



Instituto
de Salud
Carlos III

EXECUTIVE SUMMARY 2018



Unión Europea

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"Una manera de hacer Europa"



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Fondo Social Europeo
"El FSE invierte en tu futuro"



GOBIERNO
DE ESPAÑA

MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



Instituto
de Salud
Carlos III

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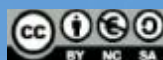
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I N T R O D U C T I O N

The Institute of Health Carlos III (ISCIII) is the main Spanish Public Research Organization in the field of Health Sciences, as well as a Scientific and Technical Support Body at the service of the Spanish National Health System (SNS). It is our mission to contribute to improving the health of all citizens and fight against diseases, through the *promotion of research and innovation* in Health Sciences and Biomedicine, and to provide *benchmark scientific and technical services and teaching programs* directed at the Spanish National Health System. For more than 30 years the institution has remained faithful to this mission, and has contributed to the transformation of health research in Spain for the benefit of all citizens. This has been possible thanks to the commitment of its staff, to the dedication and generosity of great researchers and teachers, and also, to a large extent, to the conviction and professionalism of all its directors. In this respect, I would like to express my personal and institutional gratitude to Dr. Jesús Fernández Crespo, who led the institution for much of 2018 and is responsible for many of the achievements reflected in this report.

One of the main objectives of ISCIII is the promotion of excellence in research aimed at protecting and improving health throughout the country. The actions aimed at achieving this objective are included, above all, in the call for grants of the Strategic Action in Health (AES), which takes place within the framework of the National Program for Knowledge Generation and Reinforcement of the Spanish R&D and Innovation System. In 2018, the AES allowed the continuation of long-term actions such as funding research projects and contracts for research staff. Among the latter, grants for contracts for Bioinformaticians to support research in Accredited Health Research Institutes (IIS), called for the first time in 2018, stand out for their novelty.

In addition, as a demonstration of the institutional commitment to respond to the new needs of the SNS, in 2018 calls for grants for Independent Clinical Research Projects in Advanced Therapies were launched for the first time; through these calls, eight academic clinical trials in advanced therapies (gene therapy, cell therapy, and tissue engineering) were funded, specifically aimed at advancing the treatment of various diseases.

It should also be noted that this year ISCIII continued its commitment to internationalization, both through participation in various joint European and international initiatives, and by promoting the participation of the National Health System in European programs, mainly Horizon 2020, which is increasingly gaining importance as a structural source of funding for the SNS.

Another key element of the ISCIII strategy to promote research and contribute to the cohesion of the SNS was the implementation of cooperative research structures that facilitate collaboration between the best groups in the country. Thus, the Thematic Networks for Cooperative Research and the Biomedical Research Networking Centers (CIBER and CIBERNED) are already consolidated structures, and throughout 2018 they continued their activity through consistently strong performance. It should be noted that in 2018 new groups joined CIBERNED to reinforce existing areas and to create a new area addressing Amyotrophic Lateral Sclerosis (ALS) and other motor neuron diseases.

In addition, three research foundations are affiliated to ISCIII: the CNIC, the CNIO and the CIEN Foundation, focused on research in cancer, cardiovascular diseases and neurodegenerative diseases, respectively. Both the CNIC and the CNIO are part of the network of Severo Ochoa Centers and María de Maeztu Units, and are considered to be among the world's top research centers in their areas of expertise.



Dra. Raquel Yotti Álvarez, General Director Institute of Health Carlos III

Finally, I would like to make a very special mention of the work that is carried out daily in the reference research centers of ISCIII and that makes a decisive contribution to preserving the Health of all citizens. The National Microbiology Center, the National Epidemiology Center, the National Environmental Health Center, the National Center of Tropical Medicine, the Research Institute for Rare Diseases, the Functional Unit for Research on Chronic Diseases, the Healthcare Research Unit, the Telemedicine and e-Health Research Unit, the Health Technology Assessment Agency, and the National Schools of Public Health and of Occupational Medicine, all continued in 2018 to carry out in an effective manner their three functions of providing state-of-the-art scientific and technical services to the SNS, research and teaching. Their activities are so numerous that singling out one over another would inevitably lead to oversights, so I encourage you to have a closer look at their activities and scientific production by reading this scientific report. To mention only one of the data, in 2018 the ISCIII reference centers obtained funding for 48 new projects that, added to the 209 projects that were already in force, represent a competitive financing of close to 12 million euros. This is just one of the data that reflects the high and sustained level of scientific excellence in our national centers.

I do not want to finish this introduction without acknowledging the work and dedication of all the people who make up ISCIII, and who provide the technical and administrative support that is essential to fulfill our mission of preserving and improving the health of the citizens. Thank you very much to all of you.

1.1 GOVERNANCE

The **Institute of Health Carlos III**, O.A., M.P. (hereinafter ISCIII) is a Public Research Entity (OPI) and an autonomous legal entity. In accordance with the fourth additional provision of Royal Decree 531/2017, of May 26, ISCIII reports to the Ministry of Economy, Industry and Competitiveness, and has a two-fold dependence. Functionally, it depends on the Ministry of Health, Social Services and Equality (MSSSI) for its health, planning and healthcare activities; on the other hand, it depends on the Ministry of Economy, Industry and Competitiveness through the Secretariat of State for Research, Development and Innovation, for its applied research activities that may be translated into clinical practice of the National Health System (SNS). Since the publication of RD 355/2018, of June 6, which establishes the organizational structure of the Ministerial Departments, these are respectively called the Ministry of Science, Innovation and Universities (MCIU) and the Ministry of Health, Consumer Affairs and Social Welfare (MSCBS). Since RD 595/2018, of June 22, which establishes the basic organizational structure of the Ministerial Departments, the ISCIII depends on the General Secretariat for Scientific Policy Coordination (SGCPC of the MCIU).

The **mission** of the ISCIII is to contribute to **improving the health of all citizens and fight against diseases**, through the **promotion of research and innovation** in Health Sciences and Biomedicine, and to provide **benchmark scientific and technical services** and **teaching programs** directed at the National Health System. In relation to this mission, the objectives of the ISCIII are:

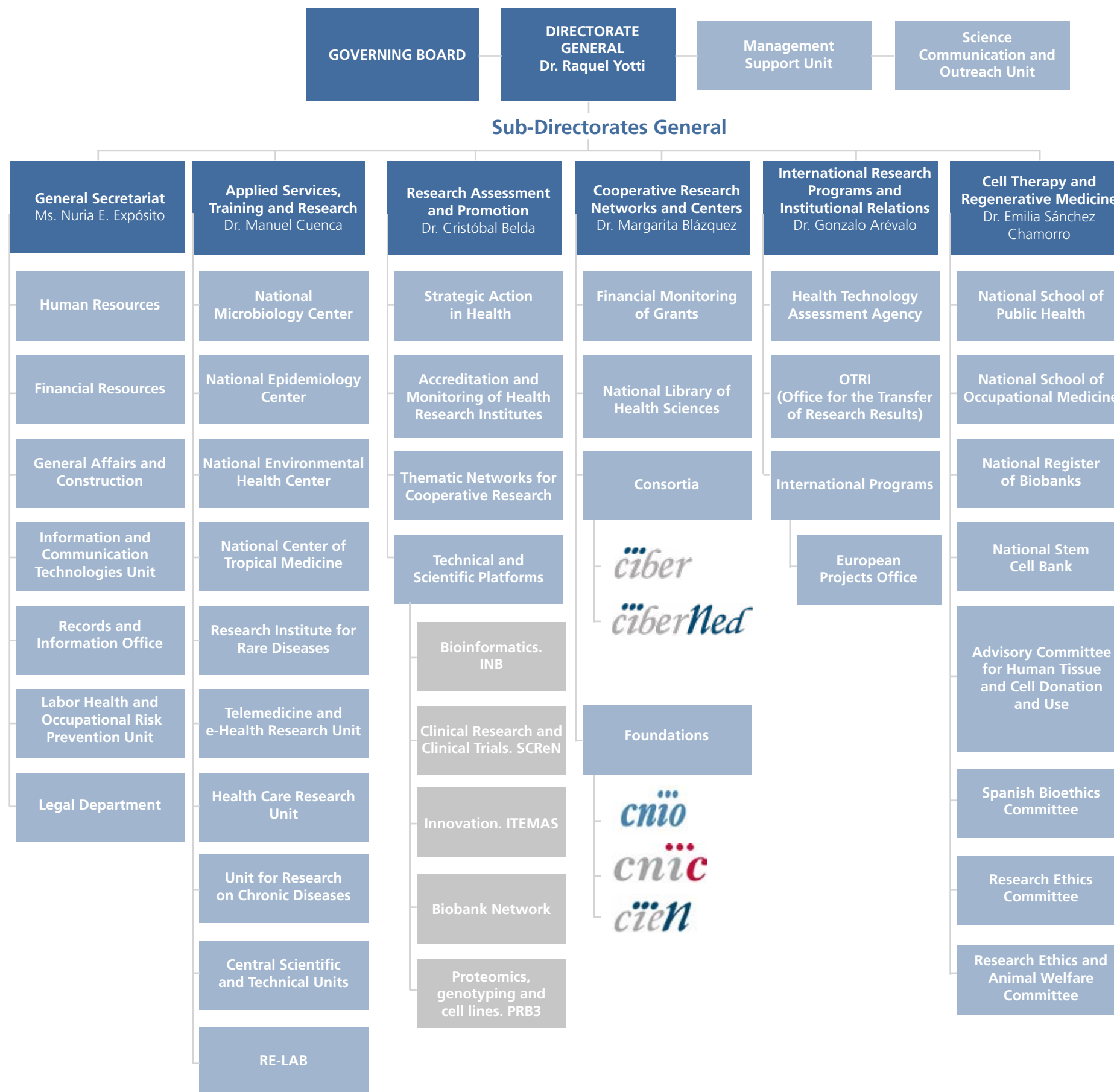
- To promote **research aimed at protecting and improving health**, by financing excellence and highly competitive research through the Strategic Action in Health of the National R&D and Innovation (R&D&I) Plan, and by enabling greater participation in international R&D&I programs and projects.
- **To provide a backbone for research within the National Health System (SNS)** through its National Reference Centers, Research Institutes, Foundations, Networks, Consortia and Platforms providing Scientific and Technical Services.

- To manage, develop and offer Spain **benchmark scientific and technical services** for the prevention and control of communicable and non-communicable diseases, environmental health, and biological products, including those potentially dangerous to **the public health**.
- To offer **scientific and technical advisory services** to support decision-making regarding health technologies and health services of the National Health System.
- To develop **teaching programs** aimed at the whole of the National Health System, and to provide **health information services and scientific documentation services**.

The vision of ISCIII is that it should serve, in close coordination with other public bodies, as the Spanish **international benchmark organization** in matters of **Public Health** and **Biomedical Research**. To achieve this vision, the activity of ISCIII must be based on the following **values**:

- **Social commitment**, understood as the defense of equity, sustainability, quality and efficiency in the fields of research and health.
- **Scientific integrity**, which ensures compliance with all ethical aspects of research, confidentiality, control of conflicts of interest, the veracity of the results, and respect for authorship and intellectual property.
- **Public responsibility**, consisting of honesty, willingness to serve, and which results in transparent management, the opening of channels for citizen participation, gender equality, continuous training, and the defense of innovation and continuous improvement.
- **Teamwork**, by the forming of and proactive participation in multidisciplinary, multi-centric, national and international teams that actively engage in the development and evolution of ISCIII and its environment in the coming years.

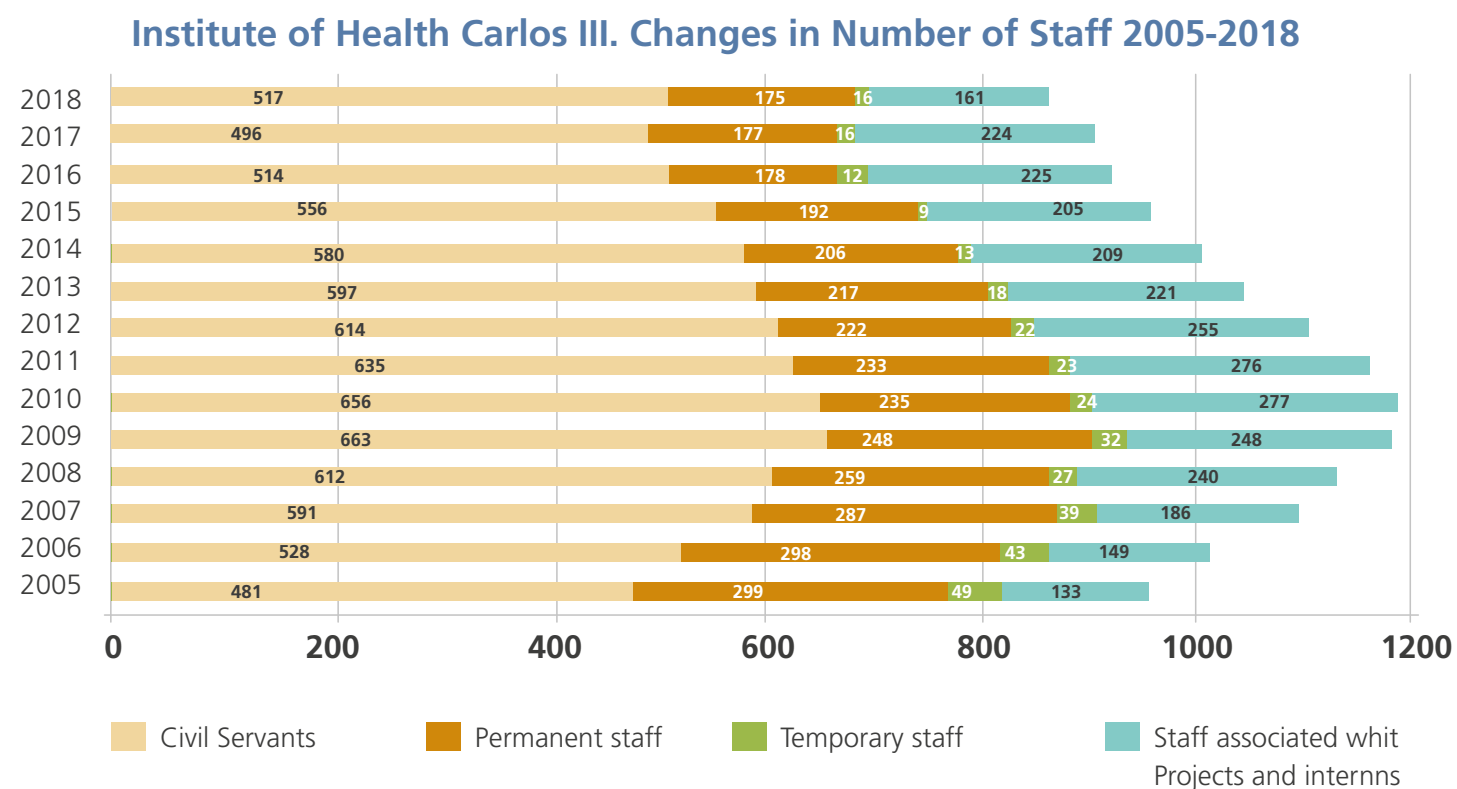
The Management Bodies of ISCIII are the Governing Board and the Director, and their functional structure is shown in the following organizational chart:



1.2 HUMAN RESOURCES

In 2018, the downward trend of ISCIII staff observed in recent years continued. On December 31, 2018, the total number of employees was 869,

which represents a cumulative decline of 4.82% with respect to the previous year, and of 17.47% with respect to 2013. The following table shows the data from 2013 to 2018, grouped by type of staff and gender:



The data at 31 December 2018, including interns, grouped by gender are listed below:

Staff ISCIII (31/12/2018)			
	Women	Men	Total
Civil Servants	349	159	508
Interim Civil Servants	5	4	9
Permanent staff	124	51	175
Temporary staff	7	9	16
Contracted staff	127	34	161
Interns	6	5	11
TOTAL	618	262	880

It can be seen that there are more women in almost all groups.

