

ETHICS AND INTEGRITY IN
HEALTH AND LIFE SCIENCES
RESEARCH

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ADVANCES IN RESEARCH ETHICS AND INTEGRITY
VOLUME 4

**ETHICS AND INTEGRITY IN
HEALTH AND LIFE
SCIENCES RESEARCH**

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United Kingdom – North America – Japan
India – Malaysia – China

Emerald Publishing Limited
Howard House, Wagon Lane, Bingley BD16 1WA, UK

First edition 2019

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British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

ISBN: 978-1-78743-572-8 (Print)

ISBN: 978-1-78743-571-1 (Online)

ISBN: 978-1-78743-918-4 (Epub)

ISSN: 2398-6018 (Series)



ISOQAR certified
Management System,
awarded to Emerald
for adherence to
Environmental
standard
ISO 14001:2004.

Certificate Number 1985
ISO 14001



INVESTOR IN PEOPLE

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SERIES PREFACE

This book series, *Advances in Research Ethics and Integrity*, grew out of foundational work with a group of Fellows of the UK Academy of Social Sciences (AcSS) who were all concerned to ensure that lessons learned from previous work were built upon and improved in the interests of the production of robust research practices of high quality. Duplication or unnecessary repetitions of earlier research and ignorance of existing work were seen as hindrances to research progress. Individual researchers, research professions, and society all suffer in having to pay the costs in time, energy, and money of delayed progress and superfluous repetitions. There is little excuse for failure to build on existing knowledge and practice given modern search technologies unless selfish “domain protectionism” leads researchers to ignore existing work and seek credit for innovations already accomplished. Our concern was to aid well-motivated researchers to quickly discover existing progress made in ethical research in terms of topic, method, and/or discipline and to move on with their own work more productively and to discover the best, most effective means to disseminate their own findings so that other researchers could, in turn, contribute to research progress.

It is true that there is a plethora of ethics codes and guidelines with researchers left to themselves to judge those more appropriate to their proposed activity. The same questions are repeatedly asked on discussion forums about how to proceed when similar long-standing problems in the field are being confronted afresh by novice researchers. Researchers and members of ethics review boards alike are faced with selecting the most appropriate codes or guidelines for their current purpose, eliding differences and similarities in a labyrinth of uncertainty. It is no wonder that novice researchers can despair in their search for guidance and experienced researchers may be tempted by the “checklist mentality” that appears to characterize a meeting of formalized ethics “requirements” and permit their conscience-free pursuit of a cherished program of research.

If risks of harm to the public and to researchers are to be kept to a minimum and if professional standards in the conduct of scientific research are to be maintained, the more that fundamental understandings of ethical behavior in research are shared the better. If progress is made in one sphere, all gain from it being generally acknowledged and understood. If foundational work is conducted, all gain from being able to build on and develop further that work.

Nor can it be assumed that formal ethics review committees are able to resolve the dilemmas or meet the challenges involved. Enough has been written about such review bodies to make their limitations clear. Crucially they cannot

follow researchers into the field to monitor their every action; they cannot anticipate all of the emergent ethical dilemmas nor, even, follow through to the publication of findings. There is no adequate penalty for neglect through incompetence, nor worse, for conscious omissions of evidence. We have to rely upon the “virtues” of the individual researcher alongside the skills of journal and grant reviewers. We need constantly to monitor scientific integrity at the corporate and at the individual level. These are issues of “quality” as well as morality.

Within the research ethics field new problems, issues, and concerns and new ways of collecting data continue to emerge regularly. This should not be surprising as social, economic, and technological change necessitate constant re-evaluation of research conduct. Standard approaches to research ethics such as valid informed consent, inclusion/exclusion criteria, vulnerable subjects, and covert studies need to be reconsidered as developing social contexts and methodological innovation, interdisciplinary research, and economic pressures pose new challenges to convention. Innovations in technology and method challenge our understanding of “the public” and “the private”. Researchers need to think even more clearly about the balance of harm and benefit to their subjects, to themselves, and to society. This series proposes to address such new and continuing challenges for both ethics committees and researchers in the field as they emerge. The concerns and interests are global and well recognized by researchers and commissioners alike around the world but with varying commitments at both the “procedural” and the “practical” levels. This series is designed to suggest realistic solutions to these challenges – this “practical” angle is the USP for the series. Each volume will raise and address the key issues in the debates, but also strive to suggest ways forward that maintain the key ethical concerns of respect for human rights and dignity, while sustaining pragmatic guidance for future research developments. A series such as this aims to offer practical help and guidance in actual research engagements as well as meeting the often varied and challenging demands of research ethics review. The approach will not be one of abstract moral philosophy; instead, it will seek to help researchers think through the potential harms and benefits of their work in the proposal stage and assist their reflection of the big ethical moments that they face in the field often when there may be no one to advise them in terms of their societal impact and acceptance.

