ACKNOWLEDGMENTS:
To all staff of ISCIII Centers, Areas and Units, for their active participation and efforts in preparing this report.

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**Presentation by the Director**

**Presentation of the ISCIII**
Following 2020, the year in which we discovered and confronted one of the greatest scientific and health crises in our recent history, COVID-19, 2021 was the year in which science as a tool to protect health prompted the development of vaccines that have protected society against the severity of the SARS-CoV-2 pandemic. The Institute of Health Carlos III (ISCIII), as in its more than 35 years of history, has done its part to address this crisis and affirm that science is the way to continue improving the health of society.

The efforts against this pandemic that were initiated and developed the ISCIII throughout 2020 continued in the past year with projects such as the CombiVacs clinical trial on heterologous vaccination, the COSMO-Spain study on the social perception of the pandemic, and the ENE-COVID Senior study on vaccines and immunity against SARS-CoV-2. Apart from COVID-19, the year 2021 was also characterized by other noteworthy issues, such as our Strategic Plan 2021-2025, the novelties in our principal tool for funding biomedical research -the Health Research and Development Strategy-, the continuation of the COSMO-Spain study on the social perception of the pandemic, the presentation of the Strategic Project for Economic Recovery and Transformation (PERTE) for Cutting-edge Health, the study of the volcano on La Palma, and the change in the Board of Directors.

As in 2020, the ISCIII has continued to play an essential role in the research, surveillance, and management of SARS-CoV-2 and COVID-19. The ISCIII 2021 activity report reflects yet another year the professionalism and expertise of the more than 900 ISCIII employees, who have continued to develop multiple projects to protect the health of all citizens through science and the generation of knowledge. If one of last year’s milestones should be highlighted here, it would be the CombiVacs clinical trial promoted by the Institute: in May, it provided the first evidence in the world of the feasibility of heterologous vaccination regimens, a combination of several different vaccines. This alternative has already been used in millions of people and is now standard in booster vaccines. The results of this study were published in the journal The Lancet and facilitated decision-making on vaccination strategy.

Another of our most prominent studies continues to be COSMO-Spain, which we launched in 2020. Throughout 2021 it published several rounds of surveys to obtain more information on the social perception and knowledge of the Spanish population regarding the pandemic. In addition, in the last quarter of the year we launched two studies on immunity in the elderly (ENE-COVID-senior study) and on persistent COVID, which will offer their results throughout 2022.
Furthermore, last year the Institute was directly involved in preparing and launching the strategy for integrating genomic sequencing into coronavirus surveillance by coordinating a national network of laboratories that enables SARS-CoV-2 sequencing capacity to be increased and new variants to be studied. In addition, the institute participated in numerous collaborative European projects related to the study of SARS-CoV-2, such as Vaccinate, which is part of the HERA initiative and seeks to reinforce a platform to facilitate clinical trials in the field of infectious diseases. These two examples show how national research must be coordinated with international efforts to advance scientific progress as much as possible.

The efforts went far beyond the pandemic, however, and placed the service that the ISCIII has been providing for more than 35 years to the scientific and health systems again in the forefront. In 2021 the ISCIII enjoyed the largest budget in its history. The year began with the publication of the ISCIII Strategic Plan 2021-2025, the roadmap to consolidate, improve, and renew the Institute's lines of work, and closed with the publication of all final resolutions of the Health Research and Development Strategy (AES by its Spanish acronym) 2021, the principal funding tool for biomedical and health research in Spain.

Last year the AES was characterized by presenting fundamental new developments such as salary improvements for the research community, a new area of Infectious Diseases in the CIBER, and a renewed model of operation of the Results-Oriented Cooperative Research Networks in Health (Spanish acronym: RICORS). In addition, the call for independent clinical research and the commitment to advanced therapies and personalized medicine have continued to be consolidated. Thanks to these and other contents of the AES 2021, the ISCIII awarded last year more than 193 million euros in grants to the science system of the National Health System (NHS), with the use of recovery funds and two extraordinary calls for proposals playing a leading role: almost 30 million euros for personalized medicine and another 15 million euros for Infrastructures. All these new developments continue to promote collaborative and multidisciplinary research in Spain.