DISTRIBUTION OF STAFF ACTIVITY (Interns Included)

	Total	Gender	Distribution
Scientific Staff	178	M	76
		W	102
Technological Staff	339	M	80
		W	259
Research Support Staff	79	M	28
		W	51
Management Staff	284	M	77
		W	207
	880		880

ISCI staff change 2013-2018

		2013			2014			2015			2016			2017			31/12/2018			Percentage change 2013 - 2018			Percentage variation 2013 - 2018		
		F	M	T	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T
Civil Servants (‘RPT’ job list or Interim Civil Servants)	A1/G1	167	124	291	165	124	289	164	117	281	153	110	263	153	103	256	174	107	281	104.19	86.29	96.56	4.19	-13.71	-3.44
	A2/G2	71	23	94	71	21	92	68	20	88	65	16	81	62	15	77	67	16	83	94.37	69.57	88.3	-5.63	-30.43	-11.7
	C1/G3	93	25	118	91	23	114	91	21	112	78	18	96	76	20	96	72	21	93	77.42	84	78.81	-22.58	-16	-21.19
	C2/G4	71	20	91	63	19	82	55	17	72	56	15	71	51	13	64	41	17	58	57.75	85	63.74	-42.25	-15	-36.26
	E/G5	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	0	2	2	0	100	66.67	-100	0	-33.33
	Total	403	194	597	391	189	580	379	177	556	353	161	514	343	153	496	354	163	517	87.84	84.02	86.6	-12.16	-15.98	-13.4
Permanent Staff	A1/G1	10	1	11	10	1	11	9	0	9	11	2	13	12	1	13	11	3	14	110	300	127.27	10	200	27.27
	A2/G2	4	0	4	4	0	4	4	0	4	3	0	3	3		3	3	0	3	75	100	75	-25		-25
	C1/G3	64	25	89	62	25	87	59	24	83	53	20	73	48	21	69	46	20	66	71.88	80	74.16	-28,13	-20	-25.84
	C2/G4	33	13	46	28	11	39	27	7	34	23	8	31	23	9	32	26	10	36	78.79	76.92	78.26	-21,21	-23,08	-21.74
	E/G5	50	17	67	47	18	65	45	17	62	43	17	60	41	19	60	38	18	56	76	105.88	83,58	-24	5,88	-16.42
	Total	161	56	217	151	55	206	144	48	192	133	47	180	127	50	177	124	51	175	77,02	91,07	80,65	-22,98	-8,93	-19,4
Temporary Staff	A1/G1	3	3	6	5	2	7	3	3	6	3	5	8	3	6	9	3	6	9	100	200	150	0	100	50
	A2/G2	0	1	1	0	0	0	0	0	0	0	0	0			0			0	0	0				
	C1/G3	4	0	4	2	0	2	1	0	1	2	0	2	2		2	3		3	75	200	75	-25		-25
	C2/G4	1	0	1	1	0	1	1	0	1	0	1	1	3		3			0	0	300	0	-100		-100
	E/G5	4	2	6	1	2	3	0	1	1	0	2	2		2	2	1	3	4	25	150	66.67		50	-33.33
	Total	12	6	18	9	4	13	5	4	9	5	8	13	8	8	16	7	9	16	58,33	150	88,89	-41,67	50	-11,1
Sum permanent and temporary staff		173	62	235	160	59	219	149	52	201	138	55	193	135	58	193	131	60	191	75.72	96.77	81.28			
Staff associated with Projects	A1/G1	110	38	148	102	36	138	109	34	143	128	40	168	117	42	159	91	32	123	82.73	84.21	83.11	-17.27	-15.79	-16.89
	A2/G2	8	3	11	6	3	9	4	3	7	3	3	6	2	1	3	1	0	1	12.5	0	9.09	-87.5	-100	-90.91
	C1/G3	55	7	62	56	6	62	50	5	55	60	11	71	55	7	62	35	2	37	63.64	28.57	59.68	-36.36	-71.43	-40.32
	C2/G4	0	0	0	0	0	0	0	0	0	0	0	0			0			0	0	0				
	E/G5	0	0	0	0	0	0	0	0	0	0	0	0			0			0	0	0				
	Total	173	48	221	164	45	209	163	42	205	191	54	245	174	50	224	127	34	161	73.41	70.83	72.85	-26.59	-29.17	-27.2
TOTAL	A1/G1	290	166	456	282	163	445	285	154	439	295	157	452	285	152	437	279	148	427	96.21	89.16	93.64	-3.79	-10.84	-6.36
	A2/G2	83	27	110	81	24	105	76	23	99	71	19	90	67	16	83	71	16	87	85.54	59.26	79.09	-14.46	-40.74	-20.91
	C1/G3	216	57	273	211	54	265	201	50	251	193	49	242	181	48	229	156	43	199	72.22	75.44	72.89	-27.78	-24.56	-27.11
	C2/G4	105	33	138	92	30	122	83	24	107	79	24	103	77	22	99	67	27	94	63.81	81.82	68.12	-36.19	-18.18	-31.88
	E/G5	55	21	76	49	22	71	46	20	66	44	21	65	42	23	65	39	23	62	70.91	109.52	81.58	-29.09	9.52	-18.42
	Suma...	749	304	1053	715	293	1008	691	271	962	682	270	952	652	261	913	612	257	869	81.71	84.54	82.53	-18.29	-15.46	-17.5
Total		1053			1008			962			952			913			869			82.53			-17.47		
		2013			2014			2015			2016			2017			31/12/2018								

F=Female; M=Male; T=Total

1.3 FINANCIAL RESOURCES

The evolution of the approved budget and its balance in the period 2008-2018 is shown below. In 2018, the income derived from the Sixth Additional Provision of Royal Legislative Decree 1/2015 (contributions by sales volume of the pharmaceutical industry) is apparently greater, because a payment corresponding to the previous year was received and now considered for 2018.

The percentage expenditure remains at a high level, in line with previous years.

Evolution of the execution of the Institute of Health Carlos III budget (in thousands of euros)

Expenditure

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Initial credit	367,246.84	369,704.33	332,412.38	300,052.03	293,446.46	279,965.92	286,762.84	273,820.83	272,128.90	269,957.38	271,339.18
Credit amendments	24,050.61	4,296.20	1,457.00	1,000.00	57.65	10,550.16	7,909.44	5,279.46	4,632.11	4,279.80	4,541.63
Final Credit (FC)	391,297.45	374,000.53	333,869.38	301,052.03	293,504.11	290,516.08	294,672.28	279,100.29	276,761.01	274,237.18	275,880.81
Net liabilities recognized (NLR)	371,785.88	354,328.54	315,322.57	290,551.31	272,760.22	273,278.58	271,977.10	271,730.91	262,716.23	257,642.51	260,730.85
% NLR/FC	95.01%	94.74%	94.44%	96.51%	92.93%	94.07%	92.30%	97.36%	94.93%	93.95%	94.51%

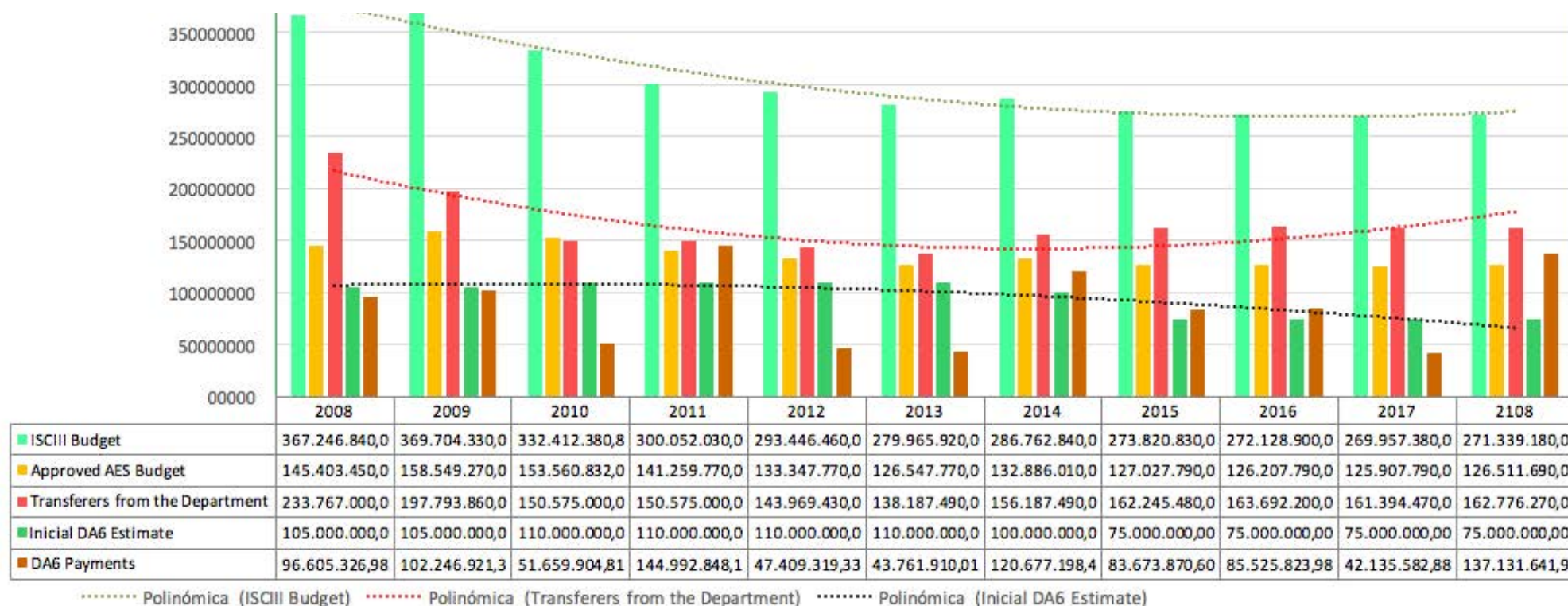
Income

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Initial forecasts	367,246.84	369,704.33	332,412.38	300,052.03	293,446.46	279,965.92	286,762.84	273,820.83	272,128.90	269,957.38	271,339.18
Credit amendments	24,050.61	4,296.20	1,457.00	1,000.00	57.65	10,550.16	7,909.44	5,279.46	4,632.11	4,279.80	4,541.63
Final forecasts (FF)	391,297.45	374,000.53	333,869.38	301,052.03	293,504.11	290,516.08	294,672.28	279,100.29	276,761.01	274,237.18	275,880.81
Net assets recognized (NAR)	371,712.90	327,819.35	230,697.78	315,736.61	226,552.63	224,278.53	354,107.01	283,753.13	275,272.66	222,471.91	365,284.75
% NAR/FF	94.99%	87.65%	69.10%	104.88%	77.19%	77.20%	120.17%	101.67%	99.46%	81.12%	132.41%

The graph below shows the evolution of the budget and the dependency of the funding of the ISCIII budget on the income derived from what is established in the sixth additional provision of Royal Legislative Decree 1/2015, of July 24, which approves the revised text of the Law on guarantees and rational use of medicines and health products. Payments are made every quarter, and usually ISCIII only receives income from the payments of the first and

third quarter of each year; this results in the collection in a fiscal year of the amounts corresponding to the third quarter of the previous year and the first quarter of the current year. This income, which constitutes the main source of income of the Institute after the transfer from the Department, has a direct impact on the Institute's annual budget.

**Evolution of ISCIII budget and main sources of funding
(€) 2008-2018**



2.1 HEALTH RESEARCH AND DEVELOPMENT STRATEGY

The **Health Research and Development Strategy** (hereinafter, AES) is one of the two Strategic Actions that are part of the **extension** of the Spanish National Plan for Scientific and Technical Research and Innovation 2013-2016 (hereinafter, the National Plan). The National Plan comprises four National Programmes, divided into State Subprogrammes, and two R&D Strategies, including the aforementioned AES. These R&D strategies are integrated into the National R&D&I Programme Aimed at the Challenges of the Society.