While the research community can be highly imaginative both in the fields of study and methodological innovation, the structures of management and funding, and the pressure to publish to fulfill league table quotas can pressure researchers into errors of judgment that have personal and professional consequences. The series aims to adopt an approach that promotes good practice and sets principles, values, and standards that serve as models to aid successful research outcomes. There is clear international appeal as commissioners and researchers alike share a vested interest in the global promotion of professional virtues that lead to the public acceptability of good research. In an increasingly global world in research terms, there is little point in applying too localized a morality, nor one that implies a solely Western hegemony of values. If standards “matter,” it seems evident that they should “matter” to and for all. Only then

can the growth of interdisciplinary and multinational projects be accomplished effectively and with a shared concern for potential harms and benefits. While a diversity of experience and local interests is acknowledged, there are existing, proven models of good practice which can help research practitioners in emergent nations build their policies and processes to suit their own circumstances. We need to see that consensus positions effectively guide the work of scientists across the globe and secure minimal participant harm and maximum societal benefit – and, additionally, that instances of fraudulence, corruption, and dishonesty in science decrease as a consequence.

Perhaps some forms of truly independent formal ethics scrutiny can help maintain the integrity of research professions in an era of enhanced concerns over data security, privacy, and human rights legislation. But it is essential to guard against rigid conformity to what can become administrative procedures. The consistency we seek to assist researchers in understanding what constitutes “proper behavior” does not imply uniformity. Having principles does not lead inexorably to an adherence to principlism. Indeed, sincerely held principles can be in conflict in differing contexts. No one practice is necessarily the best approach in all circumstances. But if researchers are aware of the range of possible ways in which their work can be accomplished ethically and with integrity, they can be free to apply the approach that works or is necessary in their setting. Guides to “good” ways of doing things should not be taken as the “only” way of proceeding. A rigidity in outlook does no favors to methodological innovation, nor to the research subjects or participants that they are supposed to “protect”. If there were to be any principles that should be rigidly adhered to they should include flexibility, open-mindedness, the recognition of the range of challenging situations to be met in the field – principles that in essence amount to a sense of proportionality. And these principles should apply equally to researchers and ethics reviewers alike. To accomplish that requires ethics reviewers to think afresh about each new research proposal, to detach from pre-formed opinions and prejudices, while still learning from and applying the lessons of the past. Principles such as these must also apply to funding and commissioning agencies, to research institutions, and to professional associations and their learned societies. Our integrity as researchers demands that we recognize that the rights of our funders and research participants and/or “subjects” are to be valued alongside our cherished research goals and seek to embody such principles in the research process from the outset. This series will strive to seek just how that might be accomplished in the best interests of all.

By
Ron Iphofen (Series Editor)

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ABOUT THE SERIES EDITOR

Ron Iphofen, FAcSS, is Executive Editor of the Emerald book series *Advances in Research Ethics and Integrity* and edited Volume 1 in the series, *Finding Common Ground: Consensus in Research Ethics Across the Social Sciences* (2017). He is an Independent Research Consultant, a Fellow of the UK Academy of Social Sciences, the Higher Education Academy, and the Royal Society of Medicine. Since retiring as Director of Postgraduate Studies in the School of Healthcare Sciences, Bangor University, his major activity has been as an adviser to the European Commission (EC) and its agencies, the European Research Council (ERC), and the Research Executive Agency (REA) on both the Seventh Framework Programme (FP7) and Horizon 2020. His consultancy work has covered a range of research agencies (in government and independent) across Europe. He was Vice Chair of the UK Social Research Association, updated their Ethics Guidelines and now convenes the SRA's Research Ethics Forum. He was scientific consultant on the EC RESPECT project – establishing pan-European standards in the social sciences and chaired the Ethics and Societal Impact Advisory Group for another EC-funded European Demonstration Project on mass transit security (SECUR-ED). He has advised the UK Research Integrity Office; the National Disability Authority (NDA) of the Irish Ministry of Justice; the UK Parliamentary Office of Science and Technology; the Scottish Executive; UK Government Social Research; National Centre for Social Research; the Audit Commission; the Food Standards Agency; the Ministry of Justice; the BIG Lottery; a UK Local Authorities' Consortium; Skills Development Scotland; Agence Nationale de la Recherche (ANR the French Research Funding agency) among many others. Ron was founding Executive Editor of the Emerald gerontology journal *Quality in Ageing and Older Adults*. He published *Ethical Decision Making in Social Research: A Practical Guide* (Palgrave Macmillan, 2009 and 2011) and coedited with Martin Tolich *The SAGE Handbook of Qualitative Research Ethics* (Sage, 2018). He is currently leading a new €2.8M European Commission-funded project (PRO-RES) that aims at promoting ethics and integrity in all non-medical research (2018–2021).

