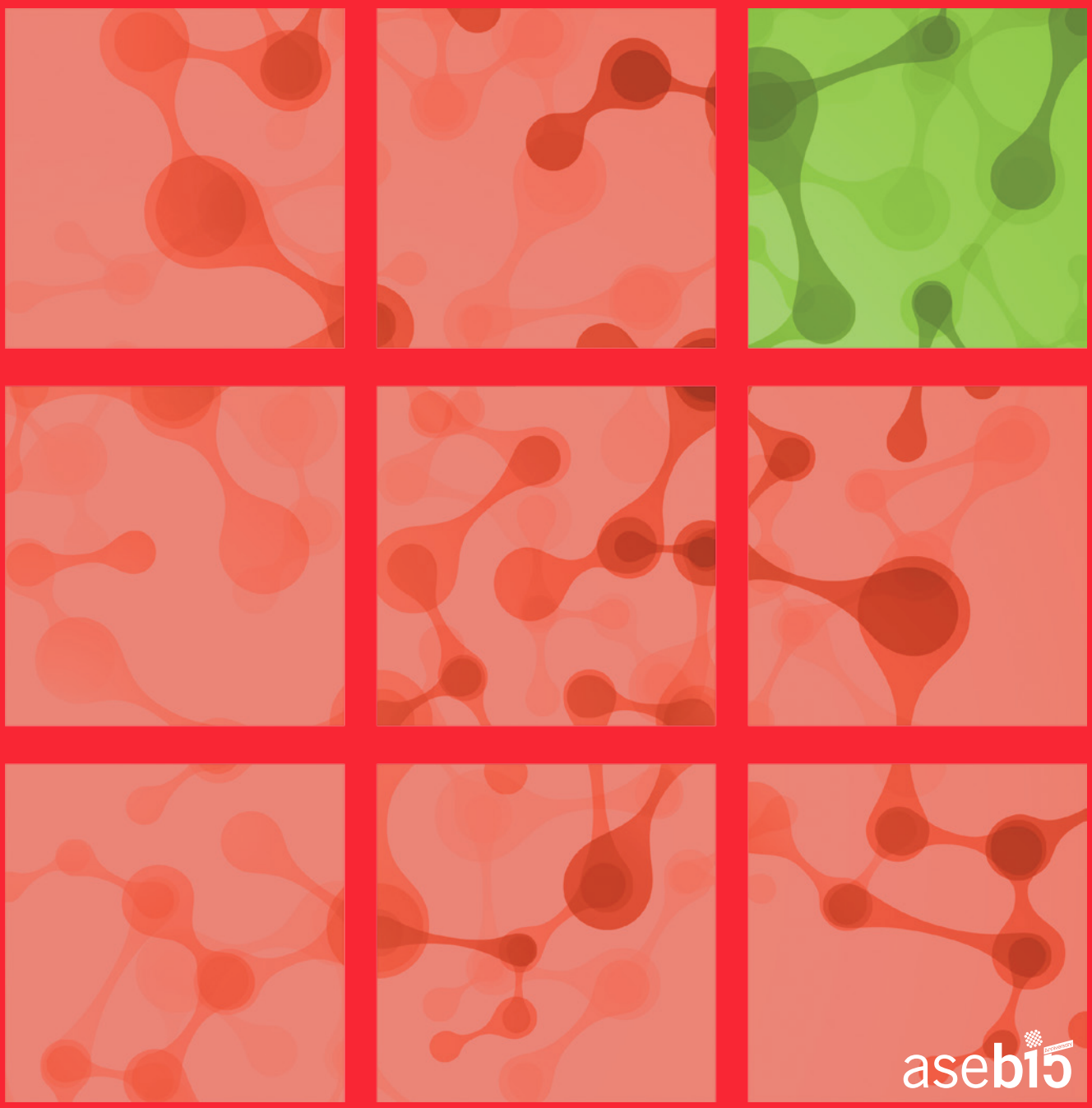
ASEBIO REPORT 2013

News and trends from
the Spanish Biotech Sector
and company guide



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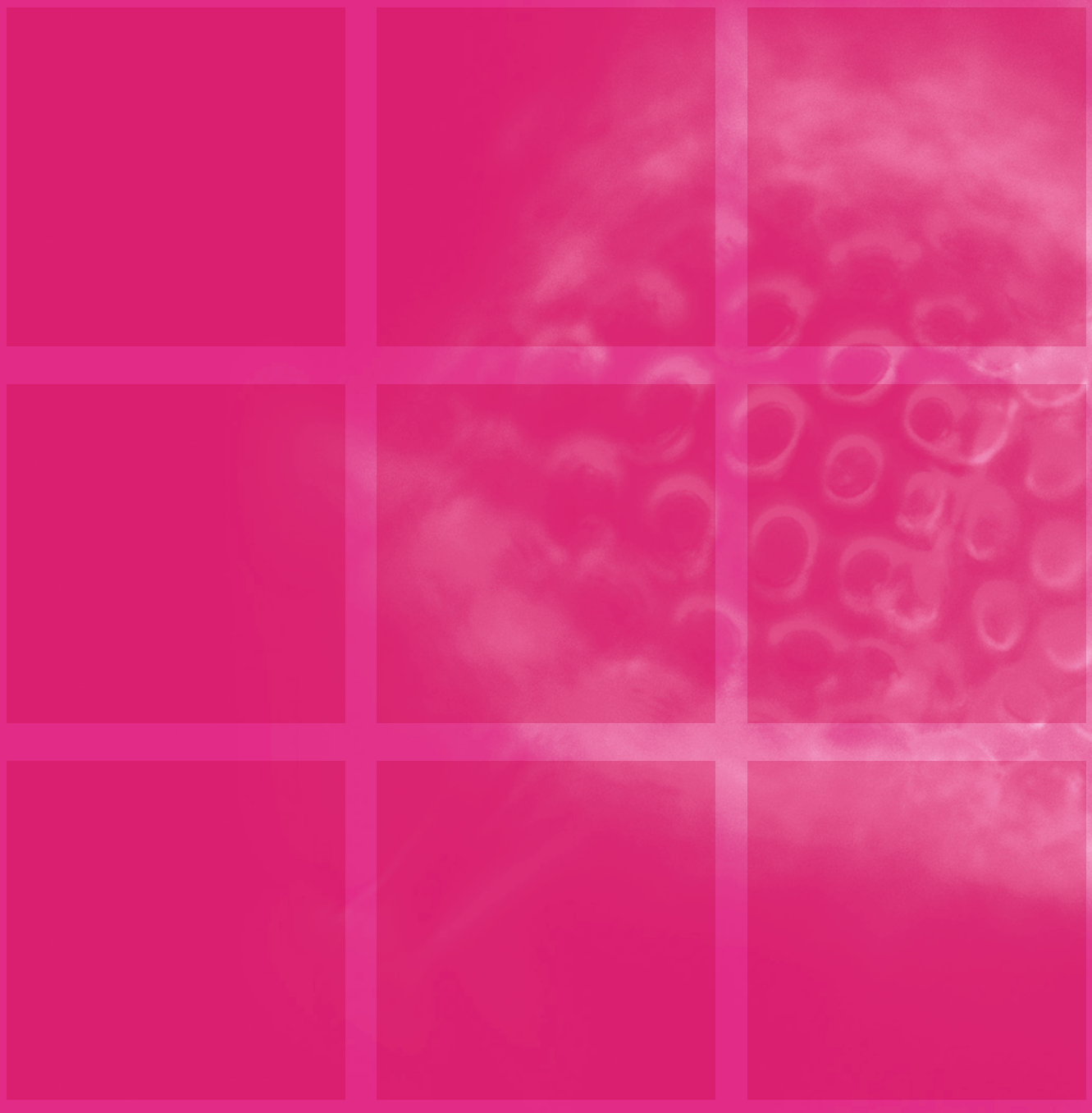


01 Status of the Spanish *biotechnology sector*

Status of the Spanish biotechnology sector

Overall, the results published in this report show a continuing positive evolution of the primary indicators for the sector, although at a significantly slower rate than in previous years:

- The number of companies engaged in biotechnology related activities remains practically the same as last year. There has been a slight increase, bringing the total up to 3070 companies (+1.48%).
- 625 companies have indicated that biotechnology is their main and/or only activity (they are often referred to as biotechs), a 5.3% decrease compared to 2011 (the first decrease of this indicator in the history of the sector in Spain).
- 726 new job positions were created in 2012, making it a slight increase of 0.36% compared to the previous year.
- The total turnover for biotechnology user companies rose to 80.312 million euros in 2012 (+5.58%).
- Focusing exclusively on the biotechs, the number of people employed by this type of company has increased by almost 5%, while turnovers have grown by 10.8%. This puts the fall in the number of companies into context, but what does continue to worry is the latest decrease in internal expenditure on R&D (-2.7%) following on from last years (-5.3%).
- The impact of Spain's biotechnology user companies on national GDP has risen to 7.8% from 7.15% last year. We should remember that in 2008 this indicator did not exceed 3%, which again illustrates the vibrancy of the sector.

Table 1 reflects the evolution of the main baseline indicators for the sector. In general, the overall results continue to be positive, although some indicators for R&D activities show the emergence of a worrying new trend. Figures 1 and 2 show the evolution in the number of people working for the sector and the total turnover in the last few years.

Table 2 shows the relationship between those indicators and other variables such as whether biotechnology is the primary and/or exclusive activity (biotechs), a secondary activity or just a necessary tool.

Main variables	*Under 250 employees*	*Over 250 employees*	*2012 total*	*2011 total*	*Variation*	*Growth rate*
Companies engaged in biotechnology-related activities	2,968	102	3,070	3,025	45	1.48%
Companies engaged in biotechnology as main and/or sole activity (biotechs)	604	21	625	660	-35	-5.30%
Companies engaged in biotechnology as a second line of business	263	25	288	368	-80	-21.73%
Companies engaged in biotechnology as a production tool	2,100	56	2,156	1,997	159	7.96%
Companies engaged in biotechnology R&D	965	71	1,036	1,041	-5	-0.48%
Total employment	76,414	126,562	202,976	202,250	726	0.36%
Turnover (in millions of Euros)	13,721	66,592	80,312	76,069	4,243	5.58%
Biotechnology R&D staff (no, of employees)	6,812	2,176	8,988	8,800	188	2.14%
A) Total by role						
Researchers	3,998	1,372	5,370	5,124	246	4.80%
Technicians and assistants	2,815	804	3,618	3,676	-58	-1.57%
B) Number of women	3,694	1,282	4,976	4,853	123	2.53%
Researchers	2,106	732	2,839	2,648	191	7.21%
Technicians and assistants	1,588	550	2,137	2,205	-68	-3.08%
Internal expenditure in biotechnology R&D (in thousands of Euros)	381,561	141,783	523,344	537,884	-14,540	-2.70%

Main variables	Under 250 employees	Over 250 employees	2012 total	2011 total	Variation	Growth rate
A) Type of expenditure						
Current expenditure	328,422	135,535	463,956	467,542	-3,585	-0.77%
- salaries for researchers	127,007	58,043	185,050	181,686	3,365	1.85%
- Salaries for technicians and assistants	60,763	23,605	84,368	86,895	-2,527	-2.91%
- Other current expenses	140,652	53,887	194,539	198,961	-4,422	-2.22%
Capital expenditure	53,139	6,248	59,387	70,342	-10,955	-15.57%
- Land and buildings	23,433	1,555	24,988	14,869	10,119	68.05%
- Equipment and devices	28,013	4,529	32,542	52,395	-19,854	-37.89%
- R&D-specific software	1,694	164	1,858	3,077	-1,219	-39.61%
B) Source of funding						
Funding from Spain	327,516	119,579	447,095	465,550	-18,455	-3.96%
- Own funds	211,077	89,438	300,515	315,372	-14,857	-4.71%
- Companies	22,077	11,312	33,389	41,160	-7,771	-18.88%
- Public funding	87,452	17,922	105,373	102,901	2,472	2.40%
- Universities	665	0	665	113	552	488.49%
- Private non profit institutions	6,245	907	7,153	6,004	1,149	19.13%
Funding from overseas	54,045	22,204	76,249	72,333	3,916	5.41%
- EU programmes	14,974	2,433	17,407	9,831	7,576	77.06%
- Other overseas funding	39,071	19,771	58,842	62,502	-3,660	-5.85%
% Companies having filed biotechnology patent applications	7%	24%	7%	5%	NA	NA
Number of patents filed	506	122	628	430	198	46.04%

Table 1. Main results for the biotechnology section of the 2012 Survey on Innovation in Companies

	Principal			Secondary			Tool				
Principal variables	Value in 2011	Value in 2012	% Over total in 2012	Value in 2011	Value in 2012	% Over total in 2012	Value in 2011	Value in 2012	% Over total in 2012	Total in 2012	Total in 2011
Units engaged in biotechnology related activities	660	625	20.36%	368	288	9.38%	1,997	2,156	70.23%	3,070	3,025
Units engaged in biotechnology R&D	524	465	44.88%	198	205	19.79%	319	366	35.33%	1,036	1,041
Biotechnology staff (no. employees)	6,266	7,141	41.55%	2,529	2,016	11.73%	6,945	8,028	46.72%	17,185	15,739
Biotechnology expenditure (in thousands of Euros)	544,997	535,736	62.79%	132,005	112,908	13.23%	160,409	204,542	23.97%	853,185	837,412
Internal R&D expenditure in biotechnology (in thousands of Euros)	372,736	353,373	67.52%	83,022	74,878	14.31%	82,126	95,093	18.17%	523,344	537,884
% Companies filed biotechnology patent application	17.8	22.6	NA	4.1	10.4	NA	1.5	2.4	NA	7.3	5.4
Number of patents filed	320	389	NA	49	118	NA	61	121	NA	628	430
Turnover (in thousands of Euros)	7,944,597	8,801,580	10.96%	45,360,438	38,387,308	47.80%	22,764,341	33,123,662	41.24%	80,312,549	76,069,376
Total number of employees	33,183	34,827	17.16%	56,056	49,848	24.56%	113,011	118,301	58.28%	202,976	202,250

Table 2: Distribution of main indicators for the sector in 2012 by type of biotechnology activity

The indicators included in Table 1 show a stabilisation and levelling-off of the growth experienced over recent years. Although many indicators continue to be positive (except those for R&D investment), symptoms of a change in trends continue to worry, particularly when we analyse their evolution over recent years and take into account that the data provided by the National Statistical Office (INE) is for 2012.