The Sub-Directorate General for Research Assessment and Promotion (SGEFI) of ISCIII is the body competent for managing this procedure, while ISCIII is the managing body for the activities arising from the AES, which are carried out through a single competitive call. As a **novelty** in the 2018 AES, grants were awarded for Independent Clinical Research Projects in Advanced Therapies, included in the National Subprogram for Knowledge Generation.

The following actions were developed under the AES in 2018:

National Programme for the Promotion of Talent and Its Employability in R&D&I

State Subprogramme for Training:

- Predoctoral contracts for training in health research (PFIS and i-PFIS)
- Grants for Training in Health Research Management (FGIN)
- 'Río Hortega' contracts

State Subprogramme for Incorporation:

- Contracts for health research management in IIS (GIS)
- 'Miguel Servet' contracts
- 'Sara Borrell' contracts
- 'Juan Rodés' contracts
- 'José María Segovia de Arana' contracts
- Bioinformatic technical support staff contracts for research at ISS.

State Subprogramme for Mobility:

- Mobility grants for research staff

National Programme for Fostering Excellence in Scientific and Technical Research

State Subprogramme for Knowledge Generation

- Health research projects
 - A. Health research projects
 - B. Technological development projects in health
- Complementary Actions to the international joint programming initiatives
- Independent Clinical Research Projects in Advanced Therapies

State Subprogramme for Institutional Strengthening

- Incorporation of new groups into the CIBERNED Consortium

**Distribution of the grants of the State Subprogramme
for Training success rates and funding by Autonomous Community and gender**

Autonomous Community	PFIS 2018								i-PFIS 2018								Río Hortega contracts							
	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %
	F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)	
Andalucía	11	8	19	5	1	6	494,400	31.58	4	6	10	2	3	5	412,000	50.00	29	11	40	7	6	13	698,516	32.50
Aragón	4	2	6	0	0	0	0	0.00	2	0	2	1	0	1	82,400	50.00	4	1	5	1	1	2	107,464	40.00
Asturias	3	1	4	0	1	1	82,400	25.00									1	0	1	0	0	0	0	0.00
Baleares	1	1	2	1	0	1	82,400	50.00																
Canarias	1	1	2	0	1	1	82,400	50.00																
Cantabria	1	0	1	0	0	0	0	0.00	0	1	1	0	1	1	82,400	100.00								
Castilla y León	6	2	8	0	1	1	82,400	12.50	0	1	1	0	0	0	0	0.00	4	2	6	3	0	3	161,196	50.00
Castilla-La Mancha	0	1	1	0	0	0	0	0.00									1	0	1	0	0	0	0	0.00
Cataluña	49	13	62	21	7	28	2,307,200	45.16	6	2	8	3	1	4	329,600	50.00	32	17	49	17	10	27	1,450,764	55.10
C. Valenciana	14	5	19	7	2	9	741,600	47.37	1	3	4	0	1	1	82,400	25.00	16	6	22	5	2	7	363,592	31.82
Extremadura	0	0	0	0	0	0	0	0.00																
Galicia	7	4	11	3	1	4	329,600	36.36	2	1	3	1	0	1	82,400	33.33	11	1	12	3	0	3	161,196	25.00
Madrid	32	12	44	9	3	12	988,800	27.27	8	4	12	4	2	6	494,400	50.00	32	17	49	8	7	15	805,980	30.61
Murcia	2	5	7	1		1	82,400	14.29	1	0	1	0	0	0	0	0.00	1	2	3	0	1	1	53,732	33.33
Navarra	8	5	13	3	1	4	329,600	30.77									2	1	3	0	0	0	0	0.00
País Vasco	1	2	3	0	0	0	0	0.00	0	1	1	0	1	1	82,400	100.00	1	2	3	0	0	0	0	0.00
Rioja (La)	0	0	0	0	0	0	0	0.00																
TOTAL	140	62	202	50	18	68	5,603,200	33.66	24	19	43	11	9	20	1,648,000	46.51	134	60	194	44	27	71	3,814,972	36.60

(M= hombre, M= mujer; T= total)

**Distribution of the grants of the State Subprogramme for Incorporation (IIS),
success rates and funding by Autonomous Community and gender**

Autonomous Community	GIS 2018								Juan Rodés 2018								Bioinformatics 2018							
	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %
	F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)	
Andalucía	1	0	1	0	0	0	0	0	7	3	10	4	1	5	900,000	50	1	5	6	0	2	2	107,464	33.3
Aragón									0	1	1	0	0	0	0	0								
Cantabria	1	0	1	1	0	1	80,598	100									1	0	1	0	0	0	0	0
Castilla y León									1	0	1	0	0	0	0	0								
Cataluña	3	2	5	2	2	4	322,392	80	3	4	7	1	4	5	900,000	71.43	2	7	9	1	3	4	214,928	44.44
C. Valenciana									1	3	4	1	3	4	720,000	100	1	0	1	1	0	1	53,732	100
Galicia	1	0	1	1	0	1	80,598	100	3	1	4	2	1	3	540,000	75	0	2	2	0	1	1	53,732	50
Madrid									9	6	15	6	4	10	1,800,000	66.67	5	6	11	2	3	5	268,660	45.45
Murcia																	0	2	2	0	1	1	53,732	50
País Vasco																	0	3	3	0	2	2	107,464	66.67
TOTAL	7	2	9	4	2	6	483,588	66.67	24	18	42	14	13	27	4,860,000	64.29	10	25	35	4	12	16	859,712	45.71

**Distribution of the grants of the State Subprogramme for Incorporation,
success rates and funding by Autonomous Community and gender**

Autonomous Community	Miguel Servet type I 2018								Miguel Servet type II 2018							
	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %
	F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)	
Andalucía	12	9	21	2	3	5	1,212,500	23.81	3	0	3	3	0	3	283,500	100.00
Aragón	1	1	2	0	0	0	0	0.00								
Asturias	3	0	3	1	0	1	242,500	33.33								
Baleares	1	1	2	0	0	0	0.00	0.00								
Canarias	0	1	1	0	0	0	0.00	0.00								
Cantabria	2	0	2	1	0	1	242,500	50.00								
Castilla y León	3	3	6	0	0	0	0	0.00	1	0	1	1	0	1	91,125	100.00
Castilla-La Mancha	1	0	1	0	0	0	0	0.00								
Cataluña	16	10	26	2	3	5	1,212,500	19.23	11	4	15	11	4	15	1,437,750	100.00
C. Valenciana	11	2	13	2	0	2	485,000	15.38	1	4	5	0	4	4	405,000	80.00
Galicia	3	4	7	1	0	1	242,500	14.29	0	1	1	0	1	1	91,125	100.00
Madrid	15	11	26	4	2	6	1,455,000.00	23.08	1	1	2	1	0	1	91,125	50.00
Murcia	0	2	2	0	0	0	0	0.00	1	0	1	1	0	1	91,125	100.00
Navarra	2	1	3	0	1	1	242,500	33.33	1	0	1	1	0	1	101,250	100.00
País Vasco	5	2	7	1	0	1	242,500	14.29								
Rioja (La)	1	0	1	0	0	0	0	0.00								
TOTAL	76	47	123	14	9	23	5,577,500	18.70	19	10	29	18	9	27	2,592,000	93.10

**Distribution of the grants of the State Subprogramme for Incorporation (SNS),
success rates and funding by Autonomous Community and gender**

Autonomous Community	Sara Borrell 2018								Segovia de Arana 2018							
	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %
	F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)	
Andalucía	23	14	37	2	3	5	402,990	13.51	2	6	8	1	3	4	120,000	50
Aragón	2	0	2	1	0	1	80,598	50								
Asturias	2	3	5	0	0	0	0	0.00								
Baleares	1	2	3	0	0	0	0	0.00								
Canarias	0	1	1	0	1	1	80,598	100	0	1	1	0	0	0	0	0
Cantabria									0	1	1	0	0	0	0	0
Castilla y León	3	0	3	2	0	2	161,196	66.67	0	2	2	0	1	1	30,000	50
Castilla-La Mancha	2	1	3	1	0	1	80,598	33.33	0	1	1	0	0	0	0	0
Cataluña	41	17	58	5	4	9	725,382	15.52	1	7	8	1	5	6	180,000	75
C. Valenciana	11	7	18	1	3	4	322,392	22.22	0	4	4	0	3	3	90,000	75
Extremadura	0	1	1	0	0	0	0	0								
Galicia	2	1	3	0	0	0	0	0								
Madrid	27	13	40	7	1	8	644,784	20	1	8	9	1	5	6	180,000	66.67
Murcia	4	1	5	2	0	2	161,196	40								
Navarra	4	1	5	0	0	0	0	0								
País Vasco	4	4	8	0	0	0	0	0	1	1	2	0	0	0	0	0
TOTAL	126	66	192	21	12	33	2,659,734	17.19	5	31	36	3	17	20	600,000	55.56

**Distribution of the grants of the State Suboprogramme for Mobility,
success rates and funding by Autonomous Community and gender**

Autonomous Community	M-BAE 2018								M-AES 2018							
	Eligible Applications			Funded				Success rate %	Eligible Applications			Funded				Success rate %
	F	M	T	F	M	T	Amount (€)		F	M	T	F	M	T	Amount (€)	
Andalucía	2	3	5	0	1	1	5,400	20	3	1	4	3	1	4	77,920	100.00
Aragón	2	1	3	2	1	3	21,280	100	2	0	2	1	0	1	9,360	50.00
Canarias									1	0	1	1	0	1	9,680	100.00
Cataluña	9	8	17	7	5	12	206,240	70.59	18	8	26	17	5	22	233,200	84.62
C. Valenciana	1	1	2	0	1	1	5,940	50	3	0	3	1	0	1	7,600	33.33
Galicia	1	1	2	1	1	2	21,920	100	1	1	2	0	1	1	14,480	50.00
Madrid	1	4	5	1	2	3	29,680	60	6	0	6	6	0	6	69,120	100.00
Navarra	1	0	1	0	0	0	0	0								
País Vasco	1	1	2	1	1	2	33,180	100								
TOTAL	18	19	37	12	12	24	323,640	64.86	34	10	44	29	7	36	421,360	81.82

A summary of all data on the **State Subprogramme for Knowledge Generation** is detailed in the following 2 tables:

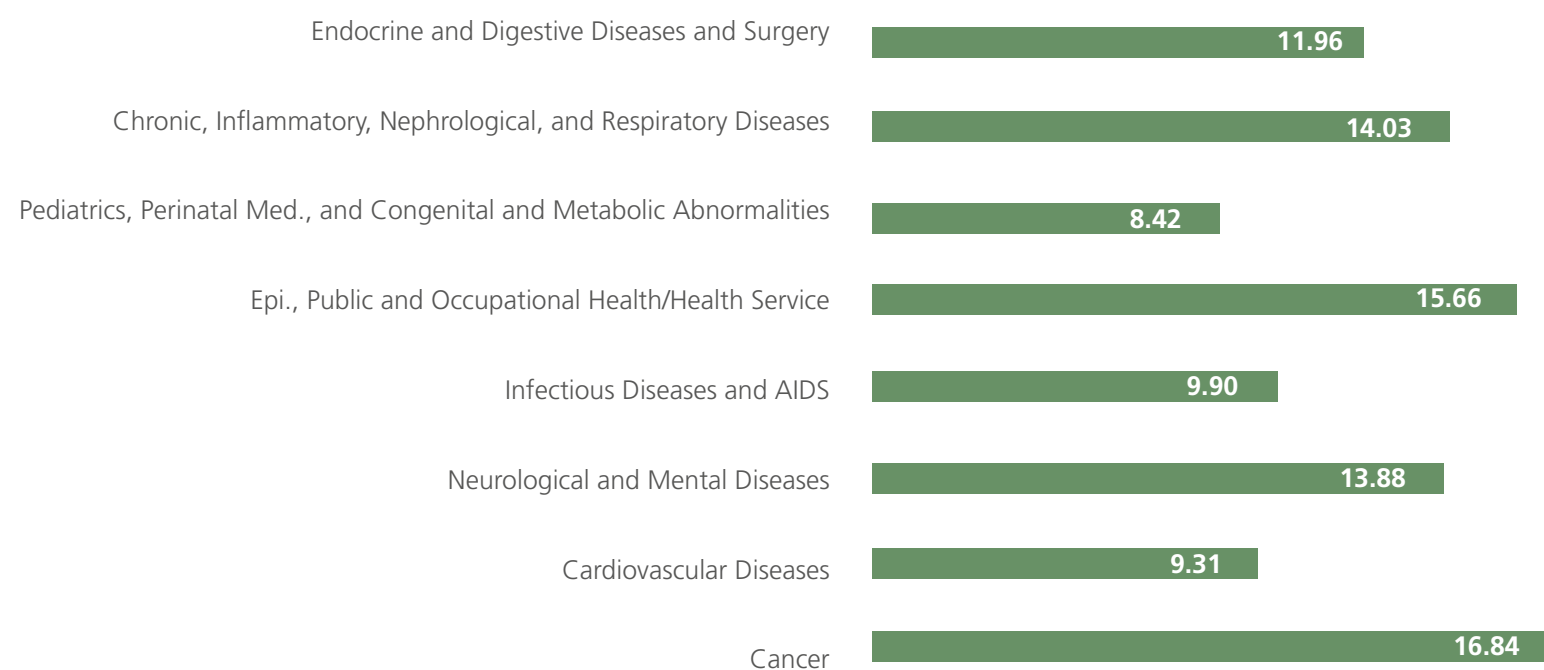
Distribution of the grants of the State Subprogramme for Knowledge Generation, success rates and funding by type of grant and gender

Action	Eligible	Eligible Women	Eligible Men	Awarded	% Awarded	Awarded Women	Awarded Men	% Awarded Women	% Awarded Men	Amount (€)
DTS	127	45	82	27	21.26	8	19	29.63	70.37	2,149,950
PI	1,582	717	865	677	42.79	313	364	46.23	53.77	75,754,524
AC	101	39	62	28	27.72	8	20	28.57	71.43	4,016,527
PIC	18	2	16	8	44.44	0	8	0.00	100.00	4,491,727
TOTAL	1,828	803	1,025	740	40.48	329	411	44.46	55.54	86,412,728

DTS: Technological development projects in health; PI: Health research projects; AC: Complementary Actions to the international joint programming initiatives; PIC: Independent clinical research projects in advanced therapies.

