen by at least one Research Ethics Committee or Institutional Review Board. Furthermore, different kind of research can be subject to the oversight of other bodies and institutions, such as the Regulatory Authority, the National Public Health Institute or others (see Chapter 2: Ethics, Law and Scientific Integrity).

While it is generally the responsibility or the PI or appointed study coordinator to proactively and reactively communicate with such bodies, it is an organizational responsibility to create an institutional culture where individual researchers and staff are aware of the relevance of timely and transparently communication to these bodies, either for planned tasks (such as submitting initial protocols and amendments, sending yearly reports, etc.) or unplanned tasks (such as promptly communicating any events or occurrence that can impact on the feasibility, acceptability or findings of the research project).

3. *Communication toward the research community*

The 2021 CIOMS Consensus on Clinical Research in Resource-limited Settings indicates the need of formal plans on how to communicate with participants and their community in continuum and in a meaningful way; and the 2016 CIOMS International ethical guidelines (commentaries on Guideline 24)[31] state that "Researchers must also communicate the results of their work to the lay public. Ideally, researchers should take steps to promote and enhance public discussion. Knowledge resulting from the research should be made accessible to the communities in which the research was conducted, either through publication in scientific journals or through other channels". Therefore, it is recommended that the Communication Plan describes how the research plans, tools, conduct and findings will be practically communicated and discussed with the research communities, on an ongoing basis.

This will ideally include details on who will be responsible for this task; which relevant stakeholders (such as patients' associations, local associations, community opinion leaders, community advisory boards, etc.) would be engaged locally; by which means the communication will be channelled and discussions will be organised (such as through structured meetings, mailings, local media, etc.); how scientific contents will be translated into lay language; and – importantly – *a* budget line specifically dedicated to activities needed for engaging the research community(ies).

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[30] Pre-prints are preliminary reports of work not yet peer-reviewed. They are uploaded in dedicated free-access servers, such as https://www.medrxiv.org/

[31] Council for International Organizations of Medical Sciences (CIOMS) *International ethical guidelines for health-related research involving humans*. 2016

1795 **4. *Communication toward mainstream and social media***

1796 Research institutions or consortia can decide to use a general or study-specific website, to inform
1797 the public on an ongoing basis about a given research program. They can also use press releases
1798 for rapidly communicating to the general public about the start of a given research program, or the
1799 achievement of a milestone during the research, or the key-facts of the research findings.
1800 Depending on the nature and mandate of the institution, the press-releases are often drafted by
1801 communication or public relation experts; however, to keep up with the principles of transparency,
1802 accountability and honesty, it is highly recommended that scientists (PI and other key-researchers)
1803 review the contents for accuracy, and that other key-information including the full protocol, analysis
1804 plan and detailed results, are rapidly made publicly available.

1805 Any information about a research undertaking or findings which is publicly available, can be
1806 retrieved by mainstream and social media. These will further spread knowledge, but there are
1807 risks that the nature or significance of findings is misunderstood or overemphasized. Therefore,
1808 at least for those research projects that are likely to get media attention, it is highly recommended
1809 that the Communication Plan includes details on how the research plans, conduct and findings
1810 will be communicated through the media, i.e. who will be *responsible* for this task (for instance the
1811 PI, assisted by the Communication Unit or officer if any); which mainstream and/or social *media*
1812 would be preferentially targeted; by which means the contents would be channelled, e.g. a
1813 dedicated website, press-releases, messages on social media etc.; and *a* dedicated *budget line*.
1814 As scientists are often not trained in communication, it is also advisable to identify in the research
1815 team one or more trained spokesperson(s) responsible for communicating with the media.

1816 **5. *Communication toward policy-makers in health systems***

1817 Policy-makers in health systems – including but not limited to Ministry of Health, National
1818 Regulatory Authorities, health insurances, reimbursement commissions, those drafting standard
1819 diagnostic and treatment guidelines etc. – significantly rely on research findings for translation into
1820 policies and practices, by making decisions that are relevant to recommendations on clinical care,
1821 health and social policies, or resource allocation, and ultimately for advancing individual and public
1822 health. Therefore, it is recommended that the Communication Plan includes details on how the
1823 research plans, challenges and findings will be practically communicated to relevant policy
1824 makers. This will include details on who will be responsible for this task; which relevant
1825 stakeholders would be engaged locally, nationally or internationally; by which means the
1826 communication will be channelled and discussions will be organised (such as through policy briefs,
1827 structured meetings, sharing of de-identified key information etc.); and a dedicated budget line.