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ABOUT THE EDITOR

Zvonimir Koporc has international recognition for expertise on research in life sciences (immunology) and professional standards in research ethics. His primary consultative activity in ethics and life sciences at present is for the European Commission (EC) Ethics Unit, Directorate General for Science and Innovation, the Research Executive Agency (REA), and the European Research Council (ERC). He has acted as Consultant, Adviser, and/or delivered training on research ethics at the European and national level. He has worked in several life science teams in Europe, and his PhD in Chemistry was awarded by the Technical University of Vienna, Austria. At the beginning of 2007 he returned to his home country through the national program called “Return of the scientists,” which was announced from the Croatian Ministry of Science. As a scientist he took up a position at the prominent Croatian scientific institution – Institute Rudjer Boskovic, Zagreb. Receiving his university tenured track position, he moved then to the Department of Biotechnology, University of Rijeka, where he stayed until 2015. From that year on, he joined Catholic University of Croatia Zagreb where he currently holds a position of University Associate Professor in Physiology where he is also a member of the Ethics Review Board. He has published extensively on immunology. Over and above the life sciences, his current professional interests are in research ethics and scientific integrity. Developing a fruitful cooperation with the Croatian Data Protection Agency in October of 2017, he organized a symposium on “Data protection in research – an insight in to the EU General Data Protection Regulation (GDPR) 25/5/2018” where he acted as a president of the organizing committee. Another fruitful cooperation has been developed with the Croatian National Agency for Mobility and EU Programmes funds where Dr Koporc regularly holds guidance workshops on ethics and research integrity for scientists and research professionals intending to apply for EU funds.

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INTRODUCTION: RESEARCH PRODUCTION IN LIFE SCIENCES

Zvonimir Koporc

THE RESEARCH PRODUCTION PROCESS IN LIFE SCIENCES

I would like to open this fourth volume in the *Advances in Research Ethics and Integrity Series* with some personal impressions about life sciences research based on my experience working in this field. Life science research teams in many ways resemble small factories. In factories, each part of the production chain is dedicated to another and each part of the production chain is strongly dependent on the efficiency of a preceding one. Just as with industrial factories, life sciences research teams are pressed with upcoming deadlines, productivity output (measured in terms of both patents and publications), and a constant struggle to finance their activities. Life science research is costly and often strongly dependent on very expensive chemicals and high-tech equipment. In such a competitive and challenging environment, only the most efficient research teams can survive.

Some might not see that as an issue of ethics or of integrity, but it is, and it is more than just a problem of the additional stress and pressure on the team members. Life science more often than not has to deliver a solid product in terms of research results, a patent, a treatment, a vaccine, a therapeutic model, or similar, and the team has to think and act together as a small quasi-commercial, and often commercial, enterprise. This can make for a more rigid decision-making process – the need to hone and refine the research “products” and ensure that obligations to funders are met. In other research fields, such as the social sciences or humanities, there may appear to be greater freedom for more “independent” thinking about research directions – although there may be similar constraints to “deliver” the outcomes specified by contractors – none more so than in market research.

As in the preceding volumes in this Series, this all points to how vital the institutional research infrastructure is to the integrity of the scientists involved. The ability to pursue particular lines of thought is intricately linked to organizational pressures and the individual career trajectory of the researcher.

Particularly, costly elements in life sciences involve the fundamental resources needed to even begin the research. To give an example, the annual price of monoclonal antibody (mAb) therapies is about \$100,000 higher for research in oncology and hematology than for researching other disease states (Hernandez et al., 2018), making research in these fields even more expensive. Different research kits such as ELISA, biochemical assay kits, or Flow cytometry kits, together with the equipment purchase and its maintenance, can sometimes exhaust the whole planned annual research budget.