The number of companies declaring biotechnology related activities over last year rose by 1.48%. Meanwhile, for the first time in the history of the sector, the number of biotech companies decreased by -5.3% (which means 35 less companies), as did (-0.5%) the number of companies engaged in biotechnology R&D.

From a macro perspective, both turnovers and the number of people employed by the sector continue to increase, though at much lower rates (+5.58% and +0.36%). Taking a closer look at the type of user company, we see that companies of under 250 employees continue to predominate (96.68% of the total). If we consider the impact of the sector on national GDP (the turnover of user companies as a proportion of Spain's GDP), we see that it continued to increase over the year, up to 7.8% of GDP (compared to 7.15% the previous year and taking into account that in 2008 it was at 3%).

The good news comes from the micro perspective, because when we focus exclusively on the evolution of biotechs over the last year, we find that the number of people

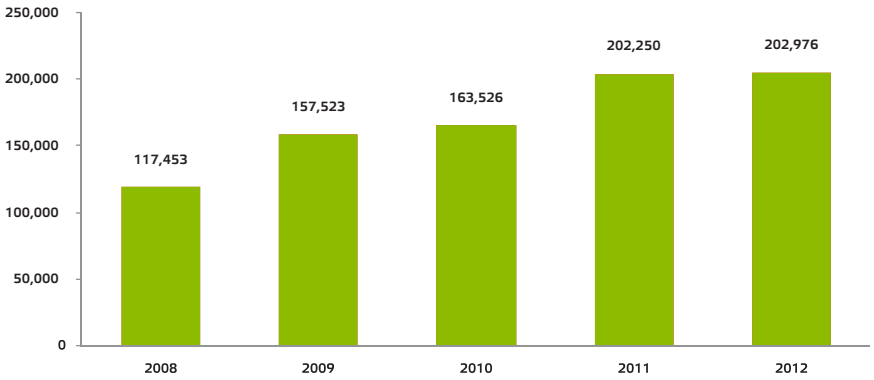


Figure 1: Evolution of employment (number of employees)

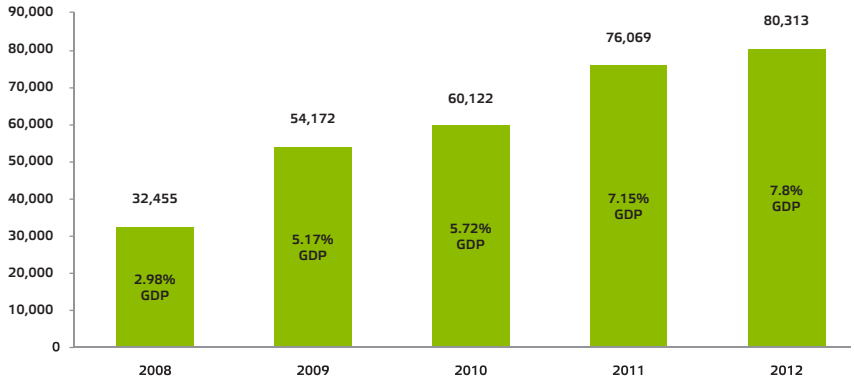


Figure 2: Evolution of the turnover (in millions of euros)

Figure 3: Evolution of expenditure in R&D (in millions of euros)

employed grew by almost 5% and that their turnovers have increased by 10.78%.

As shown in Figure 3, the most worrying figure comes from a key element for the future competitiveness of the sector, internal expenditure on biotechnology R&D. In 2012 the number fell by 2.70% following on from another decrease the previous year (-5.3%) and nearly dropping to 2009 levels.

The most significant fall is in subcontracted R&D (-18.88%).

If we analyse the source of the investment in R&D we see that most sources of funding are Spain-based (85.43%), as in previous

years. Within national sources of funding the proportional distribution is also similar to that of the previous year: own funds (67.21%), Public Administration (23.57%), other companies (7.47%) and non-profit institutions and universities (1.75%).

The latest survey by the Spanish Statistical Office shows that the total turnover for the Spanish biotechnology sector mainly comes from those companies which state that biotechnology is a secondary line of business for them (47.8%) and those which consider biotechnology to be a necessary tool for production (41.24%). Biotechs only contribute 11% of the total.

In terms of employment, the business type to distribution ratio varies according to the volume of business: tool for production (58.28%), secondary activity (24.6%) and main activity (17.2%).

The number of patent applications filed increased significantly over the year (+46.15%). Such volatility, along with the big 33.2% drop the previous year, suggests that the statistical sample obtained from the data collection method has a very big impact on the final number.

Interestingly, in terms of gender balance, the percentage of women working in biotechnology R&D remains steady at 55% (for the fourth year in a row).

Finally, Figures 5 and 6 show the sectoral distribution of biotechnology user companies and biotechs. It is noticeable, on the one hand, that food industry (68.5%) and healthcare companies (19.7%) predominate within the user sectors, while for another year, the order is inverted when it comes to *the* biotechs, as has been the case in recent reports: healthcare (52.6%) and food (32.3%).

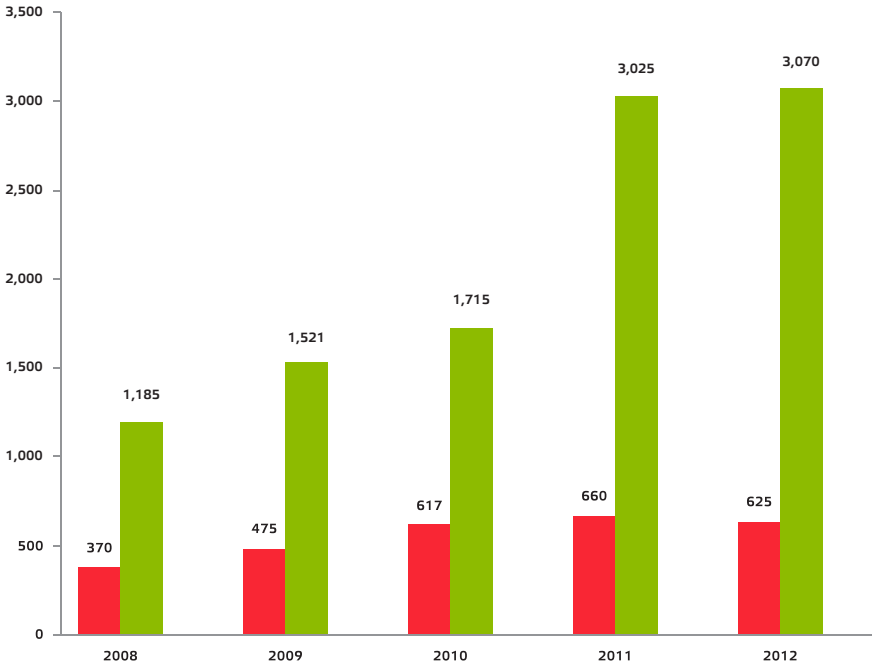


Figure 4: Evolution of the number of companies engaged in biotechnology

Figure 5. Percentage of user companies based on the final application of the biotechnology

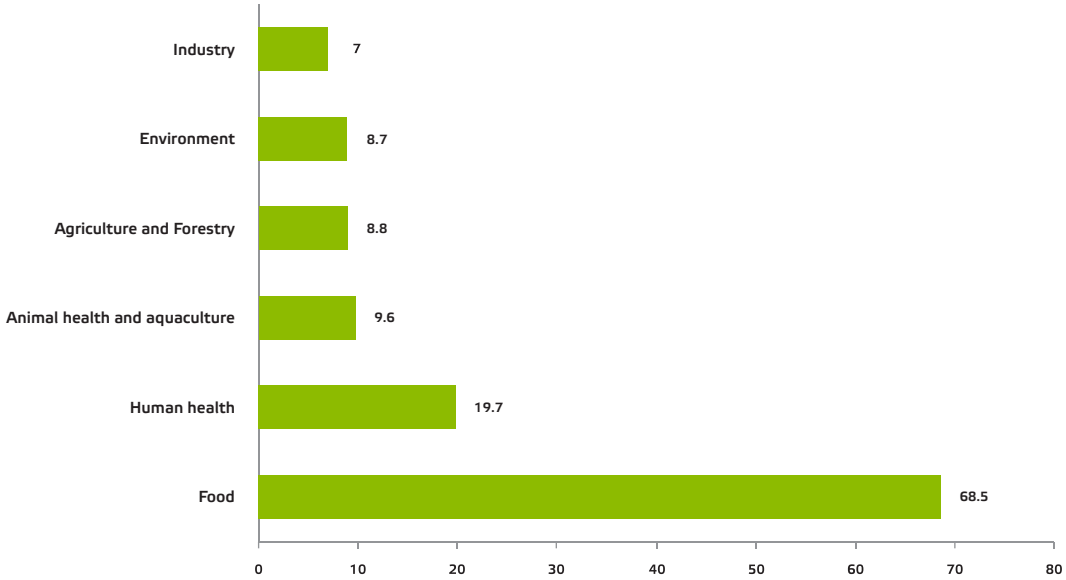
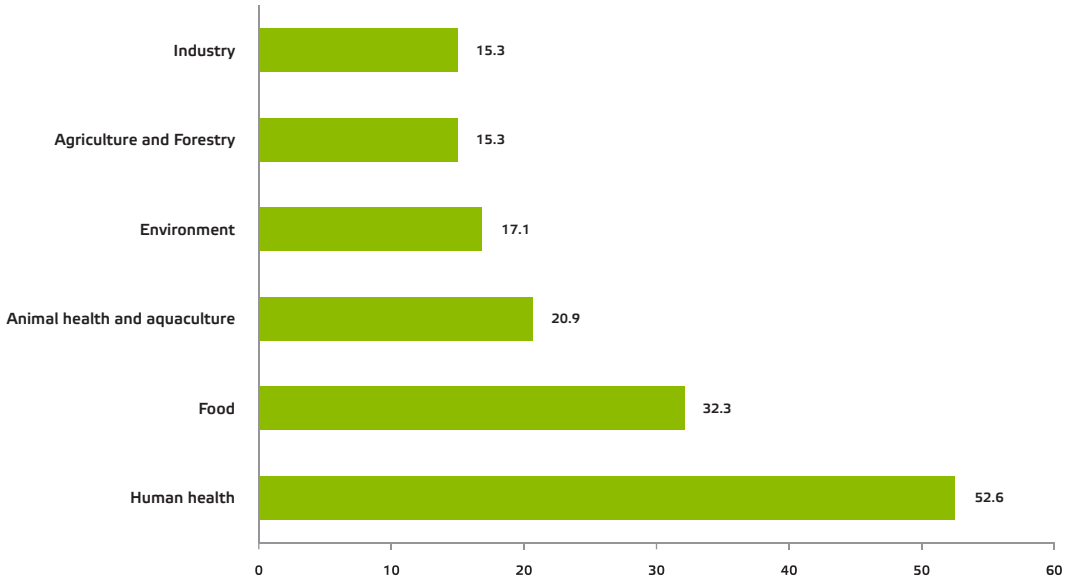


Figure 6. Percentage of biotechs based on the final application of the biotechnology



A geographical analysis of the indicators

Figure 7 shows that Catalonia is in the lead in terms of the concentration of biotechnology user companies (18.61%). Followed, like last year, by Andalusia (which now accounts for 14.6% of the total) and Madrid (13.14%). They are followed by the Basque Country (9.73%), Castile-Leon (6.94%), Galicia (6.78%) and Valencia (6.29%).

From a methodological perspective we should bear in mind that those areas with a less developed industrial fabric show significant variations vis-a-vis other annual reports. The variations could be the result of the previously mentioned random statistical sampling method. We should mention that in 2010 the Spanish Statistical Office introduced a methodological change in that the companies used in its reports were no longer collected from the census and instead have gone on to being collected through a random sampling.

Figure 8 shows that the geographical distribution of the leading group for biotechs also follows the same pattern as that of user companies. Catalonia leads the rankings (with 21.76% of the total), followed by Andalusia (16.15%), Madrid (15.91%) and the Basque Country (10.91%), which in this area is part of the leading group. For the number of biotechs, the next group includes Valencia (8.95%) and Galicia (5.07%).