1828
1829 ## 26. Institutional policies

1830 All the above tasks will be easier to plan and implemented at project level, if framed into clearly-
1831 spelled out institutional policies and practices for communication. These policies would ideally
1832 include (but not be limited to):

1833 - Institutional endorsement of relevant methodological, ethics and integrity guidelines;
1834 - Standard operating procedures or equivalent guidance for communication with research
1835 communities and with policy-makers in health systems;
1836 - Training for junior staff, junior researchers, master and PhD students and others, on
1837 research integrity (see Chapter 8: Education and Learning);
1838 - Researchers' evaluation criteria that do not foster an ethos of 'publish or perish';
1839 - The establishment of a Communication Unit or Focal Person to advise and support
1840 individual research projects.

1841 Such an institutional framework will be useful to support researchers and research institutions
1842 when reactive communication is needed in case of crisis, e.g. in case of a safety incident during
1843 a clinical trial or in case of unproven allegations of misconduct.
1844

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Chapter 8: Education and Learning

Key words

Capacity Building – Continuing Education – Education – Learning – Planning – Qualification – Training – Responsible employer – Responsibilities – Skills and expertise – Training records

Background and Principles

With the rapid advancement in health sciences, increasing complexity of research methods, elevating need of multidisciplinary research, and more and more stringent ethical, regulatory, administrative and quality requirements worldwide, health-related research is becoming more demanding. To fulfill their scientific and social purpose, research institutions increasingly need to ensure that their staff, as well as the staff of their collaborating partners, possess the qualifications, skills, experience and expertise needed to adequately and properly carry out their respective tasks in each research project. Effective governance of qualifications and learning of research personnel could help research institutions to uphold their research standards, in terms of scientific/methodological soundness and ethical, regulatory and quality compliance, at all stages of health-related research– from protocol development to project execution, until dissemination of findings and translation into policies and practices. In addition, it may also bring extended long-term benefits for the institutions and their research personnel, including but not limited to strengthening their reputation and facilitating future funding and research opportunities.

Therefore, it is recommended that the following activities are carefully planned, executed and monitored by the research institution, in line with its institutional mandate and goals:

- **Learning Opportunities**: Give all research staff access to adequate learning opportunities, based on their background and tasks, and on a continuous basis;
- **Expertise and Skills**: Put in place mechanisms to ensure that research staff have acquired the necessary expertise and skills to carry out their respective tasks in research projects, whether in research methods (e.g. clinical, epidemiological, qualitative or mixed-methods; good clinical/laboratory practices, etc.) or in research-related disciplines or activities (e.g. research ethics, research integrity, data management, scientific writing, planning, research contracts, administration etc.);
- **Professional Licenses**: Put in place mechanisms to ensure that where necessary, the research staff have the appropriate professional licenses to practice in compliance with the national laws and regulations;
- **Training/Learning Records**: Put in place mechanisms to document the training/learning activities and qualifications of all staff involved in research.

Within individual research projects, the principal investigators (PIs) have a particular responsibility for the overall conduct and supervision of their research projects. Thus, it is important that they check the skills and qualifications of the members of their research teams, and arrange any required training/re-training, prior to the commencement of (and, if needed, during the period of) the research project; and that they ensure proper documentation of all qualifications and learning activities.

Appropriate qualifications and learning are important pre-conditions to the achievement of the purposes of research. It is important to underline that the responsibility of research institutions to ensure that all research staff are competent and skilled in conducting their tasks, is mirrored by research staff's responsibility to acquire and maintain such knowledge and skills. Therefore, anybody involved in performing, coordinating, managing or overseeing any research-related activities under a research institution– whether clinical researchers, epidemiologists, qualitative researchers, health economists, research coordinators, quality assurance officers, lab

technicians, data managers, research administrators, legal experts, field data collectors, community health workers, translators or otherwise – need to acquire and maintain the relevant qualifications and knowledge in three core domains including:

- basic professional qualifications;
- research concepts and standards;
- project-specific requirements.