Distribution of the grants of the State Subprogramme for Knowledge Generation awarded by Autonomous Community

Autonomous Community	DTS		PI		AC		PIC		TOTAL	
	No. of grants	Amount (€)	No. of grants	Amount (€)	No. of grants	Amount (€)	No. of grants	Amount (€)	Nº of grants	Amount (€)
ANDALUCÍA	4	295,900	82	8,883,772	5	781,610			91	9,961,282
ARAGON	1	45,650	16	1,386,963					17	1,432,613
ASTURIAS			10	629,079					10	629,079
BALEARES			7	560,351					7	560,351
CANARIAS			6	434,995					6	434,995
CANTABRIA	2	110,000	8	1,190,459					10	1,300,459
CASTILLA - LA MANCHA	1	50,600	8	1,017,610					9	1,068,210
CASTILLA Y LEON			20	2,255,743	1	200,000	1	767,963	22	3,223,705
CATALUÑA	8	714,450	243	28,977,504	12	1,692,192	3	1,875,940	266	33,260,086
COM. VALENCIANA	2	199,100	49	5,068,206	1	140,481			52	5,407,787
EXTREMADURA			4	442,860					4	442,860
GALICIA	2	150,150	19	2,130,024	1	149,798			22	2,429,972
MADRID	5	443,850	154	17,801,399	8	1,052,446	3	1,538,724	170	20,836,419
MURCIA			9	980,100			1	309,100	10	1,289,200
NAVARRA			15	1,690,612					15	1,690,612
PAIS VASCO	2	140,250	26	2,228,620					28	2,368,870
RIOJA (LA)			1	76,230					1	76,230
TOTAL	27	2,149,950	677	75,754,524	28	4,016,527	8	4,491,727	740	86,412,728

Health Research Funded Projects 2018**PI: % Concession by thematic area**

Complementary Actions to the International Joint Programming Initiatives

The objective of this action is to fund research projects in the international joint programming initiatives in health. These projects are carried out within the framework of the transnational consortia in which ISCIII is committed to support relevant collaborative projects, where Spanish research teams participate together with teams from other countries. In the international calls for participation in the framework of the additional actions, 101 applications were received; 28 received funding for an amount of € 4,016,527. These are listed in the following table:

Calls for 2018 International Joint Programming Initiatives Projects

Programme	Groups funded	No. of Researchers	Budget Awarded
JPND-JPco-fuND	1	1	96,909 €
JPND-EU JPND-NIH USA	1	8	99,946 €
JPI HDHL	3	16	437,858 €
ERA PerMed	5	31	696,281 €
EuroNanoMed	7	41	1,156,028 €
NEURON	2	6	349,448 €
ERA-CVD	2	7	240,548 €
E-RARE	1	4	199,045 €
TRANSCAN	2	12	248,980 €
EU-CELAC	3	20	398,314 €
AAL - 3 years	1	4	93,170 €
Total	28	150	4,016,527 €

State Subprogramme for Institutional Strengthening:

Incorporation of new groups into the CIBERNED Consortium

This action aims to boost and strengthen the CIBERNED Consortium by reinforcing the areas of Neurodegenerative Diseases, Alzheimer's and other degenerative dementias, Parkinson's and other neurodegenerative motor disorders, the cellular and molecular bases of neurodegenerative processes, and creating a new area of Amyotrophic Lateral Sclerosis (ALS) and other motor neuron diseases. According to the call, 6 research groups will be selected; 4 of these must be addressing ALS or other motor neuron diseases, and 2 the other areas.

2.2 THEMATIC NETWORKS FOR COOPERATIVE RESEARCH IN HEALTH

The thematic networks for cooperative research in health (RETICS) are organizational structures formed by the association of a variable set of biomedical research centers and groups with ISCIII. The biomedical research centers and groups are of a multidisciplinary nature, depend on different public administrations or the private sector, and belong to a minimum of four Autonomous Communities; it is their objective to carry out cooperative research projects, while at the same time facilitating the structuring of research in the SNS. There are currently 14 RETICS, and they are listed below:

Nomenclature	Thematic network-ISCIII	Website
REDIAPP	Primary Care Prevention and Health Promotion Research Network	www.rediapp.org
REIPI	Spanish Network for Research in Infectious Diseases	www.reipi.org
OFTARED	Eye Diseases Network: Prevention, early detection, treatment and recovery of Ocular Pathology	www.oftared.com
REDINREN	Kidney Research Network	http://redinren.org
RICET	Collaborative Tropical Disease Research Network	www.ricet.es
INVICTUS+	Cerebrovascular Diseases Network	www.redinvictus.es
REEM	Spanish Network Of Multiple Sclerosis	www.reem.es
RIER	Network for Inflammation and Rheumatic Disease Research	https://red-rier.org/
ARADyAL	Asthma, Adverse Reactions and Allergies Network	http://aradyal.org/
SAMID	Spanish Maternal and Child Health and Development Research Network	www.redsamid.net
REDISSEC	Health Services Research on Chronic Patients Network	www.redissec.com
RIS	Spanish Aids Research Network	www.redris.es
TERCEL	Cell Therapy Network	www.red-tercel.com
RTA	Addictive Disorders Network	www.redrta.es

The main activities of each Network are given in their respective websites and are summarized in the ISCIII Annual Report for the year 2018.

2.3 PLATFORMS TO SUPPORT RESEARCH IN HEALTH SCIENCES AND TECHNOLOGY

The platforms that support research in health sciences and technologies are stable collaborative network structures that aim to provide scientific and technical network services for carrying out cooperative and transversal research projects. The purpose of the PLATFORMS is to provide high-level scientific, technical and technological support to R&D&I projects in Health Sciences and Technologies, to promote transversal projects within their area of activity, to promote Spanish participation in international programs and platforms, and to promote innovation in health technologies as an instrument that contributes to the sustainability of the SNS. There are currently 5 platforms to support research in health sciences and technology, which are detailed below:

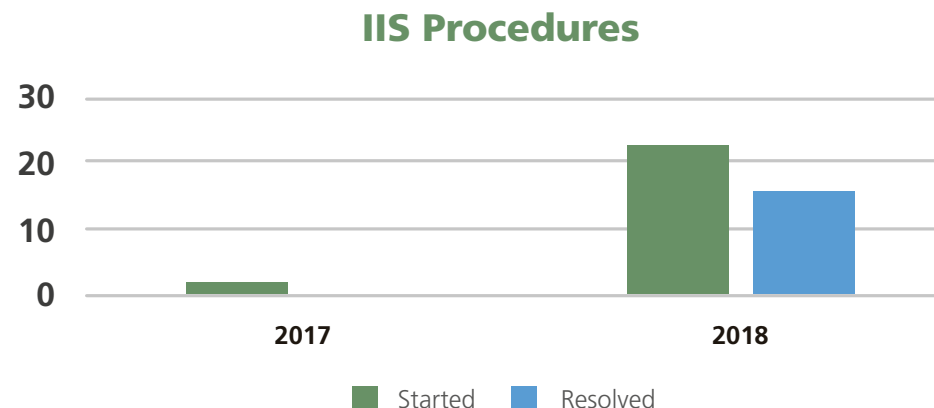
Platform	Website
Biobanks Platform (RNB)	www.redbiobancos.es
Bioinformatics Platform (INB)	https://inb-elixir.es
Clinical Research and Clinical Trials Units Platform (SCReN)	www.scren.es
Innovation in Medical and Healthcare Technology Platform (ITEMAS)	www.itemas.org
Proteomics, Genomics, and Cell Lines Platform (PRB3)	www.prb3.org

The main activities of each Platform are given in their respective annual reports and websites, and are summarized in the ISCIII Annual Report for the year 2018.

2.4 HEALTH RESEARCH INSTITUTES

According to the Statute of ISCIII approved by RD 375/2001, of April 6, it corresponds to ISCIII, as a scientific and technical accreditation public health body, to grant scientific and technical accreditation to those entities and centers that reach the level of public health services and research set forth by law. RD 279/2016, of June 24, on the accreditation of biomedical or health research institutes (IIS), regulates the procedure for accreditation and monitoring of activities for the maintenance, revocation, and renewal of accreditations of the IIS. The examining body of these procedures is the SGEFI, through the Evaluation, Accreditation and Monitoring of Health Research Institutes Programme.

In 2018, 2 new IIS were accredited: the Healthcare Research Institute of Navarre (IdISNA), and the Balearic Islands Health Research Institute (IdISBa). The accreditation of 10 of the 29 existing accredited IIS was renewed. Thirteen requests for authorization of significant changes were received; they were submitted by nine (31%) IIS and 11 of them (84.5%) were resolved favorably. The graph below shows the procedures set out in RD 279/2016, of June 24, distributed by year and situation (started and resolved):



3.1 FOUNDATIONS

The following Foundations are affiliated to ISCIII: the Spanish National Cancer Research Center Foundation Carlos III (CNIO; <https://www.cnio.es>), the Spanish National Center for Cardiovascular Research Foundation Carlos III (CNIC; <https://www.cnic.es>), and the Spanish National Center for Research on Neurodegenerative Diseases Foundation (CIEN; <https://www.fundacioncien.es>). They carry out their activities in the fields of oncology, cardiovascular disease, and neurological research, respectively. The main activities of these foundations are given in their respective annual reports and websites, and are summarized in the ISCIII Annual Report for the year 2018.

3.2 PUBLIC CONSORTIA OF BIOMEDICAL RESEARCH NETWORKING CENTERS

The CIBER consortia are stable cooperative research structures that were created at the initiative of the ISCIII as public research consortia possessing legal personality with the purpose of promoting research of excellence in priority areas of Biomedicine and Health Sciences, which is carried out in the SNS and in the Science and Technology System. There are currently two Consortia that carry out collaborative research of excellence: The Consortium Biomedical Research Networking Center, CIBER (www.ciberisciii.es), which comprises 11 Thematic Areas: Mental Health (CIBERSAM), Respiratory Diseases (CIBERES), Physiopathology of Obesity and Nutrition (CIBEROBN), Diabetes and Associated Metabolic Diseases (CIBERDEM), Epidemiology and Public Health (CIBERESP), Bioengineering, Biomaterials and Nanomedicine (CIBERBBN), Rare Diseases (CIBERER), Liver and Digestive Diseases (CIBEREHD), Cardiovascular Diseases (CIBERCV), Fragility and Healthy Aging (CIBERFES), Oncology (CIBERONC), and Neurodegenerative Diseases (CIBERNED; www.ciberned.es). The main activities of each CIBER consortium are given in their respective annual reports and websites, and are summarized in the ISCIII Annual Report for the year 2018.

4.1 INTRAMURAL RESEARCH

Intramural research refers to research carried out at ISCIII's own centres and joint units associated through competitive research projects, management delegation agreements, and collaboration agreements.

The data presented in this section, listed in the Research Coordination Area of the Sub-directorate General for Applied Services, Training and Research (SGSAFI), show the scientific production of the ISCIII centers and schools: analysis of scientific publications, research projects, and the recruitment of research and research support staff.

Projects granted in 2018 calls by programme

Funding	Programme	No. of Projects	Total Funding (€)
External Funding	International *	11	2,184,212.67
	National R&D&I Plan	4	578,900.00
	Other	3	170,976.19
	Autonomous Communities	4	148,416.47
ISCIII Funding	AESI Projects	23	1,649,051.00
	Other intramural	3	338,106.42
TOTAL		48	5,069,662.75

* 5 projects and 6 subprojects (EU, ECDC, etc.)

Current projects granted by Programme - 2018

Funding	Programme	No. of Projects	Funding (€)	
			Total	2018
External Funding	International *	49	10,091,691.59	2,584,731.03
	National R&D&I Plan	31	4,404,475.42	1,281,460.70
	Ministry of Health (MSCBS)	1	54,844.00	7,000.00
	Autonomous Communities	7	284,512.93	49,592.74
	Other	8	792,238.46	123,335.00
ISC Funding	FIS	5	589,286.00	0.00
	AESI Projects	84	7,423,420.08	1,710,311.00
	NETWORKS	12	3,756,680.25	753,236.13
	Other	12	460,119.72	105,080.58
TOTAL		209	27,857,268.45	6,614,747.18

* 39 projects and 10 subprojects (EU, etc.)

TECHNICAL AND SCIENTIFIC ACTIVITIES

Projects granted by thematic area - 2018

Thematic Area	No. of Projects
Infectious diseases: Bacteriology	7
Infectious diseases: Mycology	2
Infectious diseases: Parasitology	2
Infectious diseases: Virology	9
Rare diseases	4
Immunology	1
Nursing research	1
Public health research	6
HIV/AIDS research	4
Others (FIS, ENS, OPE, OTRI, Biobanks, Bioethics)	8
Telemedicine	3
Environmental toxicology	1
TOTAL	48

Human resources calls 2018

Number of contracts awarded per center

Center	National R&D&I Plan (*)	Autonomous Communities	Others	AESI-HR	TOTAL
CNM	7	8		10	25
CNE	2			2	4
ENS				1	1
IIER	3	2			5
UFIEC	8	4	1		13
CNMT				1	1
CNSA	1	1			2
INVESTEN	1				1
SGSAFI	2				2
OTRI	1				1
TOTAL	25	15	1	14	55

(*) Calls pending resolution were excluded

Current projects by thematic area - 2018

Thematic Area	Nº Proyectos
Cellular and Developmental Biology	3
Infectious diseases: Bacteriology	14
Infectious diseases: Mycology	12
Infectious diseases: Parasitology	19
Infectious diseases: Virology	18
Neurological diseases	1
Rare diseases	15
Tropical diseases	4
Epidemiology of infectious diseases	1
Cancer epidemiology	3
HIV/AIDS epidemiology	2
Health technology assessment	2
Genomics, microscopy and bioinformatics	2
Immunology	14
Cancer research	7
Nursing research	3
Public health research	17
HIV/AIDS research	19
Others (FIS, ENS, OPE, OTRI, biobanks, bioethics)	42
Molecular pathology	1
Telemedicine	4
Environmental toxicology	6
TOTAL	209

Publications and Theses in 2018

Center	Publications	Theses
CNM	210	9
CNE	179	-
ENS	35	-
IIER	32	1
UFIEC	37	1
CNMT	9	-
INVESTEN	7	-
AETS	4	-
CNSA	7	-
ENMT	2	-
TELEMEDICINE	4	-
TOTAL	526	11

4.2 CENTERS AND UNITS

The most notable activities of the Centers and Units of ISCIII are detailed below. Outstanding publications and the most relevant training activities of each Center/Unit are included in the annual report, but are not included in this executive summary.