Figure 7. Geographical distribution of biotechnology user companies

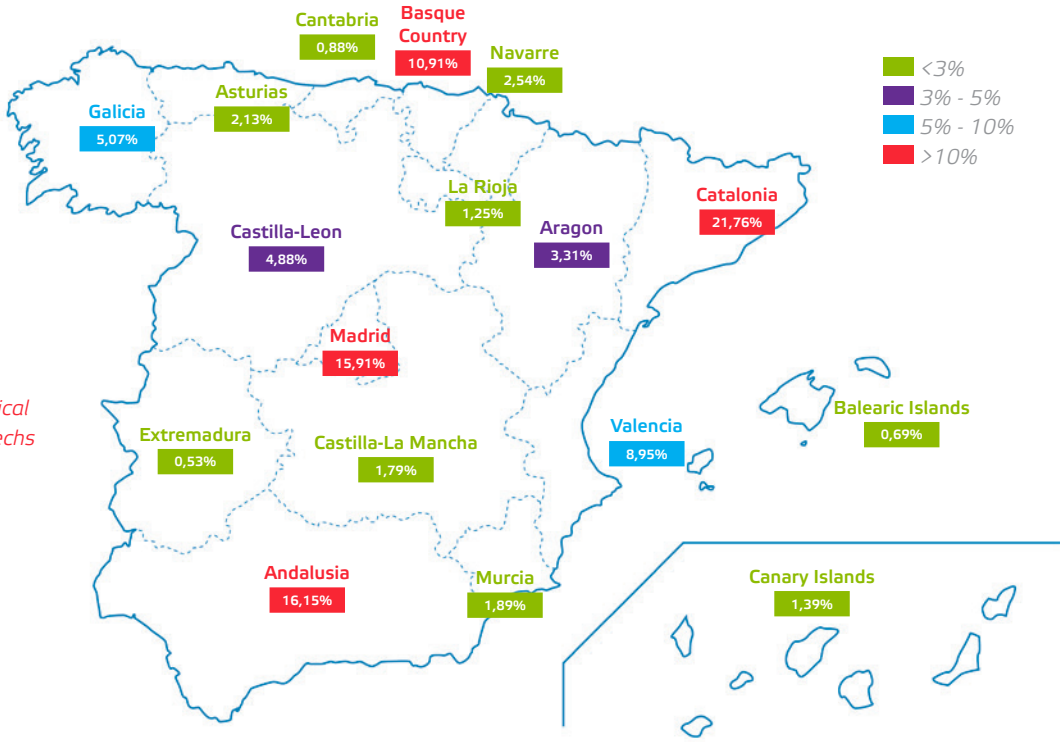


Figure 8. Geographical distribution of biotechs

Competitive cooperation in the Spanish biotechnology sector

For over three years the ASEBIO report has been analysing the performance and evolution of the so-called 'innovative biotechnology companies', that is, those which responded that they brought about technology innovation through the use of biotechnology (either in products or processes) during the two years before the date of the survey.

According to our analysis of the sample of 625 biotechs which made up the sector in 2012, 52% state that they have carried out some sort of technological innovation over the two previous years, 190 of those having collaborated in some way with other organisations. Figure 9 is the product of an in-depth analysis of this latter group, in it we look at who have been the most active agents in these collaborations with innovative biotechnology companies. Topping the list are collaborations with public sector entities: universities and other higher education institutions (73.32%) — typically public institutions — as well as public research institutions (65.16%). They are followed by collaborations with clients, consultants and laboratories, competitors, providers, other companies belonging to the same group and public sector clients.

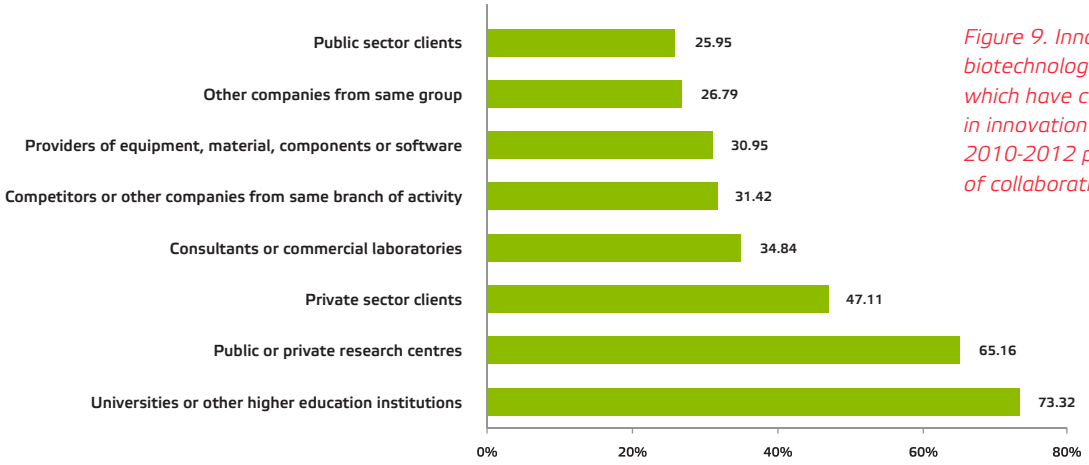


Figure 9. Innovative biotechnology companies which have cooperated in innovation during the 2010-2012 period, by type of collaboration

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02 Companies *created in 2013*

Companies created in 2013

In the analysis done by ASEBIO in collaboration with other entities, 2013 saw the creation of 71 new companies whose activities include biotechnology.

The following entities collaborated in the study: BIC Asturias, Área de Planificación Sectorial de la Junta de Castilla y León, SODENA, CEEI Valencia, BIOVAL, Parque Científico de Madrid, BIOGA, BIOCAT, Barcelona Science Park, Dirección General para la Innovación Consejería de Industria, Innovación y Empleo del Gobierno de La Rioja, SPRI, Instituto de Fomento de la Región de Murcia, Grupo Sodercan, Clúster Biotecnológico de las Islas Baleares (Bioibal), Zona Especial Canaria (ZEC), Agencia IDEA, Bioregión de Andalucía and the Parque Tecnológico de Albacete.

Among the autonomous communities, Catalonia had the largest number of new companies (26), followed by Andalucía (14), six new companies were launched in Galicia and five in the Basque Country.

Madrid and Valencia witnessed the creation and launch of four new companies (each).

Table 3 shows the complete list of new biotechnology companies launched in 2013 by autonomous community and area of activity.

Company	*Autonomous community*	*Activity*
ABIOPEP	Murcia	Disease diagnosis and products for the protection of crops.
Acellera	Catalonia	Marketing, distribution, sale and installation of IT equipment and software solutions for science.
AD3-ENERGY	Andalusia	Development of an effective system of anaerobic digestion for agrifood industry residues with high concentrations of suspended solids.
ALGAFUTURE INCIATIVAS SOSTENIBLES	Andalusia	R&D on known and productive species of microalgae for the productions of high added value products for the pharmaceutical, cosmetics and agrifood markets – in both human and animal orientated products.
ALSOL THERAPEUTICS	Andalusia	Providing innovative services in the field of rare diseases.
Artintvet	Basque Country	Development and commercialisation of products and services related to regenerative veterinary medicine, mainly oriented to pets (dogs and cats) and competition animals (horses).
BBD- Biophenix	Basque Country	Zebrafish laboratory for the pharmaceutical and biotechnology industries.
Bichos services	Murcia	Entomological and agri-environmental services for the agricultural sector. Biological plague control.
BioModel	Catalonia	Engineering firm providing prototypes for bioscience field.
BIONOS BIOTECH	Valencia	Functionality analysis of genes, ingredients and products using custom made research. Biological, microbiological and toxicological assays on animal and cell models both *in vivo* and *in vitro*. Disease modelling and drug R&D.
BIOSPINDIA	Madrid	Production of autologous growth factors.
Biotech Development	Catalonia	Solutions for biotech drug R&D. A*d-hoc* services for the promotion of projects.
BIOTONIK	Andalusia	Energy drinks and nutritional compounds.
BIOTRONIC SALUD	Andalusia	Pain treatment based on medical devices designed by Biotronic. R&D.
BLUE BIOTECH TENERIFE	Canary Islands	Culture of algae and other aquatic vegetation; conversion of products for medical, cosmetics and nutrition uses; commercialisation of cultures or products obtained; R&D of new cultures.
BOLT-ON BIOTECH	Basque Country	Development and marketing of a production system for therapeutic cells.
BRAIN HOUSE	Andalusia	Use of neurosciences and Psychophysiological variables in behavioural analysis of physical stimuli - and its marketing applications (neuromarketing).
CABANA GENETICS	Andalusia	R&D project management, scientific and technical consultancy. Design and development of biomedical devices. Molecular biology.
Cebiotex	Catalonia	Technology and services for R&D in the field of polymeric nanofibers drug delivery.
CIRCE Crystal Engineering	Balearic Islands	Specialised in polymorphs and pharmaceutical cocrystals.
Cogstate Spain	Catalonia	Clinical trials.
CORESOFT CLINIC	Andalusia	Dedicated to the development, maintenance and support of online medical registers. Data management services and all types of medical information extraction.
DERETIL VITATECH	Andalusia	Production of polyphenol extracts and combinations from various natural sources.
Developbiosystem	Galicia	Biotechnology R&D.

Company	*Autonomous community*	*Activity*
Electrochemistry for Lightweight and Integrated Analytical Solutions (ELIAS)	Andalusia	Development of biosensors and chemical sensors, manufactured and marketed as a tool for analysis and quality control in the food industry.
EmbryoTools	Catalonia	R&D and services for assisted reproduction.
ENDOASIC Technologies	Catalonia	Provides integrated circuits for medical products in endoscopy. The company focuses on technologies for non-invasive diagnosis of early stages of digestive cancer and its therapy.
ENDOTOXIN DETECTION	Basque Country	Development and commercialisation of platform for endotoxin quantification in biological reagents, pharmaceutical products and devices.
ENZYMLOGIC	Madrid	Enzymology and protein engineering providing innovative solutions for the pharmaceutical and biotechnology industries.
EVONUTRION	Andalusia	Design and development in functional nutrition for improved health, treating and preventing conditions and developing the industrial processes necessary for advanced nutrition products to develop into industrially viable food.
FENIX HEALTH SCIENCES	Madrid	Development, production and marketing of solutions for personalised medicine, clinical diagnostics and biomedical research.
Formas Naturales	Catalonia	Design and development of audiovisual content for science dissemination and education.
Galgo Medical	Catalonia	Software development for medical imaging.
Genocosmetics	Catalonia	Dermocosmetic skin treatment for the prevention of skin ageing and to obtain diagnostic information: DNASkin Matrix Mapping TM
Global and Ecofriendly Natural Extracts	Galicia	Experimental R&D in natural sciences and processes.
Health&sportlab	Catalonia	Cater for people's health and lifestyle needs by providing practical, comfortable, non-invasive tools through mobile devices.
Impetux Optics	Catalonia	Design, manufacturing and marketing of optical force measurement systems for Optical Tweezers. Their instruments measure forces exerted on an optically trapped particle by a single beam trapping system.
Indrops Laboratorio de Analisis y Calidad Medioambiental	Galicia	Assays, sample collection and pick up, in situ measurement, remote monitoring of parameters, environmental, agrifood, and quality management consultancy.
Innovamed Spain	Catalonia	Industrialisation services for single use medical devices.
LifeScience Entrepreneurs	Catalonia	Develops scientific discoveries which may provide solutions to unresolved basic health needs.
Making Genetics	Navarre	Services for genomics based studies including project design and management, genetic and epigenetic determination, interpretation of results and statistical analysis. Development and commercialisation of new genetic and epigenetic panels.
Manremyc	Catalonia	Development of Nyaditum resae®, a natural probiotic product.
Medcom Advance	Catalonia	Develops nanotechnology-based products. Its first project is a system for the immediate detection of infection causing microorganisms.
MEL Pharma	Balearic Islands	Improvement of existing products and development of new products and services to find solutions for known issues in the health field (medicine, biotechnology and food)
Mint Labs	Catalonia	Remote advanced medical image analysis and visualization platform.
MITELOS BIOSCIENCE	Catalonia	Development, registration and out-licensing of nutraceuticals, medical devices, oral care products, dermocosmetics and drugs.
Mosaic Biomedicals	Catalonia	Development of personalised cancer treatments specifically designed to target cancer stem cells.
MPA Veterinary Medicines and Additives	Catalonia	Produces exports medicines, additives and feed supplements.
NANOCUSTOM	Castile-La Mancha	Development of products based on biocompatible and environmentally friendly nanoparticles for use in soil decontamination, water purification, biomass, antimicrobial applications, and encapsulation of biologically active compounds.
Neuraltech Biopharma	Valencia	Provides support services for research, clinical diagnostics and veterinary diagnostics.
Neuropharmatest	Valencia	Using animal models Neuropharmatest evaluates the efficacy of drugs at the preclinical level for neurological and psychiatric conditions such as schizophrenia, depression, alzheimer and parkinson's.
NORTEM CHEM	Andalusia	Production of citric acid for the pharmaceutical, cosmetics and food industries using sugar beet molasses.
Oncostellae	Galicia	Research, development and marketing of products and services for the field of diagnostics and treatment of diseases, pharmaceutical development, training, scientific and technical consultancy.
Pragmatic Diagnostics	Catalonia	Consultancy and Laboratory R&D services to established companies, spin-offs and start-ups to help them in bringing new products to the market within the IVD field.
PROTEOTRON	Asturias	Researches, develops and commercialises tools to facilitate the purification, identification and quantification of proteins in biomedical samples.
Q'omer BioActive Ingredients	Valencia	Designs, develops and commercialises products and natural bioactive ingredients for the production of functional food and beverages, dietary supplements, nutraceuticals, pet food and personal care products.
Raman Health Technologies	Castile-Leon	Validation of biomarkers in blood samples using Raman laser spectroscopy and the development of a new non-invasive diagnostic technology platform for the diagnosis of Alzheimer's disease in a blood sample. The product will be targeted at the *in vitro* diagnostics market.