The above recommendations are obvious to institutions that carry out interventional clinical trials, because clinical trials are highly regulated and there are clear qualification and training requirements defined in the ICH-GCP and other applicable guidelines and regulations. Nonetheless, a well-thought and structured approach to qualifications and training is also highly beneficial to institutions carrying out other health-related research, e.g. in the field of epidemiological, behavioural and health economic research. Irrespectively of the research disciplines, a proper governance of qualifications and training creates good value to research institutions, research personnel, research participants and the public, in the perspectives of human participants' protection and ethical compliance; legal, regulatory and quality compliance; research quality and integrity; risk management; capacity building and research talents development; and advancement of research methods.

Points to consider and how to address them

27. Basic Professional Qualifications

This refers to the fundamental professional qualifications that are required for an individual to carry out tasks in health-related research, e.g. medical doctors, nurses, pharmacists, dentists, dieticians, epidemiologists, psychologists, public health specialists, qualitative researchers, health economists, legal experts etc. Research institutions need to ensure that all research staff, including but not limited to the PI, possess the necessary qualifications and continuous education to adequately and properly perform their research duties. In many instances, this will also be checked by the Research Ethics Committee – when reviewing specific research projects – to ensure that the research team as a whole possesses a suitable mix of expertise for the purpose of the project.

It is generally recommended that the responsibility to verify that adequate basic qualifications are attributed to the institution management, for instance to the head of a concerned department or unit, preferably with support of the human resources department or unit.

28. Research Concepts, Standards and Skills

This refers to the core concepts, standards and skills on health-related research, and may be classified into six areas:

- Research ethics and integrity (see Chapter 2: Ethics, Law and Scientific Integrity);
- Legal, regulatory and quality requirements (see Chapter 2: Ethics, Law and Scientific Integrity);
- Good research practice (see Chapter 3: Scientific standards);
- Public perspectives on health-related research (see Chapter 7: Communication);
- Research designs and methodologies (see Chapter 3: Scientific standards and Chapter 4: Collection, storage, and use of data and/or biological materials in health-related research);
- Research management and operations (see Chapter 1: Research Institution Management, Chapter 4: Collection, storage, and use of data and/or biological materials in health-related research, Chapter 5: Financial Management and Budgeting and Chapter 6: Collaboration).

Each of the above has different relevance, depending on the categories of staff and their involvement in research.

1957 It is recommended that research institutions cultivate a learning culture, by encouraging and
1958 supporting research personnel to learn and keep themselves updated on the above concepts and
1959 standards. This can be practically achieved by disseminating the latest regulations, guidelines and
1960 standards internally (e.g. via a website, Intranet or mailing lists) and/or by organizing in-house
1961 symposia, workshops, discussion groups, public engagement events, etc. (see Chapter 7:
1962 Communication). Furthermore, the institution can encourage and support research personnel to
1963 participate in relevant external conferences, forums, symposia, training courses, etc.

29. Project-specific Requirements

1965 This refers to the skills, expertise and qualifications needed to carry out specific tasks in a
1966 particular research project, as set out in research protocols and related manuals or documents.

1967 Ideally, a qualification and learning plan covering the required competencies for each role would
1968 be in place before the start of a research project, and no activity should start if the needed skills
1969 and expertise are not available, as checked by the PI or research coordinator. Research
1970 institutions are also recommended to oversee research duty delegation and training of research
1971 teams via their institutional research oversight mechanism (see Chapter 9: Institutional Research
1972 Oversight).

30. Institutional Governance of Qualifications and Learning

1974 All the above domains of qualifications and learning will be easier to plan and implement at project
1975 level, if framed into clearly-spelled out institutional policies for qualification and learning. Such
1976 institutional policies will also be helpful to cultivate a learning culture in a sustainable way over
1977 time, not depending on the inclination and motivation of a few individuals.

1978 These policies would ideally be produced and managed in collaboration with the Human Research
1979 department or unit, because providing ongoing professional update (whether related or unrelated
1980 to research) is part of the tasks of the institution as responsible employer. Furthermore, it is
1981 recommended that the central or departmental administration is involved in these processes, given
1982 that ensuring adequate qualification and learning comes with costs, which need to be covered
1983 either at central or project level. Table 9**:** Core domains of qualifications and learning for
1984 research personnel below summarizes the aforesaid domains, with some examples.