Such costs do threaten research integrity since the “temptations” to cut corners or ensure positive results when they are not clear are high. Certainly, governmental financial support allocated for life sciences is strong in most of the well-developed European Union (EU) countries. Without that, it would be almost impossible to build an efficient life science research infrastructure. Nevertheless, those allocations are often not sufficient to cover all necessary research costs. The recent economic crisis aggravated that already difficult situation slightly declining the percentage of the share of research and innovation (R&I) in total public budgets for the EU as a whole (1.4% 2014 vs. 1.5% 2007).¹ There is a growing tendency to expose life science research to the real market conditions globally decreasing governmental support for research and development (R&D).²

That is why even in public research institutions, life scientists are frequently forced to search for additional financial resources to support their projects.

RESEARCH WITH ANIMALS

Having worked a lot with animal research models, my own perceptions have been particularly influenced by the demands of such research. Research using animals is usually one of the most expensive forms of scientific research. Above the purchase of such animal models, the cost of their housing and the maintenance of animal facilities are factors which require careful planning and experienced project management. Besides the expense and the technical demands which follow such research, a skilled staff with a strong ability to quickly recognize and effectively respond to all ethical issues which can emanate from their research is essential for the appropriate implementation of proposed work.

Animal welfare is very important for most EU citizens as shown in the results of a recent Eurobarometer study,³ but citizens’ feelings of not being well informed about that topic can often give rise to a negative perception of all research performed with and on animals.⁴ As mentioned in the introduction to this Series, different rights, values, and principles often stand in opposition to each other. Thus, recent global actions for the fight against terrorism and the seeking of security can stand in opposition to rights of privacy (Iphofen, 2014). In similar vein, the growing concerns for animal rights may oppose to some degree the right to do

research and gain knowledge in a common public interest such as a cure for specific diseases. From the time when Russell and Burch's *The Principles of Humane Experimental Technique* was first published in 1959, in which they proposed a new applied science that would improve the treatment of laboratory animals (the 3Rs principle – **R**eplacement, **R**eduction, and **R**efinement), to nowadays when the interpretation of that principle has gone through several “updates” (Tannenbaum & Bennett, 2015), pros and cons for animal testing still stand as a hot topic for the public and for scientists alike.

For research teams working on laboratory animals, a constant struggle with often unfair and oversimplified public perceptions which sometimes places them into the category of animal rights “offenders” is another challenging factor in their endeavors. Such oversimplified views of researchers' hard work and engagements are frustrating when researchers have to go through rigorous training to obtain certificates that permit them to work with laboratory animals. Those certificates are designed to prove their knowledge and technical skills, but also their awareness of the ethical issues associated with research performed on laboratory animals.

Recently I spoke with the director of one prominent research center in the EU about that public perception. His comment demonstrates how wrong he believes that perception to be:

Even if someone would not believe our training certificates, ethical approvals, our empathy for those animals and our noble intentions, I am sure that the public will understand that we treat our animals in the best way and take the maximal care of them also because those animals are our precious and very expensive research tools.

Animal researchers are constantly working on the improvement of already established ethical practices for research on animals.⁵ For instance, a report from the Canadian Animal Care Committee demonstrated the need for the scientific community to make progress concerning the implementation of “refinement” and “reduction”, particularly in the creation and use of genetically engineered animals; addressing these roadblocks needs to be a priority (Ormandy, Dale, & Griffin, 2013). Another publication showed that a web-based Nano technical summary database called “AnimalTestInfo” offers the possibility for scientists to do large-scale analyses of planned animal studies to inform researchers and the public (Bert et al., 2017). Data drawn from that database can provide a guidance for rethinking the role of animal research models.

In regard to the large animal research models, a recent Review of Research Using Non-Human Primates (NHP) founded by the UK Biotechnology and Biological Sciences Research Council (BBSRC), Medical Research Council (MRC), and Wellcome Trust from the Panel involving prominent experts in different life science fields recommended that in their public engagement, the funders and researchers should avoid overstating and generalizing the medical benefit of NHP research, since this cannot be substantiated in many cases.⁶ It is obvious that the research community is constantly investigating the need for use of the animals in different research areas. Yet, some animal researchers don't even tell their own families about their work for fear of attack by extremists.⁷

ETHICS CODES FOR THE LIFE SCIENCES

Although a code of ethics for the life sciences (Jones, 2007) and ethical review practices concerning research with animals are well established, a dynamic and a balanced approach is needed. The approach must be “dynamic” to be able to modify and adopt the best practices and “balanced” to focus on the important and essential parts of each sets of rights. Only by implementing those two principles can the potential contrast between those rights be reconciled.