The announcements of prominent infrastructure projects to be developed and completed in the coming years were also of paramount importance in 2021, such as the renovation of the National School of Health (ENS), the construction of a P4 maximum biosafety laboratory, and the construction of new laboratories for the Center for Advanced Therapies at the Majadahonda Campus. Through these and other projects the ISCIII will improve its research and its services to the scientific and healthcare systems.
Another of the most relevant activities of the year was the presentation at the ISCIII of the Strategic Project for Economic Recovery and Transformation (PERTE) for Cutting-edge Health, in the presence of the President of the Government and the Ministers of Science and Innovation, Health, Industry, Trade and Tourism, and Finance and the Civil Service. Furthermore, the ISCIII collaborated in monitoring one of the most impactful natural phenomena of the year: the eruption of the volcano on La Palma, where the National Center for Environmental Health partook in monitoring air quality.

On a more intramural note, I cannot fail to mention that the ISCIII made a change in its Directorate in mid-year. Raquel Yotti, who had served for three years as Director, was appointed Secretary General for Research at the Ministry of Science and Innovation. I had the honor of replacing her and undertaking a task of continuity and consolidation of the immense amount of work she had done. My appointment, together with the incorporation of Rosario Perona and Pilar Gayoso into the General Sub-Directorates of Research Assessment and Promotion and of Cell Therapy and Regenerative Medicine, respectively, completed the reform of the management team initiated in the first half of 2021 with the arrival of Manuel Cuenca and Miguel Calero to the General Secretariat and the General Sub-Directorate for Applied Services, Training, and Research, respectively. People change, but the Institute’s work to improve the health of the population remains unchanged.

To mention all innovations introduced in 2021 would entail a very long list, perhaps too long for this introduction. Among the many important developments of the past year, I cannot fail to mention the creation of the Mentoring Program to promote the training of young researchers at the Institute; the creation of a Unit on Climate Change, Health, and Urban Environment; the creation of the Working Group on Equality; the entry of the ISCIII into the European initiative Science Europe; the consolidation of the Health Research Forum with regional heads of R&D and Innovation in health; and the reinforcement of joint work with Health Research Institutes (Spanish acronym, IIS), initiated with a Forum that this year has been renamed the ISS Alliance.

Finally, a few words about another of our key objectives: communication, which allows us to bring science to the people. The year 2021 was also important for the scientific dissemination carried out by the ISCIII. In addition to the three major annual activities in this area (Science Week, European Researchers’ Night, and the International Day of Women and Girls in Science), several activities were carried out to bring science closer to society, such as visits to primary and secondary schools by our researchers, as well as the signing of an agreement with The Conversation, one of the most important platforms for dissemination in Spain, which is promoting the publication of articles on current scientific issues by researchers at the Institute.

In short, last year’s work of the ISCIII was determined by the push that, like every other year, we want to give to our primary goal: to do research, train, provide funding and offer services so that science and healthcare will improve the health of the public. The work, of course, will continue in 2022.
What is the Institute of Health Carlos III working on? A look at our Chamartín Campus

ISCIII STAFF

Total 895
612 women (69.5%)
268 men (30.5%)

BUDGET
403,200,540 €

Funded by the Recovery and Resilience Fund

115,000,000 €

ERDF FUNDS
1,407 certified grants
47,200,000€ declared expenditure

ESF FUNDS
337 certified grants
7,000,000€ declared expenditure

FINANCING AND COORDINATION OF R&D&I IN THE NATIONAL HEALTH SYSTEM
1,599 Grants funded
237,795,585.74€

What is the Institute of Health Carlos III working on?
A look at our Chamartín Campus

ISCIII IN NUMBERS 2021

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ISCIII IN NUMBERS 2021

ISCIII IN NUMBERS 2021
KNOWLEDGE GENERATION
796 grants funded - 140,553,951.46€

INSTITUTIONAL REINFORCEMENT
226 grants funded - 33,016,077.88€

RESEARCH INFRASTRUCTURES AND SCIENTIFIC AND TECHNICAL EQUIPMENT
65 grants funded - 14,991,835.40€

NATIONAL PROGRAM FOR TRAINING TALENT AND ITS EMPLOYABILITY IN R&D&I

512 grants funded
Funding: 49,233,721€

NATIONAL SUBPROGRAM FOR TRAINING
216 grants funded - Funding: 18,289,851€

NATIONAL SUBPROGRAM FOR INCORPORATION
223 grants funded - Funding: 29,661,350€

NATIONAL SUBPROGRAM FOR MOBILITY
73 grants funded - Funding: 1,282,520€

NATIONAL PROGRAM FOR KNOWLEDGE GENERATION AND REINFORCEMENT OF THE SPANISH R&D&I SYSTEM

1,087 grants funded
188,561,864.74€

What is the Institute of Health Carlos III working on?
A look at our Majadahonda Campus
COLLABORATIVE RESEARCH AND ACCREDITATION OF HEALTH RESEARCH INSTITUTES (IIS)