1985 **Table 9:** Core domains of qualifications and learning for research personnel

Domain	Scope	Research Personnel Responsibilities	Research Institution Responsibilities	Examples
Basic Professional Qualifications	• Professional qualifications • Continuous education	• [Upfront] acquiring the necessary professional qualifications • [Ongoing] continuous education	• Ensuring research personnel possess the necessary qualifications • Support continuous education • Document the qualifications	• Diploma/master in epidemiology • Diploma/master in anthropology • Licence to exert the medical, nursing or allied health profession • Diploma/master in administration • Diploma/master in health economy
Research Concepts, Standards & Skills	• Research ethics • Legal, regulatory and quality requirements • Good research practice	• Learning relevant research concepts and standards via self-learning and/or participating in learning events	• Ensuring research personnel possess the necessary skills • Support training • Document training • Cultivating a learning culture	• Master/certificate in research ethics • Certificate in GCP • Certificate in data management • Master/certificate in qualitative or mixed methods

Domain	Scope	Research Personnel Responsibilities	Research Institution Responsibilities	Examples
	• Public perspectives on health-related research • Research designs and methodologies • Research management and operations.		• Disseminating latest regulations/ guidelines/standards • Supporting participation in learning events	• Master/certificate in pharmacoepidemiology and pharmacovigilance • Training in research integrity • Training in data protection • Training in research designs and methodologies • Training in CONSORT, STROBE, or other methodological guidelines • Training on SAGER guidelines • Training in research project management
Project-specific Requirements	• Project objectives, practices, procedures and requirements	• PI: ensuring team members are adequately (re)trained, and document training • Research team members: learning research protocol and related requirements	• Ensuring research personnel have been adequately (re)trained • Document training	• Training in specific data management tools (e.g. REDCap for quantitative research, NVivo for qualitative research) • Training in the study Standard Operating Procedures • Training in national research guidelines (research host country) • (Re)training in research ethics • (Re)training in GCP • Training in external or internal quality control

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Chapter 9: Institutional Research Oversight

Key words

Accreditation body – Auditing – External research oversight – Inspection – Institutional review board – Internal research oversight – Monitoring – Project oversight – Regulatory agency – Research Ethics Committee – Research waste – System oversight – Targeted checking

Background and Principles

Research institutions are accountable to the public and therefore have the responsibility to oversee their research practices and activities to ensure that good value is generated to the society whilst risks are justified. Institutional research oversight refers to the system, methods and processes of overseeing a research institution's research infrastructure, personnel, mechanisms and projects in a proactive manner. Research oversight is an integral part of good research practice and helps:

- secure ethical research conduct and participants' protection;
- uphold research data quality and integrity;
- compliance with applicable national/international guidelines, standards and regulations;
- effective utilization of limited research resources and limit research waste; and
- smooth project execution in accordance with project time plans and budgets.

The term "oversight" is used here on purpose to avoid confusion with the sponsors' monitoring obligation for drug trials according to the ICH-GCP and the national laws and regulation. The nature and level of scrutiny of the institutional research oversight depend on the nature and level of research activities carried on within – or in collaboration with – the concerned institutions. Even when institutions act as sponsors of research projects, it may be neither necessary, nor desirable that they follow the ICH-GCP model for their oversight activities outside the field of drug trials.

Research oversight could be organized and executed in two dimensions including:

- **system oversight**: overseeing the research capabilities and capacity of the research institution to make sure that researchers and research personnel are qualified and competent, come from diverse backgrounds representative of local communities, and are gender balanced, that required facilities, equipment and tools are in place and maintained in good order, and that appropriate policies and procedures are established and executed to guide the proper conduct of research activities in compliance with the applicable ethical, regulatory and quality requirements;
- **project oversight**: overseeing the setup and operation of a research project to ensure that the rights, safety and well-being of participants are protected, the project is progressing according to the time plan, funding is spent within the budget, and data is collected, documented, analyzed, reported and publicly disclosed/published properly.

Institutional research oversight upholds scientific robustness of methods employed in study conduct, protection of rights, safety and well-being of human participants, research integrity, and quality of research outcomes. Ongoing research oversight plays an important role in preventing unethical practices, research waste, fraud or falsification in the conduct of research, early detection of protocol violations, and plagiarism in reporting.