The workload and complexity of research in life science research teams requires some way of standardization which can allow the “symbiosis” between high productivity and process simplification. In such teams, each research process step and each individual research role is clearly defined. That work organization could enable high research productivity; some tasks and rules are prepared generally for the whole team. Whether this is the question of the work safety, patent and data protection, or in-vivo research on laboratory animals, the idea of such “generalized rules” is to facilitate, accelerate, and increase the efficiency of the whole research process. It is expected that each individual member will follow such rules. This means that to be productive, life science teams must be highly arranged and coordinated systems. Nevertheless, errors can happen anywhere, and life science research teams are not immune.

In such set-ups, there are two ways rule violations can happen both on the team and on the individual level. Individual violations are to be expected due to human characteristics – the flaws of self-interest, ambition, greed, and so on. The consequences of such violations are more predictable and as such could potentially be recovered if recognized in time and if the organizational controls are effective. More problematic violations are those that arise out of the organizational infrastructure which affect the whole team – whether deliberate or latent. In that case consequences are harder to address as they lead to the establishment of unwanted or unlawful practices. These influences can easily go unrecognized in some countries in which ethics review and integrity practices are not efficiently set or where they are in their early stages.

ETHICS DUMPING IN LIFE SCIENCES

The export of unethical practices from high-income regions to low- and middle-income countries is one of the critical ethical concerns we still face in the twenty-first century. This practice was recently officially termed by the European Commission as “ethics dumping” (EC, 2016). That burning issue is the core topic of the EU project TRUST which is discussed in Chapter 1 in this volume. Although problems arising from research conducted from the wealthier environments in resource-poor settings were recognized in the past (Molyneux et al., 2009), the attention to the ethics dumping is rapidly growing (Schroeder, Cook, Hirsch, Fenet, & Muthuswamy, 2018). Any research carried in a resource-poor setting brings many challenges. For instance, obtaining consent for research in such settings requires additional considerations. That is why the consenting process should be strengthened by taking into account local social, cultural, and economic

contexts in the design and administration of consent forms and processes (Boga et al., 2011). The TRUST project aimed to develop a Global Code of Conduct for Research in Resource-Poor Settings which will provide a guidance across all research disciplines. The challenges of resource-poor settings we also discuss in Chapter 2, where we investigate those settings from the viewpoint of providing health care during the largest ever outbreak of Ebola virus disease (EVD), which started during the 2013 in West African countries. This interesting chapter also provides the author's personal impressions of the situation in Lagos, Nigeria, where Dr. Petrosillo was deployed as a World Health Organization (WHO) clinical consultant on EVD. In this chapter, the author provides us with a clear table containing the issues and consequences of ethical considerations associated with dealing with EVD. The chapter clearly concludes that the epidemic would have been far worse and more people would have died without the provision of international help.

DATA PROTECTION AND THE USE OF BIG DATA IN LIFE SCIENCES

As stated previously in the Series Preface with which Iphofen opens this volume, the uneven distribution of ethics standards across whole European Research Area (ERA) (Evers, 2004) has led to the recognition of a need for a harmonization between improved review practices with the existing ones. The intention of this volume is to ensure support to life scientists, provide an overview of ethics questions and issues in some specific life science fields, and inform a broad audience about the current challenges and ongoing projects related to ethics in the life sciences. A rapid development of new technologies, expeditious development of the digital revolution and new media has also entered the field of life sciences and biomedicine. An overview of the ethics challenges in the digital era focusing on medical research in relation to the new EU General Data Protection Regulation (GDPR) 2016/679 is presented in Chapter 3. This new regulation replaces the Data Protection Directive 95/46/EC and is designed to harmonize data privacy laws across Europe, to protect and empower all EU citizens' data privacy, and to reshape the way organizations across the region approach data privacy (FRA/ECtHR/EDPS, 2018).

Huge amounts of information about patients' health, so-called Big Data, carry a tremendous potential for use in life science research even for treating the most severe diseases. It has been recognized that Big Data, as a paradigm, can be a double-edged sword in organizational and management research, capable of significantly advancing our field but also causing backlash if not utilized properly (Wenzel & Van Quaquebeke, 2018). Furthermore, the right for privacy and right for research on common benefit are in opposition. This susceptible relation is explored in Chapter 4.