Company	*Autonomous community*	*Activity*
Recombina	Navarre	Offers a range of customised services to meet specific needs of genetic engineering projects.
RGA Bio-Investigación	Castile-Leon	Research, consultancy, development and marketing of processes, products, services and technological solutions for the requirements of the wine industry and related sectors.
Rob Surgical Systems	Catalonia	Manufacture and marketing of surgical systems.
SAMURAN XXI	Basque Country	New therapeutic procedures based on plasmapheresis technology for chronic and immunology-based diseases.
SM Genomics	Catalonia	Laboratory specialised in genetics analysis for professional sportspeople and athletes to improve and increase performance.
Smalle Technologies	Catalonia	Exploit new methods and sources of clean and renewable energy that do not depend on fossil fuels or have a negative impact on the environment.
Software 4 Science Developments	Galicia	Design, development and marketing of software for the field of science; data hosting and analysis services; science and IT consultancy; technical assistance; training and dissemination of scientific and technical content.
Subtilis Biomaterials	Catalonia	Technology developed from biomaterials, biomechanics and Tissue Engineering.
Synergy Map (Hammame)	Balearic Islands	Manufacturing, marketing and distribution of cosmetic products, perfumes, beauty products, and personal hygiene products, as well as their importation and exportation.
TALEMNOLOGY	Andalusia	Development of medical devices that allow the patient to participate in the treatment process while simultaneously optimising and rationalising the activities of the health professionals.
Vetter Terapia Celular Veterinaria	Galicia	Cell therapy for the treatment of diseases in animals. Assay design and execution.
VITAGENIA HEALTH CARE	Madrid	Development and marketing of health solutions for the identification of risk of developing diseases associated with genetic profiles and prevention through nutraceuticals.
XTREM BIOTECH	Andalusia	Development of extremophilic bacteria for sustainable and environmentally friendly solutions.
ZeClinics	Catalonia	CRO offering an outsourcing solution for safe and efficient screenings of novel chemical molecules using zebrafish

Table 3: Biotechnology companies that started operating in 2013. Source: ASEBIO

03 Business *activities*

Business activities

Alliances and business development activities

This section looks at business development activities by members of ASEBIO. It includes biotechnology alliances and/or collaborations (co-marketing, co-development, product and market exchanges) with other entities initiated in 2013.

During 2013, according to our figures, there were 205 alliances of which almost 50% involved another biotech firm, 34% biotech user company and nearly 50% involved other types of organisations.

Regarding the country of origin of the partner (Figure 11), over 40% of all agreements were with Spanish companies, while 29% involved European entities, over 10% from the US, 6% were Asian companies and nearly 5% involved Latin American companies.

In terms of the objectives of the collaboration in question (Figure 12) 26.83% focused on R&D, 32.2% were 'development alliances' (clinical, field trials, etc), 25.85% were marketing and distribution agreements, 20.49% production alliances and 2.44% were agreements regarding regulation and/or industrial protection (intellectual property rights).

As we did for the 2012 ASEBIO report, we again conducted a brief survey on the barriers faced by entities engaged in alliances.

Figure 13 outlines the obstacles found by companies during alliances over the last year, both nationally and internationally.

One of the most common stumbling blocks encountered during the course of alliances in 2013 was that the economic benefits obtained were insufficient (14% never found this to be the case, 51% responded that it happened sometimes, 1% said it always the case and 34% frequently found it to be the case).

18% of companies often found that they did not have the size or financial stability to commit themselves. 16% felt they had found that they lacked the means to identify the best partner for them.

Figure 10. Distribution of alliances in the Spanish biotechnology sector in 2013 by profile of partner. Source: ASEBIO

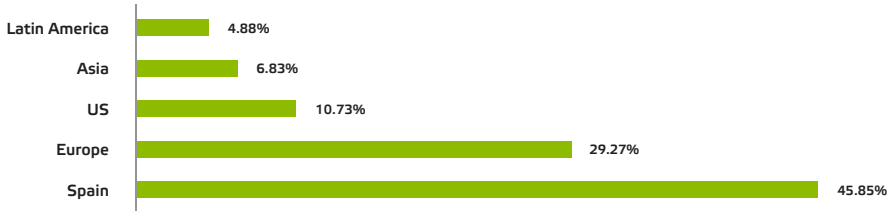


Figure 11. Distribution of alliances in the Spanish biotechnology sector in 2013 by world location of partner. Source: ASEBIO

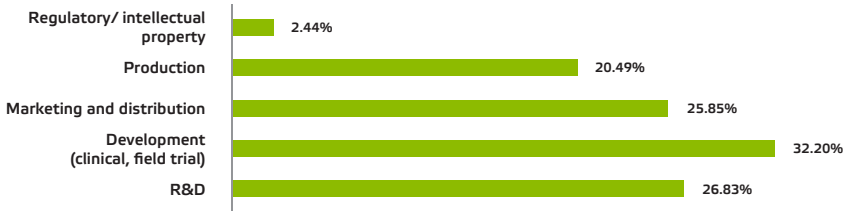


Figure 12. Distribution of alliances in the Spanish biotechnology sector in 2013 by objective of alliance. Source: ASEBIO

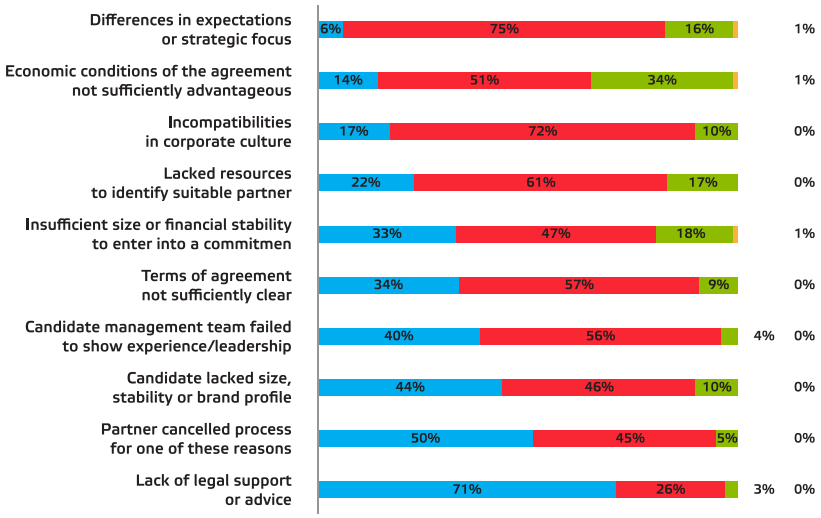


Figure 13. Barriers encountered in forming alliances by entities taking part in the survey. Source: ASEBIO

Product launches

Our records show that over 2013 a total of 126 products were launched by ASEBIO members.

Table 4 lists all launches by name of the entity, product name and description, and type of product or service.

60% of all launches were within red biotechnology or health, followed by white/industrial biotechnology which accounted for 26% of product launches and then the green or agrifood area which came to 14% of the total.

Figure 14 shows the number of launches by section and area: green, red or white biotechnology.

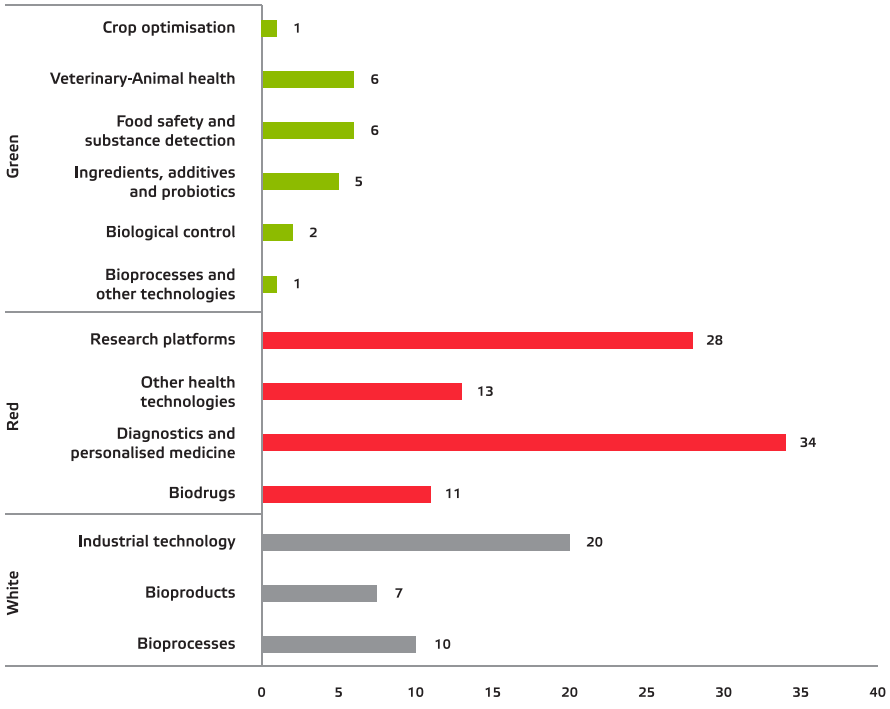


Figure 14. Products and services launched to market by ASEBIO members. Source: ASEBIO

Table 4. Products and services launched to market by ASEBIO members. Source: ASEBIO

Company	*Product name and description*	*Biotechnology area*
3P Biopharmaceuticals	AMBR 24: microreactor system for cell line development and process optimisation. HTS bioprocess development.	Red: other health technologies
3P Biopharmaceuticals	Analytical platform for GMP development process and production of biosimilars.	Red: other health technologies
3P Biopharmaceuticals	DSP mammalian: increase purification capacity of monoclonal antibodies.	Red: other health technologies
3P Biopharmaceuticals	Tech transfer services Platform: design and execution of production process technology transfer.	Red: other health technologies
3P Biopharmaceuticals	Development of cell based bioassays / qualification and quality control test.	Red: research platforms
AB-Biotics	AB-Dentalac: probiotic specifically designed to fight caries, gingivitis and halitosis or bad breath.	Green: ingredients, additives and probiotics
AbbVie	CREON: Delayed-Release Capsules for patients with exocrine pancreatic insufficiency caused by cystic fibrosis, chronic pancreatitis or pancreatectomy	Red: research platforms
AC-Gen Reading Life	HC-Gen Test: sequencing panel for the analysis of 37 genes and 89 SNP linked to hereditary cancer.	Red: diagnostics and personalised medicine
Almirall	Eklira® Genuair®: new medicine for the treatment of COPD.	Red: biomedicine
Almirall	Neurofarmagen: test for use in neurology and psychiatry that identifies the safest and most appropriate medication for each individual patient (marketed in Spain).	Red: diagnostics and personalised medicine
Almirall, S.A. and Ironwood Pharmaceuticals	Constella® (linaclotide 290mcg capsules once daily), the first approved prescription therapy in a new class of treatments for adults suffering from moderate to severe IBS-C, in Europe.	Red: biomedicine
AMGEN	XGEVA® (denosumab): for the prevention of skeletal-related events in patients with bone metastases from solid tumors.	Red: biomedicine
Azierta and GMV	Vigilazierta® is software for drug and health-product safety management and support for all phases of clinical trials guaranteeing user compliance with all current recommendations, directives and regulations.	Red: other health technologies
Biochemize	Platform for the use of ionic liquids and green solvents to carry out advanced reactions in biocatalysis.	White: bioproducts and bioprocesses
Biochemize	Platform for high performance lipases and esterases.	White: bioproducts and bioprocesses
Bioiberica S.A.	Crop-Scan®: diagnosis service of crop stress, based on aerial images obtained by thermal and multispectral cameras in manned aircraft.	Green: crop optimisation
Bioiberica S.A.	Suzukii Trap®: is a food attractant specifically designed for the capture of Drosophila suzukii. It is composed of organic acids and highly potent attractant peptides.	Green: biological control
Bioiberica S.A.	Arthrotest: clinically validated tool based on the genotyping of SNPs, which identifies the genetic predisposition of any individual patient to suffer rapid progression of primary osteoarthritis of the knee	Red: diagnostics and personalised medicine
Biogen Idec Iberia, S.L.	FAMPYRA LP (prolonged-release fampridine tablets). Treatment for symptoms of Multiple Sclerosis used to improve walking.	Red: biomedicine
Biokit	Bioelisa HIV 1+2 4.0: test for the detection of antibodies to HIV-1, HIV-2 and HIV-1 p24 antigen.	Red: diagnostics and personalised medicine
Biokit	BIO-FLASH HSV-1 IgG assay. For the diagnosis of Herpes 1 and 2.	Red: diagnostics and personalised medicine
Biomedal	AlerTox Sticks: for the detection of milk and egg allergens in foodstuffs, drinks and surfaces.	Green: food safety and substance detection
Biomedal	AlerTox ELISA Allergen: sandwich type immunoabsorbent assay designed for the detection and quantification of the allergen.	Green: food safety and substance detection
Biomedal	AlerTox ELISA Specific for wine: sandwich type immunoabsorbent assay for the quantitative determination of allergens in Wine.	Green: food safety and substance detection