La SGSAFI dispone de un sistema de gestión de calidad conforme a la Norma UNE-EN ISO 9001:2015 certificado por La Asociación Española de Normalización y Certificación (AENOR).

NATIONAL MICROBIOLOGY CENTER (CNM)

The CNM's most relevant milestones in its service and support activities in 2018 were:

- The CNM **Alert System** has been operating 24 hours per day, 7 days a week throughout the year 2018. During this time, the Alert System intervened in all health alerts activated by the Center for Coordination of Alerts and Emergencies (CCAES) of the MSCBS at the request of the Autonomous Communities, as well as on all occasions it was required to do so at the request of the RE-LAB. In this context, work continued in 2018 on the analysis of the prevalence of Crimean-Congo Hemorrhagic fever virus in *Hyalomma* ticks in different Autonomous Communities. This work was started in 2016 following the report of the first indigenous case in Spain. A study of seroprevalence in animals was initiated in 2018.
- In 2018, the first 5 indigenous cases of dengue fever in Spain were confirmed at the CNM, and together with the Community of Murcia a study was carried out to analyze the presence of the virus in larvae and adult mosquitoes of the species *Aedes albopictus* in this Community.
- Routine **massive sequencing** has been implemented in the **surveillance** of listeria, meningococcus, multidrug-resistant gonococcus, and carbapenemase-producing bacteria, following the time frames recommended by the ECDC.

- The CNM has a Laboratory Accreditation System implemented through its Quality Unit. As a consequence, in 2018 it had a total of 155 tests accredited by the National Accreditation Body (ENAC), 144 of which were according to ISO 15189 and 13 according to ISO 17025. The tests were carried out in 18 Units of the Center. In addition, 2 Units are certified by AENOR according to ISO-9001-2015.

Scientific and technical activities

- The CNM operates 23 microbiology surveillance programs for infections relevant to public health, which are revised and renewed annually. These programs generate very important data for the understanding of the monitored diseases, allowing for control and/or prevention measures to be developed by the health authorities.
- The CNM received around 50,000 requests for diagnosis and/or referral through its sample management program. It performed more than 120,000 tests in all of its activities related to surveillance programs, alerts, outbreaks, service portfolio, and contracts with institutions and businesses.
- During 2018, the CNM had a total of 98 active research projects and 23 Research Agreements with researchers participating in 2 CIBER and 9 RETICS networks.

Participation in international consortia

- The CNM collaborates in the coordination of the ViroRed thematic network of the Ibero-American Program of Science and Technology for Development (CYTED), which currently comprises laboratories from health institutes and universities in 14 Latin American countries, Portugal, and Spain.
- The CNM has the Leishmania Unit of the Parasitology Research and Reference Laboratory as a WHO Collaborating Laboratory as well as the Neisseria, Listeria, and Bordetella Unit of the Vaccine-Preventable Bacterial Disease Research and Reference Laboratory as an external Reference Laboratory for the SIREVA II Network of the Pan-American Health Organization (PAHO)/WHO.

NATIONAL EPIDEMIOLOGY CENTER (CNE)

Scientific and technical activities

- **Chronic Diseases:** The CNE provides relevant information on cancer, cardiovascular and metabolic diseases, neurodegenerative diseases and disability by monitoring mortality and investigating the main risk factors.
- **Communicable Diseases and risk behaviours:** surveillance of communicable diseases (RENAVE) and outbreaks in the EU, under the coordination of the ECDC, the WHO and the European Food Safety Authority (EFSA). The CNE collaborates among others in the elimination of tuberculosis in Spain, the surveillance of infections related to healthcare, the analysis of daily mortality, the strategic plan against hepatitis C, the evaluation of policies for early diagnosis of HIV and the evaluation of risk behaviors and socially vulnerable populations.

The main **lines of research** in Epidemiology and Public Health can be summarized by the participation in 25 research projects (15 national and 10 international), which are distributed over the following thematic areas:

- **Environmental Epidemiology of Cancer:** a) geographic distribution of cancer mortality, spatio-temporal evolution and its relationship with environmental and social determinants; b) environmental and lifestyle risk factors; c) genetic and molecular epidemiology of cancer; and d) impact of air pollution on the health of the population.
- **Applied Epidemiology:** a) aging and predictors of mortality and disability; b) dementias, parkinsonisms, and prion diseases; and c) morbidity and mortality due to external causes.
- **Cardiovascular and metabolic diseases and their risk factors:** a) impact of Law 28/2005 on Health Measures against smoking; b) addictions, obesity and cardiovascular risk factors; c) role of heavy metals in chronic diseases.
- **HIV/AIDS/STIs:** Natural history of HIV infection (CoRIS and GEMES cohorts). Epidemiology and progression of HIV infection in immigrants. Diagnostic delay of HIV infection. Reproductive health of HIV+ women. Human papillomavirus epidemiology. Methodology of longitudinal cohort studies on HIV+ subjects.
- **Risk behaviours and socially vulnerable populations:** Translation of the experience of Spain and European countries regarding policies to reduce the harm from substance use in some Eastern European countries, in collaboration with CHAFAE. Evaluation of the impact of social inequalities and different socio-economic determinants on mortality.

- **Communicable diseases:** a) effect of risk factors and evaluation of intervention measures for the prevention of communicable diseases; b) evaluation of the effectiveness of the flu vaccine in Spain and in Europe; c) development of methodology for assessing the severity of influenza epidemics and pandemics; d) co-infection of HIV and hepatitis C and B virus, papilloma virus and sexually transmitted infections; e) HIV pharmacoepidemiology; f) health inequalities of the HIV-positive population; g) use, acceptability and impact of pre-exposure prophylaxis (PreP) in the HIV-negative population at risk.

NATIONAL ENVIRONMENTAL HEALTH CENTER (CNSA)

Highlighted activities

- HBM4EU project for the development of the H2020 European Initiative on Human Biomonitoring. Members of the Steering Committee and Coordination of the Spanish Human Biomonitoring Hub. Organization and participation in the European HBM Week under the Austrian EU presidency.
- Design and coordination of the quality assurance program of chemical analysis laboratories for incorporation into the European Human Biomonitoring Strategy network, with the participation of 28 countries, more than 100 European laboratories and using 79 biomarkers of exposure.
- Accreditation of the new reference method for the determination of PM10 and PM2.5 atmospheric particles, in the framework of broadening the powers and responsibilities of the National Reference Laboratory (LNR) of Air Quality according to RD 39/2017 (transposition of Directive 2015/1480/EC).
- Participation as a National Reference Laboratory on Air Quality in the “High level dialogue on clean air” organized by the Ministry for Ecological Transition.
- European project ‘Integrated Climate forcing and Air pollution Reduction in Urban Systems’ (ICARUS) - H2020.
- Scientific and technical support and consulting for the Command Post, and in situ participation in the Joint Combined Exercise MURCIA 2018; the exercise was declared to be “of national interest” and involved the activation of “Phase 3” of the National Plans organized by the Military Emergency Unit of the Ministry of Defense.

Scientific and technical activities

- More than 150,000 analyses and more than 170 toxicity bioassays were carried out.
- Preparation, as experts in risk assessment of active substances and phytosanitary products, of more than 50 reports for the European authority (EFSA).
- Organization of three in situ nitrogen dioxide and nitrogen monoxide inter-comparison exercises with 18 air quality networks of Autonomous Communities, local entities and Portugal.
- Participation in the intercomparison exercises of National Air Quality Laboratories organized by the European Commission.
- Calibration of 29 ozone transfer standards as Associated Laboratory of the Spanish Meteorology Center (CEM) and depository of the National Ozone Standard (RD 250/2004). Presentation of the reassessment of the quality system of the National Ozone Standard in the Technical Committee for Quality (TC-Q) of EURAMET.
- Participation as a member of the Managing Council of the National Radiation Protection R&D Platform (PEPRI) and of the COST Action group "EMF-MED", a European network for cooperation in research and technology on biological effects of electromagnetic fields for medical use.
- Participation with on-site measurements in the study assessing the health impact of emissions from the Valdemingómez Technology Park.
- Assessment of the air quality after repeated episodes of bad odors in the city of Pinto.

Fundraising

- HBM4EU project for the development of the H2020 European Initiative on Human Biomonitoring with an allocation of € 74 million.
- European project 'Integrated Climate forcing and Air pollution Reduction in Urban Systems' (ICARUS) within the H2020 Program.
- LIFE WASTE4GREEN Sustainable and Green Agri-Waste based Biopesticides Project.
- AESI 2016 Project "Evaluation of the toxicological role of PAHs associated with PM10 particles through an alternative model with zebrafish embryos."
- Singular AESI Project for the creation of a "National Center for Coordinating Biomonitoring Studies of the Spanish Population".
- The management delegation agreements with the INIA (Assessment of the risk to human health of phytosanitary products), AEMET, and MAPAMA (air quality), as well as over 400 collaboration agreements for dosimetric control with different public and private entities remain active.

- Youth Employment Operational Program, co-funded by the European Social Fund and the Autonomous Community of Madrid (YEI-POEJ).

Participation in Standardization Committees and Institutional Representation

- Secretariat and memberships of the AEN/CTN 77 "Environment" Technical Standardization Committee; membership of the AEN/CTN 77/SC 01 "Water" Subcommittee; and membership of the AEN/CTN 215 "Electromagnetic Fields" committee.
- Participation in the 12, 34, and 42 WGs of the CEN/TC 264 "Air Quality".
- Members of the Steering Group for the European Human Biomonitoring Initiative (EHBMI), DG Research (EC).
- Participation in WG2 'Harmonization of Individual Monitoring in Europe' and WG3 'Environmental Radiation Monitoring'.
- Participation in WP4 'Transition to long-term recovery, involving stakeholders in decision-making process', of the CONFIDENCE Project.

NATIONAL CENTER OF TROPICAL MEDICINE (CNMT)**Highlighted activities**

Collaborative Tropical Disease Research Network (RICET):

- In 2018, RICET groups responded to two health alerts caused by emerging tropical viruses in Spain, and characterized a new case of Crimean-Congo Hemorrhagic fever and indigenous cases of Dengue virus infection. In addition, Spain's first case of primary amebic meningoencephalitis caused by *Naegleria Fowleri* was diagnosed.
- The Executive Summary of infectious diseases imported after returning from travel abroad has been published, and a manual for case management and surveillance of Leishmaniasis in the WHO European region has been prepared.
- The REDIVI network has been consolidated with more than 20,000 records of cases of infections imported by travelers and immigrants. Eight Autonomous Communities and 27 Centers participate in it, making it the most comprehensive nationwide network.
- The genome assembly of *L. infantum* has been improved through a combination of massive sequencing techniques.

- Proteins have been identified that may explain the complexity and neurological disorders in the acute and chronic phase of human fascioliasis.
- The CNMT participated in the largest genomic study of helminths carried out to date, published in the Nature Genetics.
- The CNMT demonstrated the efficacy and effectiveness of diagnostic tools such as SH-LAMP, which means that the molecular diagnosis for urogenital schistosomiasis can be easily made at low cost in remote endemic areas with limited resources.
- The CNMT has helped to demonstrate the potential efficacy of Benznidazole treatment of patients with Chagas disease, by enabling the genotypic and functional reversal of depleted T cells.
- The high-throughput screening platform has identified new natural products with antimalarial and antitrypanosomal activity, and aspects related to DNA repair mechanisms in the oxidative stress response and infectivity of *Trypanosoma brucei* have been identified.
- RICET researchers also participated in the clinical trials of the first vaccine against Ebola.
- In addition, different RICET groups, together with the Program for Control of Onchocerciasis and other Filariasis in Equatorial Guinea, have been able to verify the elimination of onchocerciasis transmission on the Island of Bioko, Equatorial Guinea.

the IIER has analyzed 37 cases of rare tumors and 15 retinoblastoma cases using gene panels.

- **Patient and organization consultation system:** In 2018, a total of 287 consultations were received, of which 52 were on issues related to rare diseases and the remaining 235 were related to toxic oil syndrome.

Lines of research in rare diseases

The IIER conducts basic and translational research in the field of rare diseases, toxic oil syndrome, and autism spectrum disorders (ASD). The main lines of research are: 1) the role of abnormalities in the innate immune system in rare diseases; 2) the study of rare pediatric tumors: genetic abnormalities and cell therapies; 3) gene and cell therapy in congenital muscular dystrophies and rare tumors; 4) the involvement of microRNAs in rare disease development and their role as biomarkers; 5) the application of new genetic analysis technologies for diagnosing rare diseases; 6) the epidemiology of rare diseases; 7) risk factors and the prevention of congenital anomalies, carried out in collaboration with the CIAC (see this center's section in the annual report); 8) collaboration in CIBERER-ISCIll research activities and the ISCIll's Biobank platform; 9) in the field of translational research, participation in different projects on quality of life of patients with toxic oil syndrome, as well as the completion of clinical practice guidelines for Fabry disease; 10) development of three-dimensional cultures (organoids) in order to model rare diseases that affect the liver; 11) identification of disease-modifying genes in rare pulmonary diseases. and 12) research into epigenetic mechanisms and genomic regulation.