7 thematic networks of results-oriented cooperative research in health

33 Health Research Institutes accredited

12 thematic areas of Biomedical Research Networking Centers (CIBER)

Participation in 4 European research infrastructures

INTRAMURAL SCIENTIFIC ACTIVITY AT ISCIII

546 indexed publications

58 projects awarded with 6,731,801.41 € of funding

24 international projects with 3,323,118.95 € of funding

204 ongoing projects with a total funding 24,744,119.73 € of which 73 international projects with a funding of 11,121,126.17 €

NATIONAL LIBRARY OF HEALTH SCIENCES

43,054 publications (bibliographic resources)
166,845 database searches
More than 82.5 million visits to SciELO España

NATIONAL SCHOOLS OF PUBLIC HEALTH

ENS
468 students
3,769 teaching hours

ENMT
909 students
1,521 teaching hours
COMMUNICATION

More than 5 million visits to the ISCIII web site

185 information news releases
5 outreach news releases

101 press releases sent to the media

56 videos published, of which 17 are live events

SCIENTIFIC AND TECHNICAL SERVICES

✓ 365 updates of the COVID-19 panel in Spain
✓ 68 reports on the “COVID-19 situation in Spain”
✓ 81 MoMo reports (Daily Mortality Monitoring System)
✓ 915 ENE-COVID reports for Autonomous Communities
✓ 68 national reports on the demographic, epidemiological and clinical characteristics of COVID-19
✓ 53 editions of the Weekly Epidemiological Bulletin
✓ 51 specific epidemiological reports
✓ 3,810 diagnostic COVID-19 tests
✓ 21,891 serological determinations from the ENE-COVID Senior, COMBIVACS and RESCUESVACS studies
✓ 6,114 SARS-CoV-2 strains detected by genomic sequencing with identification of variants
✓ 35,064 microbiological diagnostic assays within laboratory surveillance programs
✓ 102 outbreaks of pathogenic microorganisms characterized with 5,084 assays
✓ 370 microbiological analysis techniques
✓ 4,419 environmental toxicology analyses
✓ 57,922 measurements of atmospheric contamination
✓ 49,881 tests carried out by the radiation protection service
✓ 468 determinations related to human prionopathies, including 64 determinations by PCR and sequencing of the PRPN gene
✓ 376 genetic diagnoses of rare diseases
✓ 1,262 cases included in the Rare Diseases Registry and 35 cases of undiagnosed rare diseases
PERTE FOR CUTTING-EDGE HEALTH

PERTES (SPANISH ACRONYM OF STRATEGIC PROJECTS FOR ECONOMIC RECOVERY AND TRANSFORMATION) ARE NEW PUBLIC-PRIVATE COLLABORATION INSTRUMENTS FOR STRATEGIC PROJECTS THAT REQUIRE COLLABORATION BETWEEN PUBLIC ADMINISTRATIONS, COMPANIES, AND RESEARCH CENTERS TO ENSURE THE SCALING-UP OF THEIR OPERATIONS IN OUR COUNTRY.

THE PERTE INSTRUMENT WAS CREATED WITHIN THE FRAMEWORK OF THE PRTR (SPANISH ACRONYM OF RECOVERY, TRANSFORMATION AND RESILIENCE PLAN), BUT IS INTENDED TO BE PERMANENT AND TO GO BEYOND ITS TIME FRAME. THEY ARE OPEN TO ALL TYPES OF COMPANIES AND BRING TOGETHER THE COMMITMENT OF DIFFERENT MINISTRIES INVOLVED IN THEIR DEVELOPMENT. THE SIXTH POLICY LEVER INCLUDED IN THE RECOVERY PLAN IS A "PACT FOR SCIENCE AND INNOVATION. STRENGTHENING THE CAPACITIES OF THE NATIONAL HEALTH SYSTEM."
MORE THAN 982 MILLION EUROS OF PUBLIC INVESTMENT
- 487 MILLION EUROS OF PRIVATE INVESTMENT

The project is estimated to generate 4,300 million euros of GDP and 12,700 new jobs.

KEY OBJECTIVES

a) To position Spain as a leading country in the innovation and development of advanced therapies aimed at curing diseases to ensure the provision of state-of-the-art healthcare systems for all citizens and to support research, innovation, and clinical development.

b) To promote the equitable implementation of Personalized Precision Medicine, favoring the strengthening, development, and creation of competitive companies based on knowledge generation.

c) To develop a digital NHS with an integrated database to improve prevention, diagnosis, treatment, rehabilitation, and research.

d) To strengthen digital primary health care with the application of advanced technologies for all activities involving relations with the citizens and management of resources anywhere in the country and in all areas of health care.