Company	*Product name and description*	*Biotechnology area*
Biomedal	ProPure: affinity ligands and resins for antibody purification.	White: bioproducts
Biomedal	Cellena Microanalyzer: system for rapid cell analysis of individualised cells, microcolonies and cell consortiums.	White: bioprocesses
Biomol-Informatics	G4U: genome sequencing service, which from a blood test, can identify markers that show a potential predisposition to genetic diseases.	Red: research platforms
Bionaturis	BNT009: antimicrobial peptide with specific antimicrobial activity against L. Garvieae.	Green: veterinary-animal health
Bionet	CIP system for cleaning of equipment (fermentors, tangential flow filtering systems and tanks).	White: industrial technology
Bionet	Continuous esterilizable fermentation and filtration MBR_F system. For the removal of supernatant in fermentation processes subject to inhibition.	White: industrial technology
Bionet	Tangential filtering system with R50 and R500 polymer membrane. For concentrate via RO/ NF of clarified substances from fermentation. Complementary to its existing M50 and M500 UF/MF ceramic membrane product.	White: industrial technology
BTI Biotechnology Institute	New regenerative medicine implantology solutions.	Red: diagnostics and personalised medicine
CIRCE Crystal Engineering	CPS: Circe Polymorph Screening, polymorph prediction tool to identify the most stable polymorphs in an API study, making laboratory studies for their characterisation better targeted and more efficient.	Red: research platforms
CIRCE Crystal Engineering	CCS: Circe Cocristal Screening, first computational predictive tool for the search of pharmaceutical cocristals (API+coformer) from a base of 2500 coformers, reducing the coformers to test in the laboratory to 1%.	Red: research platforms
CIRCE Crystal Engineering	Neural-Mining: Hardware (FPGA) for screening of large databases for molecular patterns in the course of drug-discovery. The technology makes it possible to carry out fast and efficient screenings at very high speeds 13GBytes/second.	Red: research platforms
Coresoft Clinic S.L.	CoreTools 4.0: new version of statistical tools for research groups.	Red: research platforms
Cytognos	Four EuroFLow CE-marking screening tubes based on combinations designed by euroflow™ consortium: lst (lymphoid screening tube), alot (acute leukemia orientation tube), pcst (plasma cell screening tube), sst (small sample tube).	Red: research platforms
EntreChem	12 Chiral Synthons for medical chemistry: 8 cis amino alcohols and 4 cis diamines.	White: bioproducts
Enzymlogic	Detailed characterisation services of interactions between new pharmacological molecules and their targets . Determination of kinetic parameters and molecular mechanism in kinase inhibitors.	Red: research platforms
Era7 Bioinformatics	AG7 Method to obtain closed bacterial genomes combining illumina and Pacbio.	White: industrial technology
Ferrer inCode	Genetic diagnostics test for the detection of 12 genetic variants related to Thrombophilia.	Red: diagnostics and personalised medicine
GENOMICA	PneumoCLART® Bacteria: molecular diagnostics kit for the detection of respiratory infection causing bacteria.	Red: diagnostics and personalised medicine
GENOMICA	autoclart®: robotic system for automatic sample visualisation process.	Red: other health technologies
Glen Biotech S.L.	Integrated Control Programme for red palm weevil: sustainable and efficient solution for insect through product and application.	Green: biological control
GP Pharm	Lutrate 1 month.	Red: biodrug
Grifols	AlphaKit QuickScreen: alfa-1 antitripsina (AAT) deficiency detection kit effective within 15 minutes.	Red: diagnostics and personalised medicine
Grifols	Cell fragmentation GMP laboratory device.	White: industrial technology
Grifols	Automatic system for sterilisation of analgesic solution bag.	Red: other health technologies

Company	*Product name and description*	*Biotechnology area*
Grifols	New device to prepare vials totally automatically in kits of small and medium lots with multiple configurations.	White: bioprocesses
Grifols	Plasma Bag Opener (PBO®): new development for cleaning, thawing and emptying of biotech and biological products.	White: bioprocesses
Grifols Engineering	New aseptic vial dosifier for biotech products.	White: bioprocesses
Grupo Farmasierra	Solvilit: food supplement based on standardised extract of Hydroxytyrosol at 1.5%, recommended for cardiovascular disease.	Green: ingredients, additives and probiotics
Grupo Farmasierra	Omedrai: Omega-3 food supplement from fish oil.	Green: ingredients, additives and probiotics
Histocell	Wharton Gel Complex: new cosmetics ingredient with regenerative properties.	Red: other health technologies
Igen Biotech	iGEN FFPE kit: DNA extraction kit for use in paraffin embedded samples.	White: bioproducts
Igen Biotech	New iGENatal kit: developped as improved version of iGENatal kit eliminating need for Phenol and keeping same high performance levels.	Red: diagnostics and personalised medicine
Igen Biotech	iGEN Hemokit: DNA extraction kit developed for blood samples requiring a minimal quantity of initial sample.	Red: other health technologies
INGENASA	INGEZIM WEST NILE IgM: ELISA for the detection of IgM specific for West Nile in horse serum.	Green: veterinary-animal health
INGENASA	INGEZIM SCHMALLENBERG COMPAC: ELISA for the detection of antibodies specific to Schmallenberg in ruminant serum.	Green: veterinary-animal health
INGENASA	INGEZIM MAEDI SCREENING: ELISA for the detection of antibodies specific to ruminant lentivirus.	Green: veterinary-animal health
INGENASA	INGEZIM FVR: ELISA for the detection of antibodies specific to RIFT valley fever in ruminant serum.	Green: veterinary-animal health
INGENASA	INGEZIM Beta-lactoglobulina crom: rapid immunochromatographic test for detection of beta-lactoglobulin in foodstuffs.	Green: food safety and substance detection
INGENASA	INGEZIM caseina crom: rapid immunochromatographic test for detection of casein in foodstuffs .	Green: food safety and substance detection
InKemia IUCT group	Impurities: isolation, characterisation and synthesis of impurities in active ingredients medicinal products.	Red: research platforms
InKemia IUCT group	Plant markers: extraction, analysis and characterisation of markers in plants.	Green: bioprocesses and other technologies
Innaves, en colaboración con el CSIC	Lowpept: food supplement to help control blood pressure.	Green: ingredients, additives and probiotics
Instituto de Medicina Genómica	Skeletal Displasias NextGeneDx, multi gen panel for diagnostics of Neonatal Encephalopathy, with diagnostic quality.	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica	Childhood NextGeneDx, multi gen panel for diagnostics of Spondyloepiphyseal dysplasia , with diagnostic quality.	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica	Cardiopathy NextGeneDx, multi gen panel for diagnostics of Congenital heart defects, with diagnostic quality.	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica y BIOEF - Hospital Universitario Cruces/ BIOCRUCES	Imegen-SCAs (Ref. IMG-152): test for molecular diagnostics of neurological diseases caused by triplet repeat expansion disorders (SCA panel).	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica y BIOEF - Hospital Universitario Cruces/ BIOCRUCES	Imegen-SBMA (Ref. IMG-153): test for molecular diagnostics of neurological diseases caused by triplet repeat expansion disorders (Kennedy's disease).	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica y BIOEF - Hospital Universitario Cruces/ BIOCRUCES	Imegen-Huntington (Ref. IMG-154): test for molecular diagnostics of neurological diseases caused by triplet repeat expansion disorders (Huntington's disease).	Red: diagnostics and personalised medicine
Instituto de Medicina Genómica y BIOEF - Hospital Universitario Cruces/ BIOCRUCES	Imegen-Friedreich (Ref. IMG-155): test for molecular diagnostics of neurological diseases caused by triplet repeat expansion disorders (Friedreich's ataxia).	Red: diagnostics and personalised medicine

Company	*Product name and description*	*Biotechnology area*
Instituto de Medicina Genómica y BIOEF - Hospital Universitario Cruces/ BIOCRUCES	Imegen-DM1 (Ref. IMG-173): test for molecular diagnostics of neurological diseases caused by triplet repeat expansion disorders (Myotonic dystrophy type 1).	Red: diagnostics and personalised medicine
Laboratorios Rubió	TDAGEN+: to predict treatment response through saliva sample as well as define patient metabolic profile for medicines used for ADHD. Determine predisposition to ADHD. Determine if there is added risk of comorbidity.	Red: diagnostics and personalised medicine
Merck Serono	Immuno oncology platform integrating research, early development and strategies with biomarkers.	Red: research platforms (Screening, Enabling Technologies, CRO, Drug Delivery)
MSD	ISENTRESS tablets 100/25 mg: formula in tablet form which can be chewed for pediatric patients with HIV infection.	Red: biodrug
MSD	MONTELUKAST MSD EFG: generic montelukast formula for the treatment of patients suffering from Asthma.	Red: biodrug
Myriad Genetics	Prolaris®, prognostic test with 46 genes to determine aggressiveness of prostate cancer.	Red: diagnostics and personalised medicine
Nanoimmunotech	NITZIPPER: family of products ready for simple, effective and immediate conjugation via an innovative bioconjugation technology based on complementary characteristics of Linker U and Linker T.	White: bioproducts
Nanoimmunotech	Nitparticles: new line to find a wide variety of high quality particles (micro and nanoparticles), in a centralised manner.	White: bioproducts
nanoMyP	Tiss-Link: nanofibre tissue made through ectrospinning which is preactivated for direct covalent immobilisation of biomolecules	Red: other health technology
Neiker Tecnalia	Early detection method for the diseases: mildew, oidio and Botrytis, common in vines.	Green: food safety and substance detection
Neol	Tecnología MBO™ conversion of crude glycerol (FAME) into triglycerides through fermentation.	White: bioprocesses
Neuron BioServices (Neuron Bio Group)	Evaluation of research projects involving the use of animals for experiments in compliance with RD53/2013.	Green: veterinary-animalhealth
Neuron BioServices (Neuron Bio Group)	Analysis of the effect of ingredients and pharmaceutical drugs on the development of the central nervous system based on zebrafish embryos.	Red: research platforms
Neuron BioServices (Neuron Bio Group)	Method for the detection of adverse effects of new compounds on the eye.	Red: research platforms
Neuron BioServices (Neuron Bio Group)	Exclusive zebrafish model for the search of new medicines for epilepsy.	Red: research platforms
Neuron BioServices (Neuron Bio Group)	Measurement of anti-inflammatory/ immunological capabilities of compounds undergoing study.	Red: research platforms
Neuron BioServices (Neuron Bio Group)	Method for the detection of adverse effects of new compounds on hearing.	Red: research platforms
NIMGenetics	OncoNIM CF Cáncer Familiar: test for the detection of the presence of mutations due to large amount of deletion affecting 30 genes related to the most common hereditary cancers.	Red: diagnostics and personalised medicine
NIMGenetics	OncoNIM®Seq 50: massive sequencing panel for the identification of mutations in 50 oncogenes and suppressor genes.	Red: diagnostics and personalised medicine
OPERON	Opegen HLA B27 Strip, molecular diagnostics test using northern blot on a strip for the detection of HLA B*27 alleles associated with Ankylosing spondylitis.	Red: diagnostics and personalised medicine
OPERON	Opegen HLA B5701 Strip molecular diagnostics test using northern blot on a strip for the detection of HLA B*5701 alleles associated with hypersensitivity to the retroviral abacavir.	Red: diagnostics and personalised medicine
OPERON	Simple Norovirus, immunochromatographic test for the detection of norovirus in faeces.	Red: diagnostics and personalised medicine
PlantResponse Biotech S.L.	Stemicol ®: fitovacuna vegetal modulator of innate immune response in plants. Marketed and manufactured by LIDA plant research.	Green: ingredients, additives and probiotics
Plebiotic	Gambit: novel reverse docking platform which uses a wide collection of human proteins.	Red: research platforms