RESEARCH INSTITUTE FOR RARE DISEASES (IIER)

Scientific, technical and service activities

- **Biobank:** The National Rare Disease Biobank (BioNER) continues its activity within ISCIll's Biobank Platform and the European Eurobiobank and RD-CONNECT networks. It is currently acting as coordinator of the EURO-BIOBANK. In 2018, 118 new donors were recorded.
- **Genetic diagnosis services:** The genetic diagnosis unit is the only laboratory of the Spanish Public Health System accredited by the National Accreditation Entity (ENAC) according to the ISO15189 quality standard, for identifying genetic abnormalities in retinoblastoma. In 2018, the IIER obtained the accreditation of the Autonomous Community of Madrid as a Health Center for the diagnosis of genetic diseases. It diagnoses rare childhood tumors and alpha-1 antitrypsin deficiency. It is also in charge of genetic diagnoses for the undiagnosed rare disease program (SpainUDP). Over the course of this year, 1,887 tests were carried out on 434 cases. In addition,

Special programs

The IIER operates the following programs: 1) monitoring the toxic oil syndrome cohort of a total of 13,872 cases: 314 deaths were identified in 2018; 2) collaboration in the development of a population-based screening program for the early detection of autism spectrum disorders (ASDs) in Salamanca and Zamora provinces, in collaboration with the University of Salamanca; 3) direction and coordination of the European project on ASDs in the European Union; and 4) participation as partners in the EJP RD (European Joint Program on Rare Diseases), co-leading work packages 2 and 3.

The undiagnosed rare disease program - SpainUDP

The IIER collaborates with the Undiagnosed Diseases Network International (UDNI). The network, created in 2015, is implementing communication systems for complex cases and opening lines of collaboration among groups. The IIER has a case registration system and a process for analysing them. It

collaborates with the Puerta de Hierro University Hospital on those cases that require specific studies of the clinical phenotype. This program contributes not only to providing diagnostic services but also to research. From the year of its creation as a pilot project in 2013 (formally established in 2015) to the end of 2018, SpainUDP admitted a total of 169 cases, of which 34 were incorporated in 2018. Over the past year, 15 cases were diagnosed and in 3 cases candidate variants not previously linked to disease were found

National Rare Diseases Registry

In 2018, work on the development of the National Rare Disease Registry (ReeR) continued through participation in the meetings of the MSCBS working groups aimed at creating standardization and data validation processes. Furthermore, work on the patient registration platform continues. In 2018, 360 patient registration requests were received. Of these, 229 were processed and supplementary documentation was requested from 105 applicants. In addition, the development of two new patient registration strategies affecting large groups of pathologies was completed: immunodeficiencies and ocular pathologies in collaboration with the thematic network for eye research Oftared.

Consultation and dissemination activities

The IIER is part of the International Rare Disease Research Consortium (IRDIRC) and chairs the International Conference of Orphan Drugs and Rare Diseases (ICORD). It provides external consultancy for the Spanish Agency of Medicines and Medical Devices (AEMPS) and is an expert member of the European Medicines Agency. It also provides members to the Advisory board of FEDER and the Rare Diseases Committee of the Spanish Association of Human Genetics.

RESEARCH CENTER ON CONGENITAL ANOMALIES (CIAC)

The CIAC is a functional Unit of the IIER (Rare Disease Research Institute) for Research on Congenital Anomalies. In this Unit the ECEMC (a scientific group of ASEREMAC—the Spanish Association for the Registry and Study of Congenital Malformations) develops its activity, within the framework of the agreement established with the ISCIII, under the technical coordination of the IIER and under the supervision of the SGSAFI of the ISCIII. The ECEMC (the Spanish Collaborative Study of Congenital Malformations) is a clinical-epidemiological research program on congenital defects using a multidisciplinary and translational approach. It is structured into three sections: Epidemiology and Clinical Genetics, High-Resolution and Molecular Cytogenetics, and Clinical

Teratology. It carries out its activity in three lines of research: (a) epidemiological surveillance of congenital defects in the ECEMC and analysis of associated variables and factors; (b) clinical and etiological study of children with congenital defects; and (c) epidemiological analysis of teratogens.

Participation in research networks

The group has been a part of the Rare Disease Biomedical Research Networking Center (CIBERER) since its foundation in 2006. It also forms a part of following international networks:

- ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research; www.icbdsr.org) since 1979.
- EUROCAT (European Surveillance of Congenital Anomalies; www.eurocat-network.eu) since 1980.
- NTIS (European Network of Teratology Information Services; www.entis-org.eu) since 1990; the group is a constituent member of this network.

Highlighted activities and milestones in 2018

- Maintenance and coordination of the “Clinical Network of the ECEMC” (comprising more than 300 physicians from all over Spain).
- Clinical and dysmorphological evaluation of 784 newborn babies and fetuses with congenital defects (CD) in Spain, within the scope of the ECEMC.
- Cytogenetic study (high resolution and molecular): 168 studies (ECEMC scope).
- Handling of 908 SITTE (Spanish Telephone Information Service on Teratogens) consultations from physicians and 2,511 SITE (Telephone Information Service for Pregnant Women) consultations from the general public on risks in prenatal development.
- Epidemiological surveillance of CDs in Spain (ECEMC scope), European surveillance within the EUROCAT scope (www.eurocat-network.eu), and global epidemiological surveillance of CDs within the ICBDSR scope (www.icbdsr.org).
- Collaboration in the construction and implementation of the “ICBDSR Platform for Sharing Birth Defects Prevalence Data”.
- Participation in the international “Collaborative Project on the frequency of hypospadias” of the ICBDSR.
- Participation in the “Collaborative projects on the mortality/survival of selected non-cardiac defects” (17 subprojects), within the scope of the ICBDSR.
- Participation in the international “Global Epidemiology of Gastroschisis” project of the ICBDSR.

- Participation in the activities of the Joint Research Center-EUROCAT.
- Participation in the organization of the fourth World Birth Defects Day (WBDD) (3 March 2018) and coordination in 2018 of the fifth WBDD for 2019 (participating in the Social Media Workgroup).
- Scientific coordination of agreements on congenital anomalies with the Autonomous Communities of Cantabria, Castilla-La Mancha, Castilla y León, and Murcia.
- Participation in the CIBERER Translational Research Project “Functional characterization of non-canonical variants that alter the splicing process in patients with intellectual disabilities”.
- Participation in a research project on postaxial polydactyly in collaboration with the IIB “Alberto Sols”, CSIC-UAM.
- Participation in the National Human Biomonitoring Hub CNSA of the ISCIII.
- Participation in the Rare Disease Clinical Records Working Group, within the scope of CIBERER.
- Participation in the CIBERER transversal project proposal “PALAM Platform: A free Open Science Publishing Platform, based in Blockchain, for immediate, transparent and traceable publication and review of scientific work”.
- Collaboration with the National Epidemiology Center for the study of alcohol and tobacco consumption during pregnancy.

Participation in scientific, technical and advisory committees

International: Internal Audit Committee of the International Clearinghouse for Birth Defects Surveillance and Research–ICBDSR; EUROLINKCAT; European Medicines Agency–EMA.

National: Spanish Agency of Medicines and Medical Devices (AEMPS) Experts Network; Spanish National Commission on Assisted Human Reproduction (CNRHA); Spanish National Agency for Assessment and Forecasting (ANEP); Advisory Committee of the Spanish Federation of Rare Diseases (FEDER); Board of Trustees of the Foundation 1,000 on Birth Defects.

Awards received: “2018 ICBDSR Distinguished Service Award for longstanding excellence, service and leadership”, awarded by the International Clearinghouse for Birth Defects Surveillance and Research to Dr Eva Bermejo Sánchez, Scientific Coordinator of the ECEMC and Senior Scientist at the IIER.

TELEMEDICINE RESEARCH UNIT (UIT)

The Telemedicine and e-Health Research Unit promotes and carries out R&D&I activities and training in the field of Information and Communication Technologies (ICT) applied to health. Its lines of activity are: 1) development of PITES (Platform for Research in Telemedicine and e-Health), an open Platform for Innovation in Telemedicine and e-Health, with specific actions in the fields of active and assisted living (AAL) and mobile health (mHealth); 2) standardization and interoperability of information systems and electronic health records (EHR); 3) creation of repositories for the secondary use of information and knowledge extraction; 4) ICT training (empowerment) for patients and professionals; 5) reliability analysis of complex monitoring environments and of the safe use of medical devices in contexts of active and assisted living (AAL); 6) analysis of guarantees, protection, safety, and electromagnetic compatibility (EMC) in telemedicine applications; and 7) evaluation of mobile telehealth e-services.

Active projects

- AESI-PI15CIII/00003, 2016-2018. Innovation platform in Telemedicine and e-Health: ICT for the R&I challenges in health services - PITES-TIiSS.
- AESI-PI15CIII/00010, 2016-2018. Standardized model of shared electronic medical records for integrated health and social care. Feasibility and utility of a repository for secondary use in breast cancer.
- ERASMUS + 2017-1-IT02-KA204-036545, CARE4DEM-Dementia Caregivers Support.
- CHRODIS PLUS - JA 2017-2020. Joint Action addressing chronic diseases and promoting healthy aging across the life cycle.
- CIP-ICT-PSP-2013-7. PPI-621013. 2014-2017 (extended). STOPandGO. Sustainable Technology for Older People-Get Organized. Coordinator Ilse Bierhoff (Stichting Smart Homes, NL).
- FISPI PI16/00769. Effectiveness and cost-effectiveness at five years of complex interventions for knowledge transfer based on ICT to improve the health of DM2 Patients (INDICA-DOS).
- COST BM 1309, 2014-2018. European network for innovative uses of EMFs in biomedical applications (EMF-MED).
- SPANISH AIDS RESEARCH NETWORK (RIS) RD16CIII/0002/0003. 1 January 2017–31 December 2021.

- General Foundation CSIC, POCTEP 0348_CIE_6_E (MODULEN). Subproject 4 (Internal File DGVP29218) - Implementation of a predictive model based on monitoring the environment and daily life habits for the early detection of frailty states.
- Extraction of associations between diseases and other medical concepts (EXTRA-E) (IMIENS-2017-005).

Other activities:

- E-DUCA: Development of an app for the training of lung transplant patients.
- CAREVID: Platform for the Evaluation of Indicators of the Program for the Implementation of Best Practice Guidelines in Centers Committed to Excellence in Care.
- WEBRIS: Development of the public-private web portal of the Spanish AIDS Research Network RETIC-RIS.

HEALTHCARE RESEARCH UNIT INVESTÉN-ISCIII

The Healthcare Research Unit (Investén-ISCIII) has worked for years on promoting research in nursing care and other disciplines related to this field. Its resources are public and available for all SNS professionals interested in care research.

Strategic lines:

- Increasing the presence and visibility of care research led by nursing professionals, physiotherapy professionals and other professionals in health sciences.
- Promoting the exchange of transnational knowledge and incorporation of scientific activity in care at the European and international level.
- Promoting training in research methodology for professionals involved in the provision of care.
- Increasing scientific rigor in the research activity of nurses, physiotherapy professionals and other professionals in health sciences.
- Improving the transfer of research results in care and the application of evidence in clinical practice.

Highlighted activities:

- Two cohorts of Centers Committed to Excellence have been completed and a third was started, so that it now comprises a total of 26 centers and 271 healthcare institutions. In December 2017, an extraordinary call for the establishment of Regional Coordinating Centers closed. Three Autonomous Communities (Balearic Islands, Basque Country and Principality of Asturias) joined, adding a total of 9 new centers of these Autonomous communities to the program.
- The maximum number of students possible (full quota) enrolled for the university doctoral program in Comprehensive Care and Health Services in collaboration with the University of Jaén, the University of Lleida, the University of Vic and the ISCIII.

Active projects of the Unit

- European Project: CARE 4 DEM-DEMENTIA CAREGIVERS SUPPORT (2017-1-IT02-k214-036545).
- AESI Project: Identification of sustainability factors for the implementation of clinical practice guidelines and their evolution in the cohorts that implement them in SNS health centers. PI16CIII/00032.
- Multi-center AESI project: Effectiveness of the Otago Exercise Program applied in a group versus individually in the probability of falls of non-institutionalized people between 65-80 years old. PI16CIII/00031.
- AESI Project: Circadian health in patients admitted to intensive care units and in hospitalized patients. CHRONOHOSPIPI18CIII/00012.
- Interreg Project (Spain-Portugal). Pilot project for the establishment of a predictive model as a possible modulator of aging in health: ModulEn.
- European Collaboration: European Innovation Partnership on Active and Healthy Ageing. A2 and A3 ACTION GROUPS.
- National Collaboration: participation in the REDISSEC thematic network (RD12/0001/0016) and consolidation of our participation in CIBERFES.

FUNCTIONAL UNIT FOR RESEARCH INTO CHRONIC DISEASES (UFIEC)**Scientific and technical activities**

The UFIEC's activities are aimed at basic research into neurodegenerative diseases, cancer, and inflammatory, metabolic, and mitochondrial pathologies. It addresses aspects of regenerative medicine (stem cells, iPSCs and organoids), pharmacological targets (signalling and structural models), detection of new biomarkers, cellular senescence, animal models and computational biology. In addition, other scientific and technical activities are carried out, among which the following stand out:

- Benchmark molecular diagnosis of human prionopathies (included in the ECDC's surveillance program).
- Transversal technical support services such as the Histology Unit, the optical imaging platform for in vivo monitoring of animal models (IVIS), the Luminox platform, and structural protein analysis equipment.

Fundraising

The UFIEC's research activity has been financed through funds obtained through competitive calls from public institutions: seven projects from the former Ministry of Economy, three from the Health Research and Development Strategy (AES), and one Innovation Check from the Autonomous Community of Madrid. The following grants were obtained from private institutions: one from the Spanish Foundation for the Promotion of Research on Amyotrophic Lateral Sclerosis (FUNDELA) and two from the Spanish Association against Cancer (AECC). IDP Pharma directly finances a project on neuro-oncology, and several groups have scientific and technical support agreements with companies (AMOPHARMA LTD, TECHNICAL PROTEIN NANOBIOTECHNOLOGY SL, REGEMAT 3D SL) and collaborations with different institutions and consortia (Consortium NEUROSTEM-CM, the BT-CIEN Tissue Bank and the CIEN Foundation, the H12O (i+12) Research Institute, IdiPaz, the MinE International Consortium for the study of Amyotrophic Lateral Sclerosis, the Spanish Research Group on NeuroOncology, CIBERONC, and CIBERNED).