IN SITU ETHICS, A FOCUS ON LABORATORY WORK

Sometimes the interpretations of principles of safety and security are very limited, and are considered only as sub-criteria of other ethical principles, ignoring the public interest in safety and security. That issue we discuss in Chapter 5 where it is clearly recognized that as long as adequate inclusion of safety and security expertise in ethics panels is missing, as ethics panels are sometimes dominated by philosophers, ethicists, medical doctors, and lawyers with limited practical background in safety and security risk management of emerging technologies, ethics reviews will not contribute to effective safety and security risk management when emerging technologies are involved.

One of such new emerging technologies which will have a strong impact both on science and society in the future is gene-editing technology. The legal and ethical considerations governing gene-editing technology in the European Union are scrutinized in Chapter 6. Recently, a need for the foundation of an expert group (European Steering Committee) to assess the potential benefits and drawbacks of genome editing and to design risk matrices and scenarios for a responsible use of this promising technology was recognized (Chneiweiss et al., 2017). Consequently, on March 23, 2018, in Paris, France, the international “Association for Responsible Research and Innovation in Genome Editing” (ARRIGE) to promote a global governance of genome editing was launched.⁸ The association aims to provide a comprehensive setting for different stakeholders, including academia, private sector, patient organizations, public opinion, and governmental institutions, to allow the development of these paramount technologies in a safe and socially acceptable environment. Recognizing the importance of this event, we dedicated a separate chapter (Chapter 7) on the ARRIGE association.

Above the issue of security and safety of new and emerging technologies, the so-called dual-use issue plays a significant ethical consideration for technologies in which the future consequences of their use are not clearly predictable. The concept of dual use can be applied on almost everything that is designed and produced. Nevertheless, this concept in life sciences may have even deeper meaning, since the research products that life sciences may enter have an application already at the nanoparticle level, spreading such applications to a fully global use.

The need for a better definition of the dual-use concept, with the need to move from constraining to enabling types of policies, the move from secrecy to openness, and the move from segregation to integration of the public voice, has been previously recognized (Dubov, 2014). Also a reconsideration of dual use in life sciences should include the aspect of threats and intentions (van der Bruggen, 2012).

In Chapter 8, a dual use with focus on neuroscientific and nanotechnological research is elaborated in relation to the current and emerging tools and techniques used in brain research, presenting how they actually or potentially can be employed in settings that threaten public health and raising multiple ethical concerns. A term like neurohacking (Malin et al., 2017) is exhaustively elaborated in several research domains.

A problem of the rapidly increasing numbers of older adults with dementia and other mental health problems throughout the world will have huge implications for healthcare systems (Sorrell & Loge, 2010), consequently making clinical dementia research more demanding and more urgent.

In Chapter 9 we moved a step ahead, exploring the ethical challenges of informed consent, decision-making capacity, and vulnerability in clinical dementia research where we tried to provide an overview of the ethical framework and decision-making in clinical dementia research, and to analyze and discuss the ethical challenges and issues that can arise when conducting clinical dementia research.

Above multiple ethical challenges which are raised in this kind of research, even the nutrition of such patients must be in focus for ethical considerations. For instance, a comfort feeding (not forcing a person to eat or making them feel guilty if they don't), instead of enteral nutrition, can and must be applied when dysphagia and progressive disease processes have still not occurred. Enteral nutrition guidelines and recommendations which have been developed by the American Society for Parenteral and Enteral Nutrition and the Academy of Nutrition and Dietetics for individuals with dementia focus on patients with advanced dementia due to the dysphagia and progressive disease process. Nevertheless, the application of the enteral nutrition to all dementia patients is still widely practiced (Schwartz, 2018).

Malnutrition problems in the broad population of older adults is a growing issue, and a comprehensive assessment for early identification of malnutrition and determination of the appropriate intervention strategies is needed to address this global public health problem (Maseda et al., 2018).

According to the Second International Conference on Nutrition (ICN2), which was jointly organized by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) and was held at the FAO Headquarters in Rome, Italy, from 19 to 21 November, 2014, 795 million people remain undernourished, over 2 billion people suffer from various micronutrient deficiencies, and an estimated 161 million children under 5 years of age are stunted, 99 million underweight, and 51 million wasted. Meanwhile, more than 600 million adults are obese. Global problems require global solutions (Amoroso, 2016).