Company	*Product name and description*	*Biotechnology area*
Plebiotic	Maeras (Pharmacophores): software. Tool for drug repositioning.	Red: research platforms
Promega	GenePrint(R) 10 System: Human identification though STRs (Small Tandem Repeats).	Red: diagnostics and personalised medicine
Promega	Trypsin/Lys-C Mix, Mass Spec Grade: Digestion of proteins for identification through mass spectrometry.	Red: research platforms White: industrial technology
Promega	Quantus (TM) Fluorometer: Quantification of nucleic acids.	Red: research platforms White: industrial technology
Promega	NAD(P)H-Glo Detection System, NAD/NADH-Glo and NADP/NADPH-Glo Assays: Study of enzymes which produce or use NAD.	Red: research platforms White: industrial technology
Promega	PowerPlex(R) ESX 17 Fast and ESI 17 Fast System.	Red: diagnostics and personalised medicine
Promega	CellTiter-Glo(R) 2.0 Assay: Cell viability study.	Red: research platforms White: industrial technology
Promega	HDAC-Glo(TM) Class IIa Assay: study Histone Deacetylases activities for compound screening.	Red: research platforms White: industrial technology
Promega	GloMax(R) Discover System: Device for the measurement of fluorescence and luminescence assays (cell viability, apoptosis, ELISA, etc.).	Red: research platforms White: industrial technology
Promega	ViaFect(TM)Transfection Reagent: cell transfection reagent.	Red: research platforms White: industrial technology
PROTEOS Biotech	Development and launch of new line of business: manufacture and sale of cosmeceutics based on the activity of various recombinant enzymes produced on-site.	White: bioproducts
Reig Jofré	Nife-Par: management of preterm birth.	Red: biodrug
Reig Jofre	Blox4: Allergy relieves nasal symptoms of allergies caused by pollen and house dust mites. Provides instant protection for up to 12 hours.	Red: biodrug
Roche	Sistema FLOW: for standardised workflows with greater flexibility and intelligent data management for laboratories with a high number of samples.	White: industrial technology
Sanofi Pasteur MSD	FILA HEXYON® provides protection from six diseases (diphtheria, tetanus, whooping cough, Hepatitis B, poliomyelitis and Haemophilus influenzae type b).	Red: biodrug
SECUGEN	NGS genetic analysis of infantile epileptic encephalopathy.	Red: diagnostics and personalised medicine
Sistemas Genómicos	Onco GeneProfile 80: genetic panel to analyse up to 80 genes associated with susceptibility to hereditary cancer.	Red: diagnostics and personalised medicine
Sistemas Genómicos	GeneSys: platform for integral analysis of data from resequencing studies to identify genomic variants for every individual.	Red: research platforms
Stem Center	GID SVF-1: device to isolate stromal vascular fraction cells (that contain the adipose tissue-derived mesenchymal stem cells) from human lipoaspirate.	Red: other health technologies
Stem Center	GID700: device to harvest, rinse, filter and obtain an adipose graft.	Red: other health technologies
SYGNIS Biotech	QUALIPHI®, marketed as SensiPhi®, is used in DNA amplification techniques.	White: bioproducts
SYGNIS Biotech	New technology for the detection of interactions between proteins, it is a novel analytical platform for the development of new medicines (has obtained patents for Europe and the US).	Red: research platforms
TiGenix	ChondroCelect®, is the first cell therapy product for the treatment of cartilage; launched in Spain after obtaining national reimbursement in April 2013.	Red: other health technologies
Vircell	Respiratory Viral Screening & Identification MAb: product for the direct detection and screening and identification of the 7 main respiratory viruses.	Red: diagnostics and personalised medicine
Vircell	VirClia® Monotest: new Vircell line based on chemiluminescence technology in monodose format (53 references).	Red: diagnostics and personalised medicine

Company	Product name and description	Biotechnology area
Vircell	HELICOBACTER PYLORI ELISA IgA: immunoenzymatic assay for the semi quantitative detection of IgA antibodies to identify Helicobacter pylori.	Red: diagnostics and personalised medicine
Vircell	AmpliRun® TOTAL, 19 new references of extraction and amplification control which contain the complete inactivated microorganism in a matrix that mimics human specimens. Product delivered quantified and in lyophilized format.	Red: diagnostics and personalised medicine White: bioprocesses
Vircell	AmpliRun® DNA/RNA controls, 10 new references of amplification controls which contain the purified complete genome of the infectious agent.	Red: diagnostics and personalised medicine White: bioprocesses
Vivotecnia Research	Inhalation unit for chemical and phytomedical agents.	Red: research platforms

Strategic priorities

This section looks at the priorities of biotechnology companies that are ASEBIO members for 2014 and compares them to those for 2013.

The results of the 2014 questionnaire are shown on Table 5.

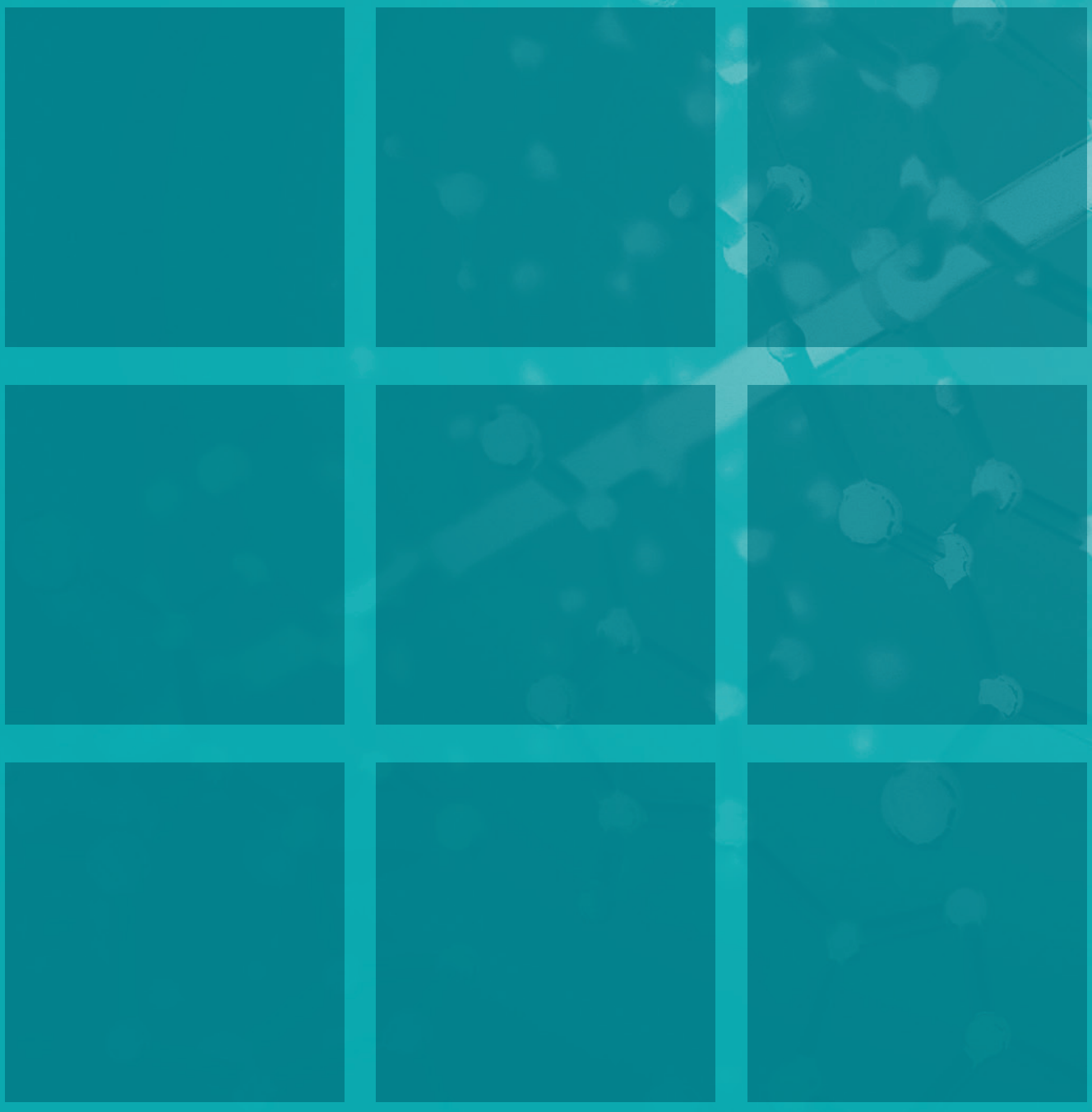
Internationalisation continues to be the top priority for biotechnology companies in 2014. It is followed by product launches, which was valued higher than last year.

Launching clinical and field trials as well as dose scaling has increased in importance by four points over 2013. On the other hand, licensing-in technology grew in importance from 2012 to 2013 but then dropped by four points in 2014.

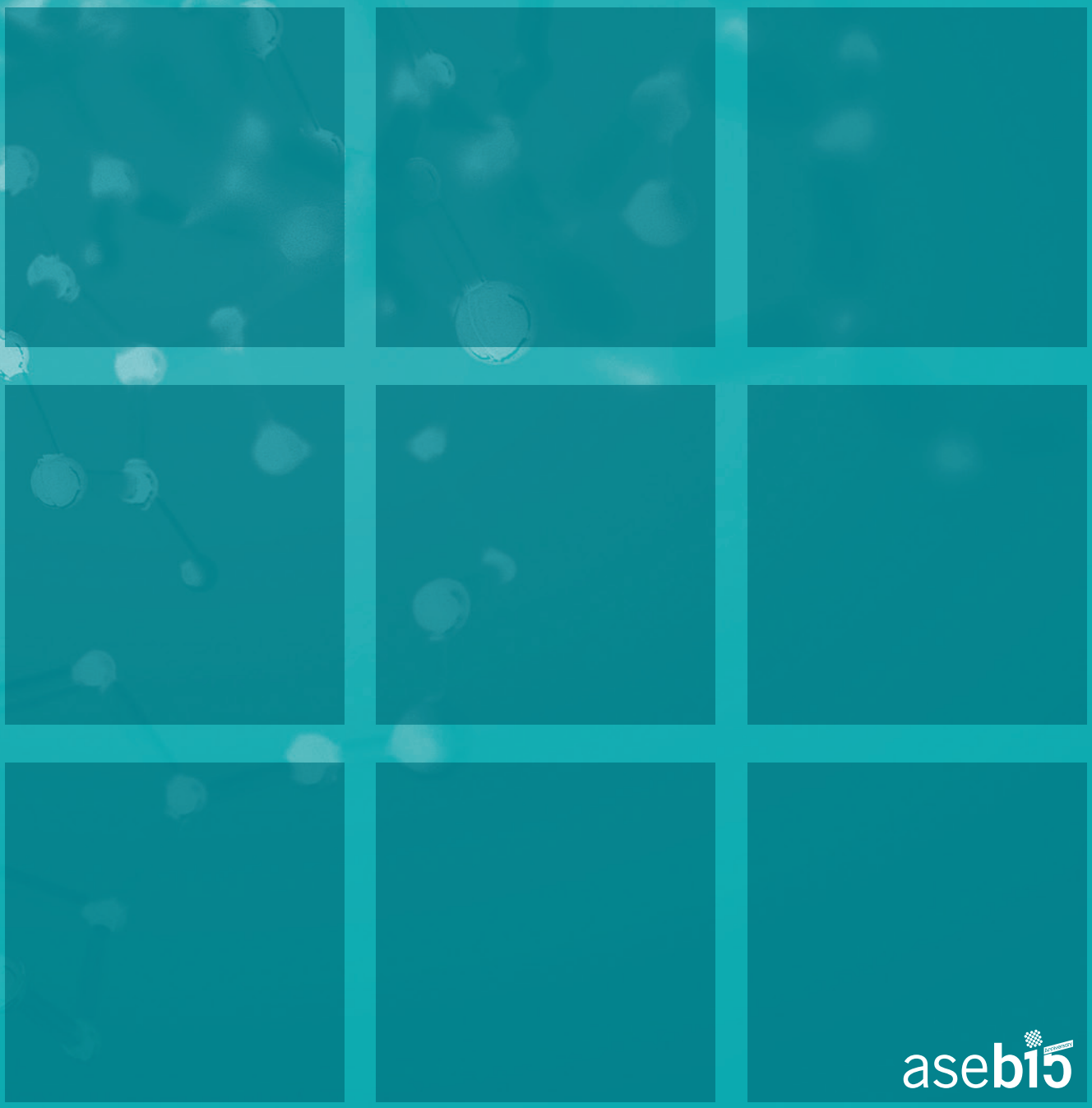
As in 2013, acquiring other companies continued to be the lowest priority.

Position 2014	Priorities	Relevance 2014	Change compared to 2013	
1	Internationalisation	3.14	/=/	0
2	Launch of products to market	2.66	↑	3
3	Acquiring knowledge and/or technology	2.57	↓	-1
4	Alliances with user companies (pharma, agrifood, etc.)	2.40	↓	-1
5	Enter into clinical phases/field trials/dose scaling	2.36	↑	4
6	Contracts or alliances with public institutions	2.26	/=/	0
7	Licencing-out technology	2.25	↓	-3
8	Alliances with other biotechs	2.19	↓	-2
9	Expand activities int other business areas	2.07	↓	-1
10	Joint venture agreements	1.49	↑	1
11	Refocus R&D	1.46	↑	2
12	Refocus product development	1.44	/=/	0
13	Licencing-in technology	1.35	↓	-3
14	Hire overseas professionals	1.30	/=/	0
15	Outsource productions	0.85	/=/	0
16	Mergers (with other companies)	0.64	↑	1
17	Reduce operations	0.51	↓	-1
18	Acquiring another company	0.44	/=/	0

Table 5. Analysis of strategic priorities for Spanish biotechnology entities for 2014. Source: ASEBIO



04 Industrial property rights *and knowledge generation*



Industrial property rights and knowledge generation

The data provided in the following Technology Watch Report was obtained using a method designed by Clarke Modet and Madrid Science Park which is based on the OECD definitions for the biotechnology sector. The methodology is the result of continuous evolution based on the experienced gained during previous studies on industrial property rights carried out in recent years.

This report was compiled using data sourced from Thomson Reuters databases.

In order to contrast the data, other public databases were used including those of: the Spanish Trademark and Patent Office (SPTO), the European Trademark Office (EPO), the United States Patent and Trademark Office (USPTO), the Japan Patent Office (JPO) and the World Intellectual Property Organization (WIPO). The date of publication of patents has also been included.