Participation in international Committees

The UFIEC is represented in the Scientific Committee of the IARC (International Agency for Research on Cancer), which belongs to the WHO, for international coordination of cancer research. It is also a national expert member of the ECDC for the surveillance and diagnosis of human prion diseases. The UFIEC participates in the EU-NETVAL (European Union Network of Laboratories for

the Validation of Alternative Methods) in the validation and implementation of methods aimed at the detection of endocrine disruptors.

CENTRAL SCIENTIFIC AND TECHNICAL UNITS AREA

The Central Scientific and Technical Units (UCCTs) Area of the SGSAFI includes the Veterinary, Bioinformatics, Electronic and Confocal Microscopy, Flow Cytometry, Histology and Genomics Units. Its main function is to provide high-quality scientific services to researchers from ISCIII's centers who request it.

Highlighted activities

The Histology Unit, until recently integrated into the Functional Unit for Chronic Disease Research (UFIEC), has become part of the UCCTs Area. The Veterinary, Electronic and Confocal Microscopy, and Flow Cytometry Units renewed AENOR certification of their Quality Management System according to ISO Standard 9001-2015. The Genomics and Electron Microscopy Units maintained their ENAC accreditation according to ISO 15189, within the CNM quality system. Furthermore, the Bioinformatics Unit has strengthened its affiliation with the ISCIII's Bioinformatics Platform, and now forms part of the TransBioNet network.

Scientific and technical activities

The units' activities are focused on training, scientific and technical assistance, and providing services to users of the various ISCIII centers. Regarding the services provided by the various units:

- The Genomics Unit carried out more than 88,000 Sanger-type individual sequencings and generated around four terabytes of sequences by means of massive sequencing.
- A large part of this data has been processed by the Bioinformatics Unit, resulting in the analysis of around 3,000 bacterial genomes, 350 human exomes, and 250 transcriptomes.
- The Electronic Microscopy Unit has done 23 diagnostic assays for the National Health System and 379 analyses requested by researchers.
- The Veterinary Unit has processed 371 requests for animal model experiments and carried out 23 botulism assays.
- The Flow Cytometry Unit has provided services to 81 users throughout the Institute

BIOLOGICAL ALERT LABORATORY NETWORK, RE-LAB

The main added value of the network is that under its control a coordinated response with the competent health authorities can be orchestrated, especially with the MSCBS Health Alert and Emergency Coordination Center and with the law enforcement agencies to give a quick and effective response to incidents of a biological nature. In 2018, the new Order PCI/1381/2018, of December 18, was published, regulating the RE-LAB.

Scientific and technical activities

- The RE-LAB Management Unit coordinated the response of the network's reference laboratories to alerts regarding mail deliveries containing possible biological threat agents that occurred in various public institutions and private entities in the country throughout the year.
- The conference "The role of the RE-LAB in the face of the threat of bioterrorism. Research funding programs" was organized in order to encourage the participation of laboratories in the H2020 Safety Challenges Calls and obtain research funding in this area.
- The Management Unit participated in the creation of the Spanish declaration on measures for promoting trust in the Prohibition of Biological and Toxin Weapons Convention (BTWC) by coordinating the information provided by laboratories in the network.

Participation in work groups and institutional representation:

- Specialized Committee on the Non-Proliferation of Weapons of Mass Destruction, a support body of the National Security Council within the framework of the National Security System, on behalf of the Ministry of Science, Innovation and Universities.
- Interception Working Group for cases of diversion of Weapons of Mass Destruction, created within the Non-Proliferation Committee.
- Interministerial Group for the Prohibition of Biological Weapons (GRUPABI), coordinated by the Sub-Directorate General of Non-Proliferation and Disarmament of the Ministry of Foreign Affairs, European Union and Cooperation.
- Interministerial Working Group for the implementation of the NRBQ Action Plan of the European Union coordinated by the Ministry for Home Affairs.

NATIONAL LIBRARY OF HEALTH SCIENCES (BNCS)

The BNCS is a specialized library that serves ISCIII researchers, students of medical and occupational health schools, and the Spanish public health system. In addition to providing traditional library services, which are currently carried out almost exclusively by electronic means, it develops initiatives to disseminate scientific production in Spanish health internationally, including:

1.1- Virtual Health Library - Spain (<http://bvsalud.isciii.es>)

IBECS	228 indexed journals
Spanish Health Sciences Bibliographic Index http://ibecs.isciii.es	174,291 articles (an increase of more than 6,000 records with respect to 2017) 31,182 links to full-text articles included in SciELO Spain and in open-access journals
SciELO	60 publications
Scientific Electronic Library Online	Over 37,000 full-text articles (html, XML, and pdf)
Collection of Spanish open-access health sciences journals. http://scielo.isciii.es	Nearly 24 million visits and over 29 million pages downloaded The SciELO website accounts for 93.49% of the ISCIII's web traffic (http://www.alexa.com/siteinfo/www.isciii.es) Integrated into the Web of Science (WoS) through the SciELO Citation Index Available on Google Scholar Available in open-access directories: Hispana/DOAJ/OAISTER/ROAR/OpenDOAR/Recolecta/OpenAire and BASE
LIS-España	Directory of health sites subject to quality control
Health Information Finder	2,365 entries in Information for professionals 1,954 entries in Information for citizens The content is integrated into the LIS-Regional portal that gathers 33,300 resources from 67 different sources
DeCS	Spanish (Spain) translation of the trilingual (ES/EN/PT) biomedical term thesaurus created by BIREME based on the National Library of Medicine's MeSH
Health Sciences Descriptors	422 new descriptors and 135 terms modified 4,135 new synonyms in already existing records 291 Scope notes modified in already existing records

1.2 National Health Sciences Catalog (CNCS)

CNCS	Launched in November 2018
National Health Sciences Catalog http://cncs.isciii.es/	Contains 140,000 bibliographic records and 363,957 collections from 267 libraries and 16,418 journals have been integrated

1.3 BNCS Social Networks

Channels	@BNCSisciii–Official corporate profile (690 followers)
TWITTER	@scielospain–Official profile of the SciELO Spain collection (4.9K followers) @bvs_spain–Official profile of the Virtual Health Library – Spain (2.4K followers)

1.4 Institutional Repository (REPISALUD)

REPISALUD	Launched in September 2018
https://www.repisalud.isciii.es	Unified open-access platform for the scientific and technical production of the ISCIII, the CNIC and the CNIO

Editorial program

Twenty titles were published in 2018: 14 monographs and 2 periodicals in electronic format, 2 informative brochures and 2 new volumes of the “More than health” collection: “Healthy Aging” and “Microscopic fungi: friends or foes?” Free access to all ISCIII’s electronic publications from 2009 on is available online at <http://publicaciones.isciii.es/>. The portal has an alert system for registered users that has 2,398 subscribers.

HEALTH TECHNOLOGY ASSESSMENT AGENCY (AETS)

The AETS addresses the SNS’ needs for scientific information and evidence related to determining the policy on healthcare benefits and improving its quality and efficiency. Since 2012, part of the AETS’ technical services has belonged to the “Spanish Network of Agencies for Assessing National Health System Technologies and Performance.”

Technical and scientific activities

Health Technology Evaluation Reports

- Study of the effectiveness and safety of cryopreservation of oocytes and ovarian tissue for the preservation of fertility in cancer patients.
- Diagnostic effectiveness and safety of elastography in the study of liver fibrosis in chronic liver disease.
- Diagnostic effectiveness and safety of different types of elastography in oncology. An overview of systematic reviews and meta-analysis.
- Use of the Denis Browne splint up to the age of 4 to prevent recurrence of congenital clubfoot.
- Analysis of the efficacy and safety of orthodontic-orthopedic maxillary expansion appliances as an alternative to adenotonsillectomy and/or pharmacological treatment in the management of Sleep Apnea-Hypopnea Syndrome in pediatric patients.
- Analysis of the efficacy and safety of peripheral neurostimulation of the sphenopalatine ganglion for the treatment of refractory chronic cluster headaches.
- Policy Analysis of the European Innovation Partnership on Active and Healthy Ageing and its impact in Spain. Achievements and recommendations for the 2016-2020 period.

- Heli-Fx EndoAnchor™-type anchor or fixation systems for the treatment or prevention of endovascular repair failure in patients with aortic aneurysm.
- Validity and Clinical Utility of the New Genomic Platform for Next Generation Sequencing (NGS) FoundationOne® in non-small cell lung cancer and other types of solid tumors.

Participation in methodological development lines:

- Quality criteria and best practices in organizations dedicated to the evaluation of health technologies: internal report. Quick response.

Monitoring Studies:

- Left atrial appendage closure device in patients with nonvalvular atrial fibrillation.
- Biodegradable esophageal stents for benign pathologies.
- Neurostimulator for refractory headaches.

New and Emerging Health Technology Detection System. SINTESIS - New Technologies:

In 2018, 13 new and emerging technologies were identified and evaluated and 4 assessment forms of new and emerging technologies of prioritized technologies were made:

- Hypoglossal nerve stimulation systems for the treatment of obstructive sleep apnea.
- Gastric Electrical Stimulation (GES) for weight reduction in patients with obesity. Abiliti® system.
- Identification of neoplastic tissue by the MasSpec Pen system and high-resolution linear ion trap mass spectrometry analysis during cancer surgery.
- Home rehabilitation program to improve arm function in patients with Multiple Sclerosis.

GuíaSalud Program for Clinical Practice Guidelines (CPG) in the Spanish Public Health System (SNS).

Research projects

- EUnetHTA Joint Action 3 - European Network for Health Technology Assessment.
- “CHRODIS-PLUS: Implementing good practices for chronic diseases”.
- REDISSEC Thematic Network for Cooperative Research “Healthcare Services for Chronic Diseases Research Network.”
- FIS PI15/01377 “Effectiveness and cost-effectiveness of a multicomponent

strategy to implement clinical practice guidelines and improve health outcomes in people with Systemic Lupus Erythematosus”.

- FIS 14/01677. Development from primary care of a risk stratification model in patients with heart failure to predict disability and hospitalization (2015-2018).

Consultation activities

- The AETS is a member of the EUnetHTA Executive Board.
- It represents ISCIII on the SNS's Commission on Benefits, Insurance, and Funding; the Committee for Designation of Reference Centers, Services, and Units (CSUR); the Advisory Committee for Orthoprosthetic Benefits; the Advisory Committee for Benefits with Dietary Products; and the AEMPS' Medicinal Products Committee.

OFFICE FOR THE TRANSFER OF RESEARCH RESULTS (OTRI)

In 2018, the OTRI carried out its activities principally in 3 areas:

- Patent Management. The OTRI has a portfolio of 73 patents, including filed and granted patents, belonging to 18 patent families. Twelve of these are Spanish and 61 are foreign or in the process of internationalization.
- Trademark Registration. The OTRI applied this year for the trademark “CNCS. National Health Sciences Catalog”.
- Materials and Know-How Licensing. Various national and international agreements were processed in order to transfer and license the use of materials.

SCIENTIFIC CULTURE AND INNOVATION UNIT (UCCIII+i)

In 2018, the UCCIII+i carried out a project funded by the Spanish Foundation for Science and Technology (FECYT) entitled 'ISCIII's Outreach for all 2018' for the third consecutive year.

Highlighted activities

- Researchers' Night: We look after your health by watching over the environment. Presentation of the activities of the CNSA held in the Plaza de Isabel II in Madrid (Plaza de Opera.)
- Co-organization of visits to ISCIII's Museum of Public Health and Hygiene; presentation of the collection of educational books “More than health” in the Juan Rulfo bookstore in Madrid. Open House at ISCIII's Majadahonda Campus.
- Workshop/training course “Disseminate your Science”
- Scientific education program in secondary education and Baccalaureate school centers “Science Goes to School”.

Through the National School of Public Health (ENS) and the National School of Occupational Medicine (ENMT), ISCIII seeks to develop teaching programs aimed at the SNS and to provide health information and scientific documentation services. To this end, it carries out training, improvement and specialization tasks of healthcare and non-healthcare personnel in the fields of healthcare and health administration and management, without prejudice to the competences of other public bodies, and it develops methodological disciplines in social and economic sciences applied to health.

2018 Training offer	Academic load (teaching hours)	ECTS
Master's Degree in Public Health (In person)	1,500 (750)	60
University Master's Degree in Healthcare Administration (Blended)	1,500 (750)	60
Master's Degree in Systems Management and Information and Communications Technology in Health (Blended)	1,500 (750)	60
Master's Degree in Bioinformatics Applied to Personalized Medicine and Health (In person)	600 (360)	30
Specialization in Health Law and Bioethics Diploma (Online)	250	10
Specialization in the Individual Rights in Health and Social Care Diploma. Bioethical and Legal Aspects (Online)	250	10
Specialization in Law for Healthcare Executives Diploma. Managing the Legal Variables in Healthcare Organizations (Online)	120	5
Specialization in Public Health for Development Aid Diploma (Online)	250	10
In-person continuing education courses	551	30

5.1 NATIONAL SCHOOL OF PUBLIC HEALTH (ENS)

Highlighted activities

- In 2018, the Blended Diploma Course 'Specialization in Public Health for Development Aid' was launched. Its objectives and contents are similar to the old International Health Diploma.
- The ENS Coordinates the European Joint Action CHRODIS+ and is an active participant in the REDISSEC Thematic Network. It is also important to highlight the collaboration in other projects focused on the prevention and promotion of health, quality of life and aging, gender-based violence, and climate change and health.