2045 **Points to consider and how to address them**

2046 *31. Methods of Research Oversight*

2047 Depending on the statutes of a research institution and the nature of its research projects, different
2048 methods of oversight – including "internal research oversight" and "external research oversight"
2049 on different levels (see **Table 1:** Example of matrix management) – may be applied. A research
2050 institution has the primary responsibility to:

2051 • establish an internal research oversight system – for the institution itself and for its
2052   researchers and research teams; and
2053 • set out practical policies and guidance to support external research oversight by relevant
2054   external stakeholders.

2055 For the avoidance of doubt, a research institution does not necessarily have to use all these
2056 methods but may just select a combination of methods that serves its own purposes – considering
2057 factors such as the institution's research objectives, the risks of its research projects, its regulatory
2058 environment, and expectations of its communities.

2059 **Table 10:** Overview of research oversight

Level of Research Oversight	Method of Research Oversight	
	Internal Research Oversight	External Research Oversight
Level 1	Self-checking by research team: As the first line project and quality control measure for a research project, targeting to discover, rectify and minimize deviations from the study protocol, applicable standards and project time/budget plans	Monitoring by sponsor: As the primary project and quality control measure for a sponsor's project team, targeting to discover and rectify deviations from the study protocol and applicable standards and oversee project progress in alignment with project time/budget plans
Level 2	Central oversight by institutional office/unit: Representing institutional governance, targeting to oversee research compliance, resources utilization and project progress on system and project levels	Auditing by sponsor/funding body/collaborator: Representing organizational oversight by sponsor/funding body/collaborator, targeting to oversee research compliance, resources utilization and project progress
Level 3	Ethical oversight by Institutional Research Board (IRB) (if applicable): Representing institutional research ethics governance, targeting to oversee research ethics and regulatory compliance and participant protection	Inspection by REC/accreditation body/regulatory agency: Representing research ethics and regulatory oversight, targeting to oversee ethics, regulatory and quality compliance and data integrity for research institutions and/or their research projects

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2062   *32. Internal Research Oversight*

2063   Whilst establishing an internal research oversight system is the responsibility of a research
2064   institution, execution of internal research oversight is the joint responsibility of all research
2065   stakeholders within the institution – including institutional management, researchers/research
2066   personnel and other delegated units/persons. Table 11 provides an outline of an internal research
2067   oversight system for reference.

2068   **Table 11:** Outline of an internal research oversight system

Level of Oversight	Primary Responsibility	Possible Delegate	Methodology & Scope	Institution's Role
Level 1: Self-checking by research team	Researcher	Study coordinator, research assistant	• Full checking • Targeted checking	• Developing guidance documents and forms for use by researchers and research teams • Establishing and operating a mechanism for advising and receiving reports from researchers
Level 2: Central oversight by institutional office/unit	Research oversight committee, central research office, quality management department, or equivalent	Internal quality specialist, contracted auditor	• System oversight: Routine or for-cause review • Project oversight: All projects or selected projects	• Delegating an institutional office/unit to perform central oversight • Establishing a mechanism to select units/teams/ projects for checking • Developing guidance documents and forms for system oversight and project oversight
Level 3: Ethical and regulatory oversight by IRB (if applicable)	IRB (if applicable)	IRB member, contracted auditor	• Ethical and regulatory oversight	• Authorizing the IRB to perform ethical and regulatory oversight • Receiving feedback/reports from IRB • Procuring relevant researchers and institutional offices/units to respond to IRB's feedback

Level 1 Oversight: Researchers play an important role in conceiving, designing, conducting and reporting research, and also assume the primary responsibility for ensuring compliance and quality of their research projects. They should therefore maintain adequate and verifiable research records and delegate team member(s) to perform first-line checking of their research works. Depending on a project's nature, risks and applicable ethical, regulatory and quality requirements, self-checking could be performed by way of:

- **full checking**: reconstructing and verifying the entire research process against the research protocol and applicable standards by checking all research-related records and data, including but not limited to source documents, clinical notes, case report forms, participant-administered questionnaires, researcher training records and equipment maintenance records; or
- **targeted checking**: checking of only pre-defined important records and process (e.g. informed consent documents, data supporting the primary objective of the project) – usually by applying a risk-based approach – to ensure that the key research data are reliable and the most important requirements and conditions are fulfilled.