Analysis of patent applications published and patents granted

Figure 15 shows that the biggest percentage of applications were published via the PCT, accounting for 30% of the total, followed by SPTO applications (27%). In 2012 the order was inverted.

If we assume that the majority of patents filed through the SPTO are priority patents and PCT applications are intended for the internationalisation of patents, we could conclude that SPTO patents can be used as advanced indicators of future applications with the international registries, which will first focus on PCT patents and then patents for the US, Japan and Europe.

Looking at patents granted, we can see that the largest percentage is still made up of applications filed with the SPTA, which accounts for 68% of the total (see Figure 16).

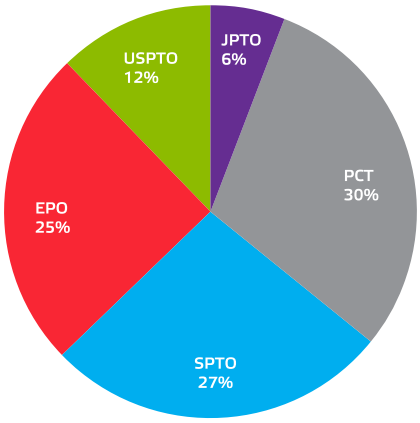


Figure 15. Distribution of filed patent applications (2013).
Source: Clarke & Modet - PCM

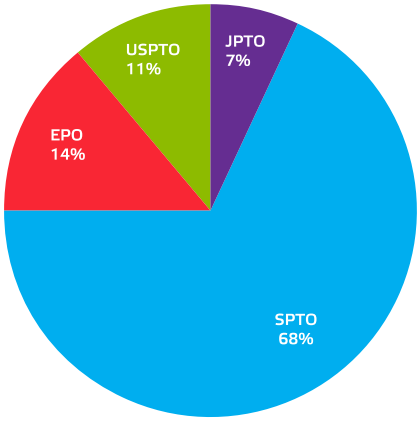


Figure 16. Distribution of patents granted.
Source: Clarke & Modet - PCM

Table 6. Number of applications and patents granted – Spanish biotechnology entities, 2013.
Source: Clarke & Modet-PCM

2013	*SPTO*	*EPO*	*USPTO*	*JPTO*	*PCT*	*Total*
Patent applications	155	143	66	33	173	570
Patents granted	226	46	37	22	0	331
Total	***381***	***189***	***103***	***55***	***173***	***901***

Analysis of patent ownership - 2013

In 2013 the business sector was the biggest player, accounting for 32% of published patents. It was followed by universities (17%), and Public Research Bodies (13%). As in previous years, both applications published and patent granted reflect this patent ownership pattern (Figure 17).

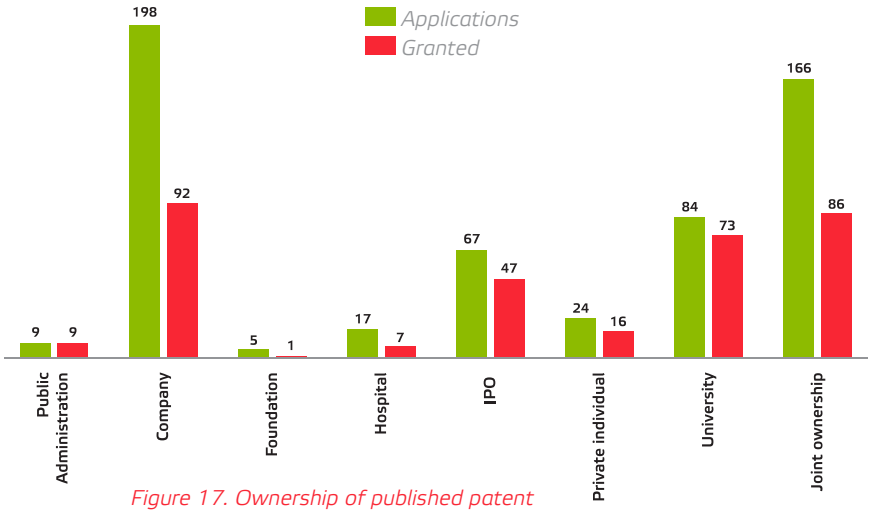


Figure 17. Ownership of published patent applications and patents granted (2013). Source: Clarke & Modet – PCM

Patent rankings by company - 2013

In 2013 a total of 142 biotechnology companies filed patent applications or had patents granted. Lipotec had the largest number of patents published in 2013, with a total of 18 applications and three patents granted, it was followed by Grifols which rose from holding 7th position in 2012 up to 2nd. The CIMA Biomedicine Project rose to 3rd position with five applications and seven patents granted.

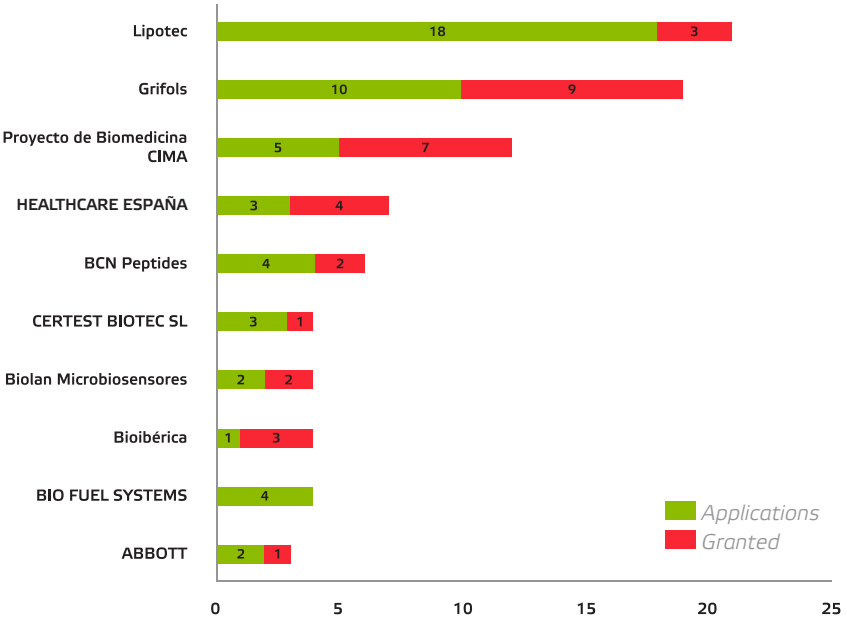


Figure 18. Companies filing patent applications and patents granted. 2013. Source: Clarke & Modet - PCM

Evolution of Industrial Property in the Spanish biotechnology sector, 2009-2013

According to the data published over the last five years, the trend in patenting activities within the biotechnology sector has experienced a sharp rise with a 109.53% growth between 2009 and 2013.This evolution not only shows that the biotechnology sector is on the rise, but also the importance of Industrial Property for the sector as a source of returns for investments. Although, as we have seen, growth is slower than in 2012 (during 2009-2012 average growth stood at 147.44%).

Taking year-on-year variations into account, there is a clear slowing in the publication of global patents from 2012 to 2013, with a decrease of 15.32% which is in line with the trend established over the previous five years but becomes more pronounced during 2012-2013.

This trend is also clearly visible in the number of applications, which grew at an average of 51.21% during 2010-2011, while during 2011-2012 growth slowed down to 23.60% and again during 2012-2013 it shrunk by a further 25.97%.

In terms of the number of patents granted we must point out the slight increase seen in 2013 of 12.59%.

The trend analysis shows the evolution experienced by each of the application routes over time.

Figure 19 shows the evolution of patents published in Spain by the biotechnology sector and the drop in the number of applications in 2013 is clear, particularly when compared to 2012.

Spanish publications (SPTO) continued their downward trend from 2012, and the rest of publications decrease in relation to the trend seen up until 2012.

Scientific Production - biotechnology companies

Every year, ASEBIO carries out a study of the publications in high impact journals by Spanish biotechnology companies and international research laboratories with a base in Spain which are ASEBIO members.

The study does not include press releases conference, poster presentations or publications by research centres or universities which do not make any references to business projects.

In 2013, biotechnology firms published a total of 260 papers, a 5% increase over the previous year, when 248 publications were recorded. Those 260 papers were published by 41 biotechnology companies.

In terms of the companies which have published most papers (Figure 20) we find MSD and PharmaMar in the top two positions with 30 and 27 publications, respectively, closely followed by BTI with 25 publications.