Students in training	2018	2017	2016
Preventative Medicine and Public Health Teaching Unit. Total number of MIR in training programs (R1, R2, R3 and R4)	9	8	8
Master's Degree and Diploma Programs	205	225	192
In-person continuing education courses	164	241	201

5.2 NATIONAL SCHOOL OF OCCUPATIONAL MEDICINE (ENMT)

During 2018, the ENMT signed and maintained agreements in the fields of training and research with Autonomous Communities, with the National Social Security Institute (INSS), INGESA, and scientific associations for the training of specialists in occupational medicine and occupational nursing, and for the continuing education in occupational diseases for primary care physicians in the form of e-learning.

Training indicators in the academic year 2018

11 courses/workshops in 2018	Format	CTC/ECTS Credits	Hours
Opening day academic year	ENMT In-person	-	5
VI Scientific Workshops on Occupational Health Review Studies	ENMT In-person	1 CTC	5
Introduction to Dermatoscopy for Occupational Health Physicians	ENMT In-person	0.9 CTC	7
Introduction to Hypoacusia for Occupational Health Physicians I	ENMT in-person	1 CTC	6
Introduction to Hypoacusia for Occupational Health Physicians II	ENMT In-person	1 CTC	6
Higher course on occupational medicine. CUSMET 2018	ENMT Blended	—	800
Practical Application of Health Surveillance Protocols Course	ENMT Online	4.5 CTC	45
Prescription of Physical Exercise for Healthcare Professionals III	ENMT Online	6.3 CTC	50
Prescription of Physical Exercise for Healthcare Professionals IV	ENMT Online	6.3 CTC	50
Introduction to the Planning of Workplace Health Promotion Interventions	ENMT Online	4.5 CTC	45
Master's Degree in Medical Evaluations of the Inability to Work and Dependency (ISCIII-UAH-INSS-IMSERSO)	ENMT Online	60 ECTS	350

Global Training Indicators 2018	2018
Total number of MIR in training programmes (R1, R2, R3 and R4)	176
Number of students in continuing in-person education	202
Number of students in online education	244
Number of students in continuing education agreements	40
Total class hours taught	1,364

ONGOING RESEARCH PROJECTS 2018

Project name	Funding entity	Participating entities
Models of occupational accidents while driving vehicles: assessment of attentional components and engines	ISCIII	ISCIII- University of Innsbruck (H.Hochzirl) – University of Barcelona - Catholic University of Valencia
CHRODIS-PLUS; tasks	ISCIII- EUROPEAN COMMISSION	ISCIII and European consortium
Objective voice assessment in professionals: comparative analysis of traditional phonation measurements and kinematic glottal measurements	ISCIII- UNED	ISCIII- UNED- University of Coimbra- University of Lisbon - University of Barcelona
Global Spine Care Initiative: Public Health and Prevention Interventions	Stanford Health Care, ISCIII, World Spine Care, UC Irvine, Cincinnati VAMC	Stanford Health Care, ISCIII, World Spine Care, UC Irvine, Cincinnati VAMC
Fatigue, falls and useful standards	ISCIII-UCV- H.CLINIC-Univ. of Navarre	ISCIII-UCV-UVEG-H.CLINIC-Univ. of Navarre

6.1 INTERNATIONAL PROGRAMS

The internationalization of the Spanish Science, Technology and Innovation System is one of the priority areas and the central focus of the Spanish Science and Technology and Innovation Strategy 2013-2020. The Sub-Directorate General of International Research Programs and Institutional Relations (SGPIRI) is working both on the promotion of participation in European and international R&D&I programs and on the joint programming of calls in the fields of International Research Infrastructures, Joint Programming Initiatives (JPIs) and ERA-Nets, and other International Consortia.

International research infrastructures

- **IARC:** International Agency for Research on Cancer.
- **ELIXIR:** European Life Sciences Infrastructure for Biological Information.
- **EATRIS-ERIC:** Distributed European Infrastructure for Translational Medicine
- **ECRIN-ERIC:** Distributed European Infrastructure for clinical trials.
- **EU-Openscreen-ERIC:** Distributed research infrastructure for Chemical Biology and Molecule Screening for Therapeutic Activity.
- **Euro-BiolImaging:** Distributed infrastructure for the digitalization of medical imaging and biological microscopy.

JPIs and ERA-Nets

In 2018, ISCIII participated as a funding agency in 11 international joint calls; the participation of 28 research groups was funded for an amount of around € 4 million. These grants are detailed in Section 2.1 (Health Research and Development Strategy) of this document.

Promotion of European Programs

One of the functions of ISCIII is to promote the structuring of the SNS. In **Societal Challenge 1** of Horizon 2020, the results of the Spanish participa-

tion have continued in 2018 in line with the good results of 2016 and 2017, in terms of both successful participation and leadership. In terms of grants obtained it is noteworthy that, using figures from the end of 2018, Spain will obtain a cumulative financing in Societal Challenge 1 of H2020 of more than € 250 million for these five years. This accomplishment keeps Spain in fifth position in the health area, only behind the United Kingdom (21.09%), Germany (15.24%), the Netherlands (13.17%) and France (9.96%). It should also be noted that ISCIII presented in 2018, 22 proposals to the different international programs, 6 of which were funded.

In addition, the call of the **EU Health Program** for 2018, adopted on January 25, has a budget of € 62 million for funding Grants, Tenders, Joint Actions, Awards and other actions. The main topics funded in 2018 were the implementation of good practices and scaling up of care, Orpha-Codes, serious cross-border threats to health, and European Reference Networks (ERN).

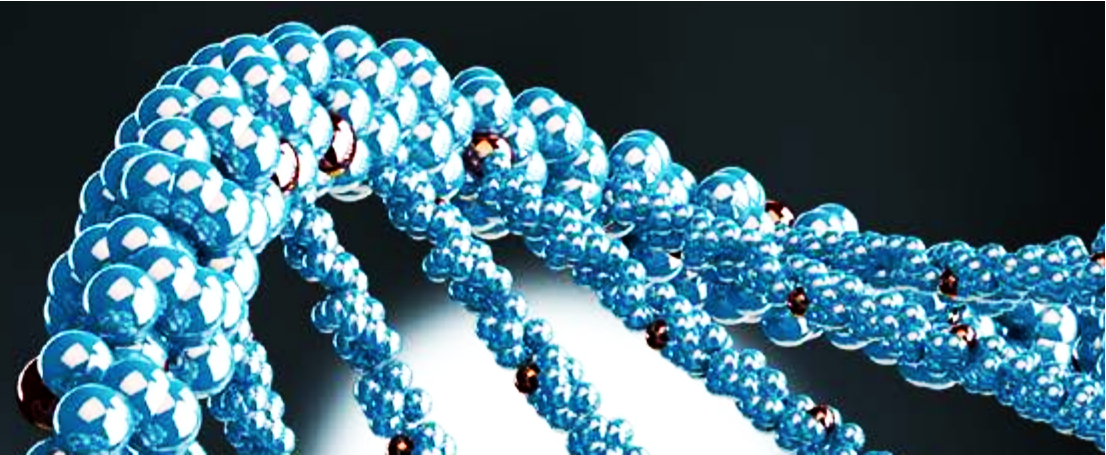
Other international consortia

These consortia are mostly related to existing programs, and the role of ISCIII is to align them with the funding activities:

- **IRDiRC:** International Rare Diseases Research Consortium
- **GloPID-R:** Global Research Collaboration for Infectious Disease Preparedness
- **CEPI:** Coalition for Epidemic Preparedness Innovation
- **TDR:** Research on Diseases of Poverty
- **ICPerMed:** International Consortium for Personalized Medicine
- **PMC:** Personalized Medicine Coalition
- **ICGC:** International Cancer Genomics Consortium

Summary table of joint programming initiatives and coordination and support actions in which ISCIII participates that are active in 2018

Acronym	Title	Period	Role of ISCIII	Total EU Funding in €	ISCIII Funding in €
JPco-fuND	ERA-NET for establishing synergies between the Joint Programming on Neurodegenerative Diseases Research and Horizon 2020	01/01/2015-31/12/2019	Partner	9,999,999.98	157,799.43
JPSustaiND	Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases	01/11/2015-30/04/2021	Partner	2,043,283.75	191,250.00
JPI-EC-AMR	ERA-NET for establishing synergies between the Joint Programming Initiative on Antimicrobial Resistance Research and Horizon 2020	01/11/2015-31/10/2020	Partner	7,858,116.00	224,812.00
EXEDRA	EXpansion of the European Joint Programming Initiative on Drug Resistance to Antimicrobials	01/01/2017-31/12/2020	Partner	2,149,202.50	119,375.00
ERA-HDHL	ERA-NET Biomarkers for Nutrition and Health implementing the JPI HDHL objectives	01/02/2016-31/01/ 2021	Partner	4,765,200.00	224,812.50
INTIMIC	ERA-Net on INtesTInal MICrobiomics, diet and health, implementing JPI HDHL objectives	01/12/2016-30/11/ 2021	Partner	3,498,825.00	224,812.50
EuroNanoMed III	ERA-NET ON NANOMEDICINE	01/11/2016-31/10/2021	Coord.	5,039,100.00	212,850.00
ERAPerMed	ERA-Net Cofund in Personalised Medicine	01/12/2017-30/11/2022	Coord.	9,508,950	224,812.50
E-Rare-3	ERA-NET rare disease research implementing IRDiRC objectives	01/12/2014-30/11/2020	Partner	5,884,310	221,827.00
TRANSCAN-2	ERA-NET: Aligning national/regional translational cancer research programmes and activities	01/01/2015-31/12/2020	Partner	6,672,187.00	215,743.00
ERA CVD	ERA-NET on cardiovascular diseases to implement joint transnational research projects and set up international cooperations	01/10/2015-30/09/2020	Partner	5,974,237.50	245,437.50
ERACoSysMed	ERACoSysMed - Collaboration on systems medicine funding to promote the implementation of systems biology approaches in clinical research and medical practice	01/01/2015-30/06/2020	Partner	4,876,821	224,812.00
Neuron Cofund	ERA NET NEURON in the area of brain-related diseases and disorders of the nervous system	01/01/2016-31/12/2021	Partner	6,772,342.50	257,812.50
EJP RD	EUROPEAN JOINT PROGRAMME ON RARE DISEASES	01/01/2019-31/12/2023	Partner	55,073,831.17	765,898.00



7. BIOETHICS

The Sub-Directorate General of Cell Therapy and Regenerative Medicine Research (SGITCYMR) coordinates all Bioethics-related Committees supported by ISCIII, as well as other related structures such as the National Stem Cell Bank (BNLC) and the National Register of Biobanks. The activity of each of them carried out during 2018 is summarized below.

ADVISORY COMMITTEE FOR HUMAN TISSUE AND CELL DONATION AND USE

This Committee is closely related to the BNLC; during 2018, a total of 30 research projects received information.

NATIONAL STEM CELL BANK

Thirty induced pluripotent stem cell lines (iPS) were deposited in the BNLC. These lines were established in the following Research Centers: 8 in the Cajal Institute of the CSIC, 6 in the Institute for Bioengineering of Catalonia (IBEC), 4 in the Pompeu Fabra University, 4 in the Foundation of the Institute of Ocular Microsurgery (IMO), 3 in the GENYO center, 2 in the Prince Felipe Research Center (CIPF), 1 in the Health Research Institute of Santiago de Compostela (IDIS), 1 in the Center for Diagnosis of Molecular Diseases of the Autonomous University of Madrid (CEDEM) and 1 in the Institute for Biomedical Research Alberto Sols (IIBM).

In 2018, the transfer of eighteen stem cell lines (seven embryonic, eleven iPS) for eight projects (four of which from foreign centers) developed by eight researchers was requested and approved.

SPANISH BIOETHICS COMMITTEE

Since its Technical Secretariat falls under the SGITCYMR, in 2018 renewal of the members of the Committee took place, as set out in Order SSI/598/2018, of May 9, which provides for the termination and appointment of members of the Spanish Bioethics Committee. Accordingly, the members of the Committee are: **1) at the proposal of the Autonomous Communities**, as agreed by the SNS Interterritorial Council: Mr. Vicente Bellver Capella, Mr. Manuel de los Reyes López, and Ms. Leonor Ruiz Sicilia; and **2) at the proposal of the Spanish General Administration**: for the Ministry of Economy, Industry and Competitiveness: Ms. Encarnación Guillén Navarro. For the Ministry of Health (MSCBS): Mr. Rogelio Altisent Trota and Mr. Álvaro de la Gándara del Castillo.

RESEARCH ETHICS COMMITTEE (CEI)

During 2018, 121 requests for reports on research projects involving human beings were evaluated. These projects came from ISCIII centers and from Foundations affiliated to the Institute.

RESEARCH ETHICS AND ANIMAL WELFARE COMMITTEE (CEIYBA)

During 2018, 30 research projects involving the use of animals were evaluated. These projects came from ISCIII centers and from Foundations affiliated to the Institute.

NATIONAL REGISTER OF BIOBANKS

On 31 December 2018, a total of 96 biobanks and 1,679 collections were included in the Register; one new biobank and 135 new collections were registered during 2018.

TECHNICAL UNIT FOR THALIDOMIDE VICTIMS

The Health and Social Services Commission of the Spanish Parliament approved on November 24, 2016 a non-legislative motion (NLP) on the protection of people affected by Thalidomide. At its meeting on November 8, 2017, the SNS Interterritorial Council created two specific working groups: the Institutional Commission for Thalidomide and the Scientific and Technical Committee for Thalidomide. The Secretary General of Health and Consumer Affairs, by resolution of February 13, 2018, entrusted ISCIII with the creation of a Technical Unit to coordinate all actions of the Evaluation Units created in the Autonomous Communities, and to establish an information system to channel the reports from persons applying to participate in the procedure vis-à-vis their final assessment by the Scientific and Technical Committee. This Technical Unit falls under the SGITCYMR of ISCIII, which has been coordinating during 2018 all the information that is being generated in this process, provides support to the Scientific and Technical Committee and collects the documentation generated by the Evaluation Units of the Autonomous Communities.

On December 31, 2018, a total of 541 applications had been received and 200 progress reports had been compiled.



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EXECUTIVE SUMMARY **2018**



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