At the same time, the PERTE establishes five cross-cutting lines aimed at strengthening and developing the capabilities of the NHS (National Health System) centers.

CROSS-CUTTING LINES

CCL1 Strengthening and developing the capacities of the NHS.

CCL2 Developing and modernizing Spain’s innovation-oriented industrial capacity.

CCL3 Collaboration and Coordination between the science and business sectors.

CCL4 Territorial cohesion.

CCL5 Training.
INSTRUMENTS

This strategic project encompasses and coordinates two specific investment agendas: one addressing the science sector and the other the business sector, particularly fostering scientific-business alliances. These investment agendas are organized around the following instruments:

a) Calls for proposals aimed at the scientific and industrial sectors and at collaborative projects that combine the two investment agendas
b) Creation of a networked R&D and Innovation structure for advanced therapies (consortium) that will allow the existing capacities throughout Spain to be structured
c) Creation of a public-private investment vehicle for advanced therapies (public-private business partnership) with the participation of companies with production capacity in Spain
d) Elements for coordination and early identification of capacities and needs of the Spanish Public Health System.
e) Innovative and pre-commercial public procurement
f) Agreements with Autonomous Communities and agreements through sectoral meetings
g) Private initiatives and projects co-programmed within the Alianza Salud de Vanguardia (Cutting-edge Health Alliance) with the leadership of the industrial sector
h) Public tenders
What is cutting-edge health?
It is the promotion and protection of health based on the development and incorporation of innovative products and procedures and digital solutions that offer added value to the prevention, diagnosis, personalised treatment and rehabilitation of patients.

The ISCIII participates with a **TOTAL BUDGET OF 177,409 M€. 18% OF THE TOTAL** public investment in the PERTE.

**ITS ACTIVITIES AND ACTIONS ARE FOCUSED ON:**

**STRATEGIC GOAL 1**

**PERSONALIZED PRECISION MEDICINE:**
- ISCIII call for R&D&I projects on Personalized Precision Medicine amounting to 111 million euros between 2021-2022

**STRATEGIC GOAL 2**

**ADVANCED THERAPIES AND OTHER INNOVATIVE DRUGS:**
- ISCIII call for Independent Clinical Research for a value of 15 million euros (2021-2022)
- Joint ISCIII-CDTI call for innovation linked to Personalized Medicine and Emerging Therapies for 20 million euros (10 million euros contributed by ISCIII in 2022)
- Creation and development of the National Consortium of Advanced Therapies CTA for a value of 22.5 million euros
- Public-Private Business Partnership (CDTI-ISCIII) ISCIII: Provision of scientific and technical content.
What do we want to achieve with the PERTE?

- Toward personalized precision medicine
  Incorporation of technological developments

- Toward an innovative and less technology-dependent industry
  Industrial transfer of scientific knowledge and R&D&I generated in the healthcare system (advanced therapies and emerging drugs)

- Toward digital healthcare
  Incorporation of digital technological capabilities for prevention, diagnosis and treatment

- Toward a healthcare system with greater and better capabilities and greater competitiveness

Cross-cutting line 1 - Strengthening and developing the capacities of the NHS

a) Agreements between the ISCIII and the Autonomous Communities to attract investments in Spain
b) ISCIII Clinical Research Platform - SCReN
c) Platform for dynamization and innovation of the industrial capacities of the SNS and their effective transfer to the productive sector ISCIII-ITEMAS for a total value of both platforms of 18 million euros (2021-2022)

Cross-cutting line 3 - Collaboration and Coordination between the science and business sectors

a) ISCIII Clinical Research Platform - SCReN
b) Platform for dynamization and innovation of the industrial capacities of the SNS and their effective transfer to the productive sector ISCIII-ITEMAS

TWO ACTIONS ARE PURSUED WITHIN THE FRAMEWORK OF THIS PLATFORM:

PORTFOLIO OF HEALTH INNOVATION PROJECTS
MONITORING SYSTEM FOR PROJECTS IN PRECLINICAL PHASES

Cross-cutting line 5 - Strengthening and coordinating new training programs between companies, the NHS, and R&D&I centers

a) ISCIII training grants in health research management for a total of 0.907 million euros between 2021-2022
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<thead>
<tr>
<th>Month</th>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>JANUARY</td>
<td>14</td>
<td>Funding opportunities in International Joint Programming 2021/Biomedicine <a href="https://www.youtube.com/watch?v=kJmKlwajZOo&amp;t=4s">Link</a> <a href="https://www.youtube.com/watch?v=pQMwxAe7k&amp;t=782s">Link</a></td>
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<td>21</td>
<td>Presentation of the Health Research and Development Strategy 2021 <a href="https://www.youtube.com/watch?v=Hjbx93kDjKk">Link</a></td>
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<td>27</td>
<td>Information day on the 2021 call for proposals of the ERA PerMed initiative on personalized medicine <a href="https://www.youtube.com/watch?v=Xgle-WcXQNs&amp;t=22s">Link</a></td>
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<td>29</td>
<td>Israel Cruz - World Neglected Tropical Diseases Day <a href="https://www.youtube.com/watch?v=F6CegVOg6gA">Link</a></td>
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<tr>
<td>FEBRUARY</td>
<td>28</td>
<td>Ignacio Pérez de Castro World Rare Diseases Day <a href="https://www.youtube.com/watch?v=15QHLOwvqkE">Link</a></td>
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<td>MARCH</td>
<td>3</td>
<td>Eva Bermejo - World Birth Defects Day <a href="https://www.youtube.com/watch?v=2kstkdqBCC">Link</a></td>
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<td>22</td>
<td>ISCIII COVID-19 Fund, one year after its call: biomedical research during the pandemic <a href="https://www.youtube.com/watch?v=ze_2cP_xfo&amp;t=958s">Link</a> <a href="https://www.youtube.com/watch?v=TwOurP5rZg">Link</a></td>
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<tr>
<td>MAY</td>
<td>18</td>
<td>Preliminary results. CombivacS clinical trial <a href="https://www.youtube.com/watch?v=VH5rTl-5ZAw&amp;t=175s">Link</a></td>
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JULY
2
Open Science Day in Health Research Institutes
https://www.youtube.com/watch?v=Qtaibh0Yizg
7
Presentation of new features in the R&D&I calls of 2021
https://www.youtube.com/watch?v=8V7qM9tpJs&t=2479s
22
Webinar EU4Health WPogramme 2021
https://www.youtube.com/watch?v=pxO0Cp9gzIs&t=5061s

SEPTEMBER
6
Cristóbal Belda. General Director Institute of Health Carlos III
https://www.youtube.com/watch?v=R0RRIod2fX4&t=7s
9
Didactic handbook on climate change and health
https://www.youtube.com/watch?v=9O34wCiHYao&t=8s
16
Visit by the Ministers of Health and Science to the CNM (in relation to granting the sequencing project)
https://www.youtube.com/watch?v=mF7Fi6W2TS8
28
Lecture by Professor Dr. Rafael Nájera Morondo at the 1st Follow-up Conference of the PhD Program in Biomedical Sciences and Public Health
https://www.youtube.com/watch?v=KyO64dmvBmk&t=209s
Course on parasitological diagnosis of tropical diseases
https://www.youtube.com/watch?v=rTpxQFiCA4

OCTOBER
1
QASP Study: Adding quality to the years
https://www.youtube.com/watch?v=8veGPpGp4kc&t=128s
28
Lecture by Professor Dr. Rafael Nájera Morondo at the 1st Follow-up Conference of the PhD Program in Biomedical Sciences and Public Health
https://www.youtube.com/watch?v=KyO64dmvBmk&t=209s

DECEMBER
10
Irene Molina, winner of the contest ‘Your thesis in 3 minutes’ 2021
https://www.youtube.com/watch?v=xLBNldlPCoM&t=6s
14
INFODAY ERA PerMed Joint Transnational Call 2022: “Prevention in Personalised Medicine”
https://www.youtube.com/watch?v=_U2WYR6Bm8
20
Rafael Nájera, virologist and first general director of the ISCIII, on his book “Epidemic, disease, pandemic”
https://www.youtube.com/watch?v=Bad5+rTAXbE
22
Conference: Funding International Health Projects 2022
https://www.youtube.com/watch?v=aa4xVuovNQA&t=5607s

JUNE
21
Spanish CombivacS Study & Vaccelerate
https://www.youtube.com/watch?v=ajRkn9AGupY&t=1981s
22
SEMINARS RIs IN BIOMEDICAL SCIENCES
https://www.youtube.com/watch?v=K78yTeUDLoa&t=3131s
Informative day on Research Infrastructures in Horizon Europe
https://www.youtube.com/watch?v=s2uUo4a4v2M&t=946s

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