Research institutions should provide guidance and support to researchers and their research teams on performing self-checking of their projects. Issuance of guidelines and checking tools (e.g. checklists, reporting forms) and organization of training are valuable options.

Level 2 Oversight: Research institutions are responsible for maintaining a research-friendly environment that helps researchers and research personnel to adopt good research practice and undertake research with good compliance and integrity. The higher the research activities are, the higher is the need to set up a central oversight system, operated by a delegated research oversight committee, central research office, quality management department, or equivalent unit. Central research oversight could be performed from the dimension of system oversight or project oversight, as introduced in the background and principles section above.

For sizeable research institutions with multiple layers/units, system review could be performed regularly as a routine exercise for individual departments/units/specialties rather than for the entire institution in one go. Extra reviews could be organized as needed, for instance, in case of any concern or complaint.

For smooth execution of project review, institutions may establish a review plan with pre-defined check-points for each research project. In case an institution is running a large number of ongoing projects, it may not be practically feasible to review every single project. In this regard, the institution may establish a mechanism for selecting a manageable number of projects for review within each defined period (e.g. annually). Again, a risk-based approach taking into consideration certain core risk factors (e.g. involvement of vulnerable participants, enrolment of a large number of participants, and application of investigational interventions) is recommended.

Level 3 Oversight: Some research institutions may establish and operate their own institutional review boards (IRBs) to oversee research ethics and regulatory matters, and in this case such IRBs may undertake a more independent role in performing another level of research oversight – in particular with focus on protecting the rights, safety and well-being of research participants and their affiliated communities. Like central research oversight as described in the previous paragraph, ethical and regulatory oversight could be performed from the dimension of systems or projects. To facilitate this, research institutions should give their IRBs due authority and establish a mechanism to require relevant researchers and institutional offices/units to cooperate with the IRBs and respond to their feedback.

33. External Research Oversight

Health-related research is more and more organized in a collaborative manner, in anticipation to generate better value for benefiting a wider population. Research projects are therefore more often subject to external oversight by collaborating parties, whether commercial sponsors, other collaborating institutions, funding bodies, accreditation bodies or regulatory agencies.

Different external bodies may have different oversight requirements, depending on their roles and involvement in the corresponding research projects or activities. For instance, commercial sponsors may have their focus on protocol compliance, whilst funding bodies may pay more attention to resource utilization and budget control.

Although research institutions are on a relatively passive role in terms of external research oversight, they should establish appropriate institutional policies and guidance for researchers and relevant institutional offices/units in facilitating such oversight activities, in particular on:

- personnel records maintenance: maintaining and retaining updated CVs, qualification certificates and training records for researchers and research personnel;
- facility and equipment maintenance: maintaining and retaining corrective/preventive maintenance and calibration records for relevant research facilities and equipment;
- research documents and records maintenance: generating and retaining all essential research records such as informed consent documents, source records, case report forms and survey forms – whether in paper, electronic or other formats – during the period of each project and the required duration after project closure.

Proper document retention is a key prerequisite for supporting external oversight. However, long-term document retention is a common challenge for researchers. Research institutions are advised to allocate/identify sufficient document storage space (within or outside the institution) and establish a research document management mechanism to facilitate long-term document archiving and document retrieval as needed.

34. Continuous Improvement

Institutional research oversight is not a one-time exercise. In addition to the subject matter of each review, it is more important for encouraging the institution's continuous improvement. It is therefore necessary to incorporate a positive feedback loop in the research oversight systems to allow:

- documentation of identified observations/findings;
- submitting amendments to relevant REC and NRA prior to implementing them;
- reporting of identified observations/findings to researchers and institutional offices/units;
- escalation of identified observations/findings to institutional management;
- evaluation of the root causes of identified observations/findings;
- implementation of corrective and/or improvement actions to attain institutional improvement in terms of research capabilities, quality and compliance.

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Annex: Points to Consider in Establishing Good Governance Practice for Research Institutions

Chapter 8: Research Institution Management

Chapter 2: Ethics, Law and Scientific Integrity

Chapter 3: Scientific standards

Chapter 4: Collection, storage, and use of data and/or biological materials in health-related research

Chapter 5: Financial Management and Budgeting

Chapter 6: Collaboration

Chapter 7: Communication

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2219 **Chapter 8: Education and learning**

2224 **Chapter 9: Institutional Research Oversight**

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