Recognizing raising global health problem related to nutrition, we included in this volume two additional chapters: one describing the ethical and moral responsibility related to diet therapy (Chapter 10) and another, bolder chapter which tries to move a step further, moving from the "conventional box" of relations between nutritional and medical practices (Chapter 11).

In this volume, we have tried to identify some of the most important cross-roads between the life sciences and the issues of ethics and integrity they must confront. Certainly, this task was not easy given the broad range of research fields which appertain to life sciences. However, we did not want to renege upon that challenging adventure. As each great journey starts with a first step, we hope that this volume will encourage professionals in this field in their professional endeavors to further their work with integrity. We also hope this volume

offers some insight on the ethical problems facing the life sciences for the interested general reader. Each chapter here warrants another volume of its own and will be returned to later in the series.

NOTES

1. Retrieved from https://ec.europa.eu/research/openvision/pdf/rise/veugelers-saving_away.pdf
2. Retrieved from https://digital.rdmag.com/researchanddevelopment/2018_global_r_d_funding_forecast
3. Retrieved from http://ec.europa.eu/public_opinion/archives/ebs/ebs_270_en.pdf
4. Ipsos MORI Social Research Institute. Public attitudes to animal research in 2016. A report for the Department for Business Innovation & Skills. July 2016. Retrieved from <https://www.ipsos.com/sites/default/files/publication/1970-01/sri-public-attitudes-to-animal-research-2016.pdf>
5. http://digital.rdmag.com/researchanddevelopment/2018_global_r_d_funding_forecast?pg=1#pg1
6. https://wellcome.ac.uk/sites/default/files/wtvm052279_1.pdf
7. Retrieved from <https://www.theguardian.com/education/2007/feb/13/businessofresearch.highereducation>
8. Retrieved from <https://arrige.org/>

REFERENCES

- Amoroso, L. (2016). The Second International Conference on Nutrition: Implications for Hidden Hunger. *Hidden Hunger: Malnutrition and the First 1,000 Days of Life: Causes, Consequences and Solutions*. H. K. Biesalski and R. E. Black. Basel, Karger. 115, 142–152. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/27197665>
- Bert, B., Dorendahl, A., Leich, N., Vietze, J., Steinfath, M., Chmielewska, J., ... Schonfelder, G. (2017). Rethinking 3R strategies: Digging deeper into animal test info promotes transparency in in vivo biomedical research. *PLoS Biology*, 15(12), e2003217.
- Boga, M., Davies, A., Kamuya, D., Kinyanjui, S. M., Kivaya, E., Kombe, F., ... Mwalukore, S. (2011). Strengthening the informed consent process in international health research through community engagement: The KEMRI-Wellcome Trust Research Programme Experience. *PLoS Medicine*, 8(9), e1001089.
- Chneiweiss, H., Hirsch, F., Montoliu, L., Muller, A. M., Fenet, S., Abecassis, M., ... Saint-Raymond, A. (2017). Fostering responsible research with genome editing technologies: a European perspective. *Transgenic Research*, 26(5), 709–713.
- Dubov, A. (2014). The concept of governance in dual-use research. *Medicine, Health Care and Philosophy*, 17(3), 447–457.
- Evers, K. (2004). Codes of conduct – Standards for ethics in research. European Commission Luxembourg: Office for Official Publications of the European Communities, 2004. Retrieved from https://www.researchgate.net/publication/301609039_Codes_of_Conduct_Standards_for_ethics_in_research
- FRA/ECtHR/EDPS. (2018). Handbook on European data protection law. Retrieved from https://www.echr.coe.int/Document/Handbook_data_protection_02ENG.pdf
- Hernandez, I., Bott, S. W., Patel, A. S., Wolf, C. G., Hospodar, A. R., Sampathkumar, S., & Shrank, W. H. (2018). Pricing of monoclonal antibody therapies: higher if used for cancer? *American Journal of Managed Care*, 24(2), 109–112.
- Iphofen, R. (2014). Ethical issues in surveillance and privacy, Chapter 5. In A. W. Stedmon & G. Lawson (Eds.), *Hostile Intent and Counter-Terrorism: Human Factors Theory and Application* (pp. 59–71). Aldershot: Ashgate.
- Jones, N. L. (2007). A code of ethics for the life sciences. *Science and Engineering Ethics*, 13(1), 25–43.