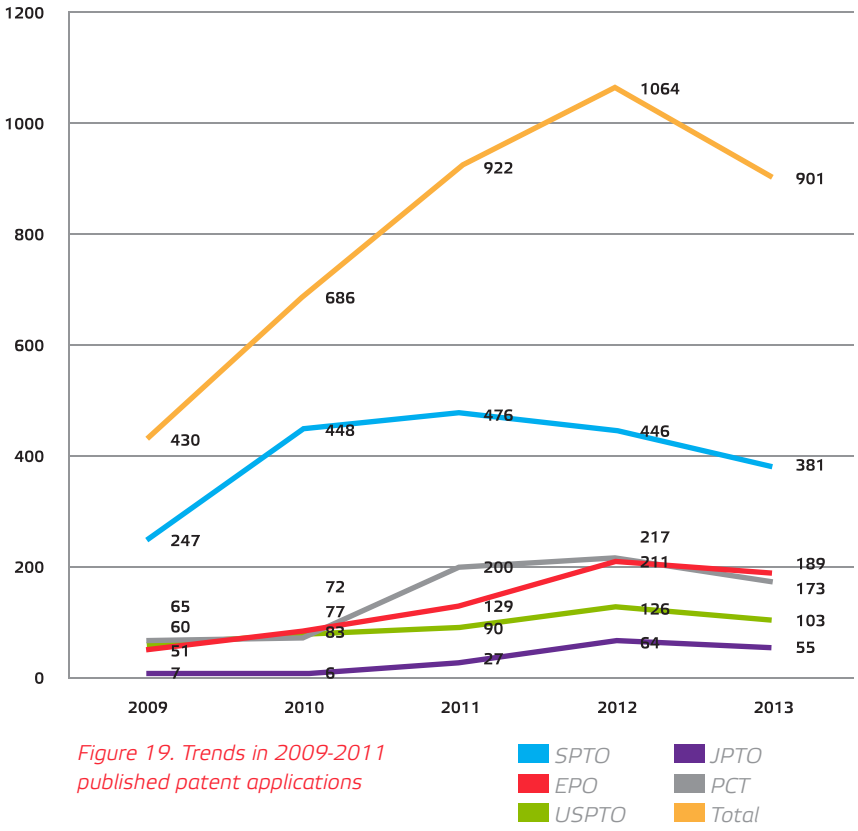


Figure 19. Trends in 2009-2011 published patent applications

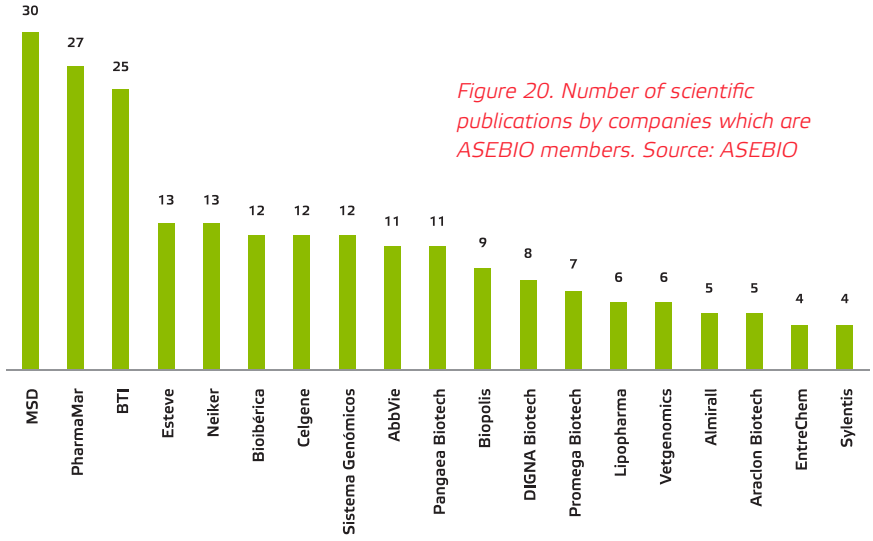
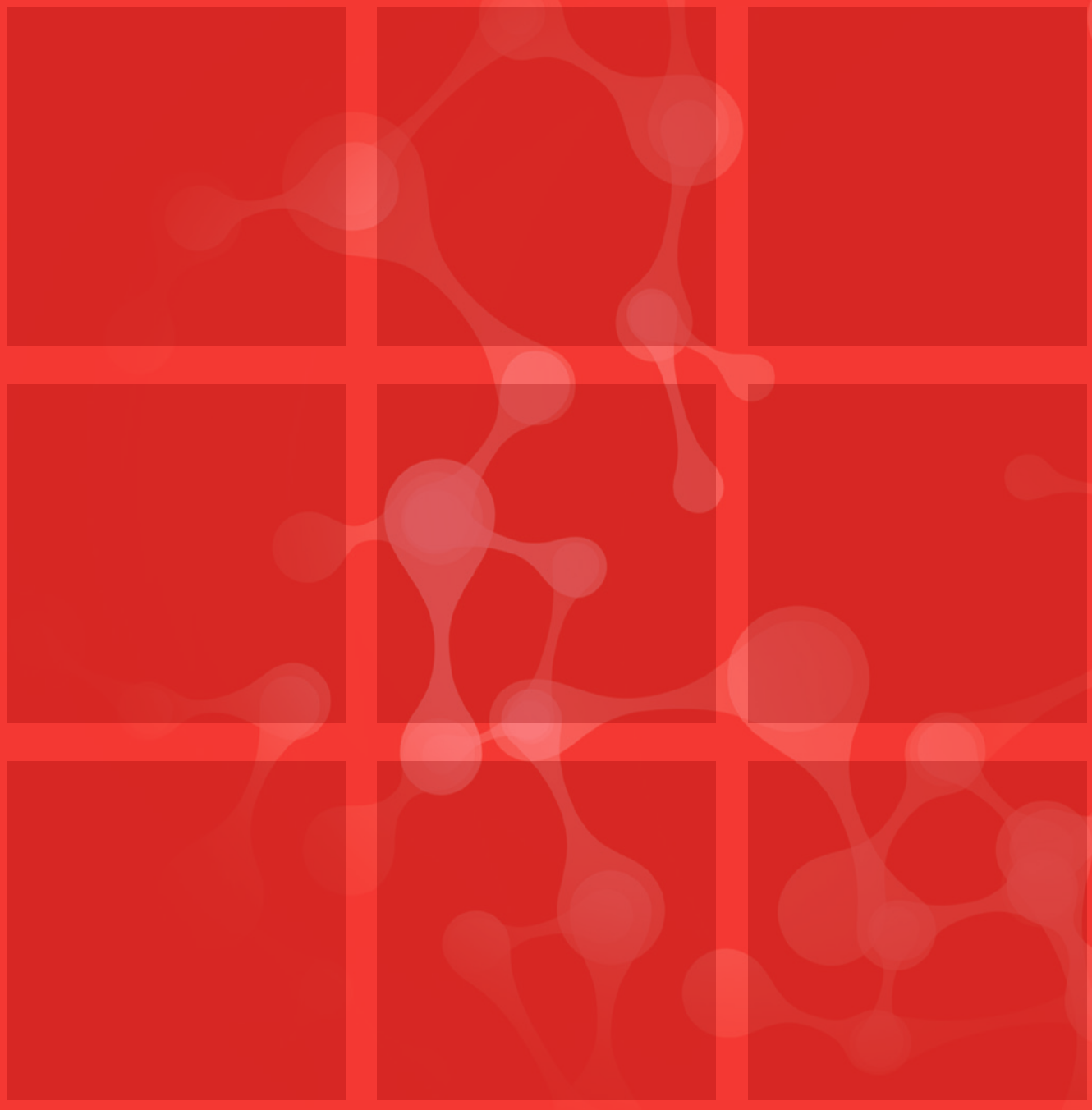


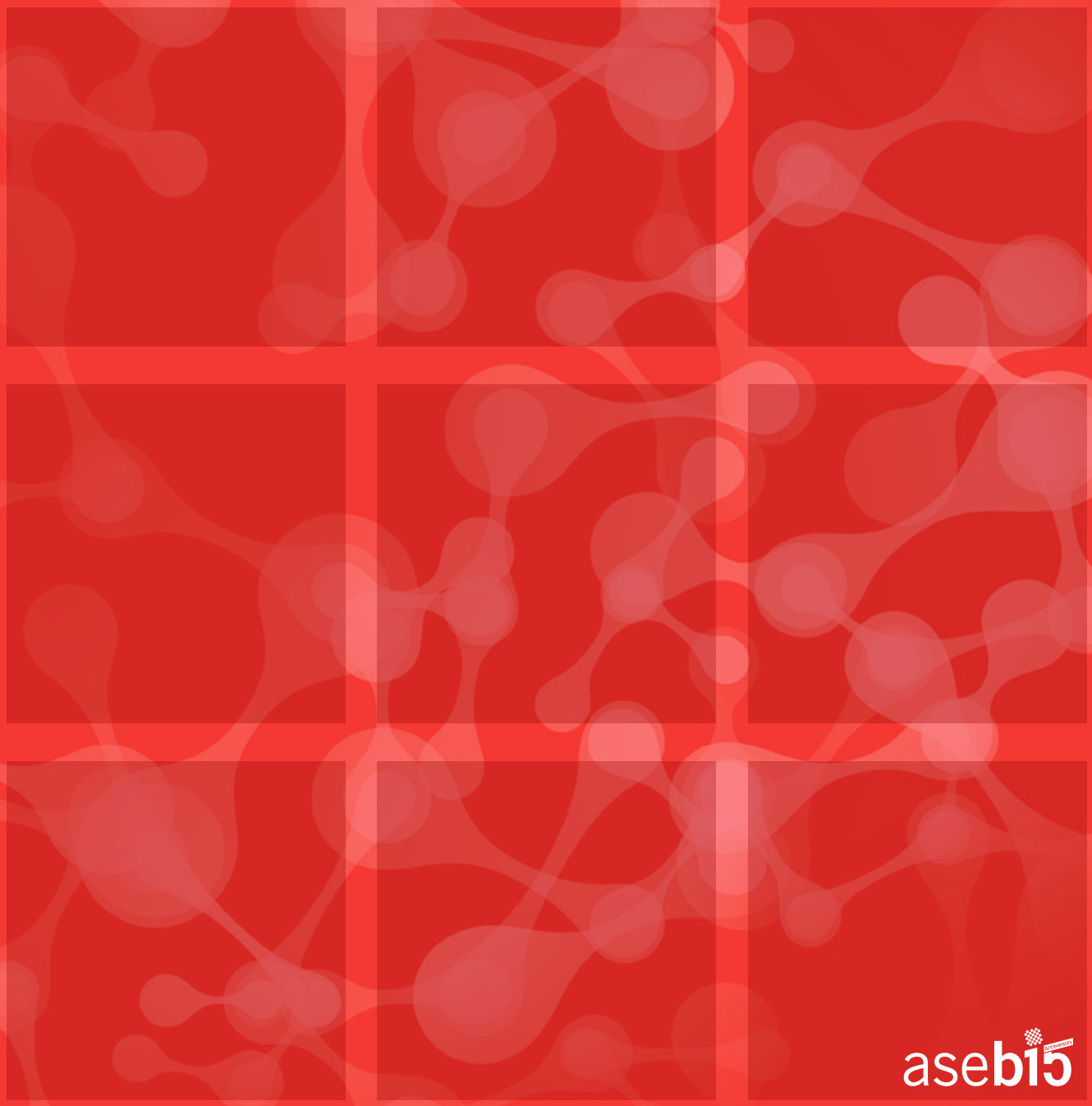
Figure 20. Number of scientific publications by companies which are ASEBIO members. Source: ASEBIO

Esteve and Neiker are next, with 13 publications each, while Bioiberica, Celgene and Sistemas Genómicos all published 12 papers. Both AbbVie and Pangaea Biotech contributed 11 publications each.

Although in theory they are not included in this analysis due to the fact that they are not companies, it is still worth pointing out the number of scientific publications by institutions such as the Institut Químic de Sarriá, which published 29 papers, the Instituto Maimónides de Investigación Biomédica de Córdoba (25 publications), Fundación INBIOMED (25 publications), Francisco de Vitoria University and GAIKER (7 publications each), Fundación MEDINA (5 publications) and the Centro Tecnológico Leitat (4 publications).



05 Health
Red biotechnology



Health - Red biotechnology

Molecular diagnosis and personalised medicine

The latest advances in molecular biology have allowed us to identify a whole series of biomarkers which have brought about a very significant improvement in the diagnosis and prognosis of medical conditions, which in turn has led to a more thorough understanding of various pathologies and the development of targeted therapies and treatments. This has allowed medicine to move forward both in terms of cost-effectiveness and efficacy.

With the objective of analysing the current situation and future expectations of Spanish hospitals in relation to the use of genomic and proteomic markers, ASEBIO launched the "SUMMA Project: the identification of early demand for personalised health technologies (advanced markers) in the National Health System"; an initiative which counts with the support of the Ministry of Industry, Energy and Tourism (MINETUR) through the "Innovative Business Groups" programme which was sponsored by Merck and counted with the collaboration of REGIC and the Spanish Biotech Platform.

The results provided by SUMMA identified the pathologies which represent the best business opportunities for the development of biomarkers in two main areas (haematology and oncology) which were identified as not covered by current technologies. Clinicians' interest in technologies currently being developed or already developed by the Spanish biotechnology sector was also looked at.

It is a fundamental tool for the coordination of future public procurement projects, as it serves to draw the attention of the various health sector agents to the need for innovation in biomarkers in order to make the most of the benefits they bring to patients and optimise the resources of the Spanish National Health System.

These biomarkers have also allowed us to make advances across a whole range of greatly varied areas and pathologies. Below, are named several examples of the most outstanding achievements in the field of molecular diagnostics and personalised medicine developed by entities within the biotechnology sector over 2013.

Scientists from the Maimonides Institute for Biomedical Research (IMIBIC) working in collaboration with other entities are studying an early cancer detection system which uses our breath. It is a multidisciplinary project which could be used to diagnose lung and colon cancers, amongst many other diagnosis applications.

Vircell launched VirClia® Monotest, a new screening product for the identification of the seven main respiratory viruses. It is a new product line based on chemiluminescence technology, an ideal solution for infectious serology. Vircell also participated in the European HERACLES Project with prestigious hospitals and research centres to diagnose Echinococcosis in humans. One of the project objectives is to develop a recombinant antigen from *Echinococcus granulosus* which can then be applied to a rapid test.

Grifols unveiled AlphaKit QuickScreen, a device capable of detecting alfa-1 antitrypsin (AAT) deficiency within 15 minutes. AAT deficiency is a hereditary condition which often goes undiagnosed, with only 5% of sufferers being correctly diagnosed. This is because AAT and Chronic Obstructive Pulmonary Disease (COPD) have similar symptoms and not treating AAT deficiency correctly can lead to emphysema and COPD in adults, as well as liver disease in children.

Andalucia-based Biomedal has developed a kit which measures the presence of a marker associated with the failure of liver transplants and haematopoietic stem cell transplantation, for instance in bone marrow.

Almirall began marketing Neurofarmagen in Spain, Neurofarmagen is a pharmacogenetic test developed by AB-Biotics which can be used in psychiatry and neurology to help to identify the optimal medication for each patient. The test helps

to narrow down the number of pharmacological options and estimates the most adequate dosage for an individual patient while also providing information about possible adverse effects.

Biokit announced the launch of BIO-FLASH HSV-1 IgG assay, a new member of the BIO-FLASH family. It is the first reagent of a group of three products to help in the diagnosis of Herpes 1 and 2.

Bioiberica Farma launched the first DNA test to predict the progression of knee osteoarthritis. A saliva sample is all that is needed to identify certain genetic alterations associated with the rapid progression of the disease, helping healthcare providers to choose a personalised treatment for any given patient, including proactive treatment to reduce or delay the need for prosthetic surgery and thereby improving quality of life.

Scientists from CIMA (University of Navarra) and the University Clinic of Navarra have described a biomarker that may lead to the early diagnosis and prognosis of lung cancer. Their findings showed that the C4d protein is linked to a higher mortality rate and that levels of the protein are reduced after surgical removal of the tumor. C4d also increases the risk of lung cancer in asymptomatic individuals, meaning that it could be used as a biomarker for the early detection and treatment of the disease.

Onco GeneProfile 80 is a new gene panel developed by Sistemas Genómicos which can analyse up to 80 genes linked to a high risk of suffering from inherited cancer, facilitating the early diagnosis and implementation of preventative measures and therapies in cancer patients and/or at high risk of suffering from hereditary oncological diseases. This panel includes the most common hereditary tumors but also other, less well known hereditary disorders such as Li Fraumeni syndrome, ataxia telangiectasia and juvenile polyposis syndrome amongst others. In 2013 the Reproductive Genetics unit at Sistemas Genómicos also became the first Spanish company to receive ISO accreditation to carry out Preimplantation Genetic Diagnosis (PGD) testing for all monogenic diseases.

Biomol-Informatics announced the launch of a genomic sequencing service for the Spanish market. From a simple blood test allows the search for markers that indicate potential genetic diseases. The system, called Genomika4U, allows individual genomic sequencing to uncover potential predisposition to genetic diseases which may affect the patient and also those which could be passed to their children.

The discovery of fetal cells in maternal blood has made it possible to avoid amniocentesis (amniotic fluid test) by using TrisoNIM, a test created by Nimgenetics. TrisoNIM is a noninvasive prenatal test which provides early detection of chromosome abnormalities such as Down's, Edwards and Patau's syndromes.

Developing therapies for human health

Oncology

Within the oncology therapy field, there have been developed a whole series of advances and improvements in various types of cancer treatment which have been researched and developed by the biotechnology sector during 2013.

VCN Biosciences presented preclinical results which show that VCN-01 used in combination with the chemotherapy drug gemcitabine (registered for the treatment of pancreatic cancer) substantially increased its efficacy vis-a-vis the separate use of the two treatments.

PharmaMar, which is part of Zeltia Group, announced that its partner Janssen Research & Development, LLC had completed patient enrollment for SAR-3007, a registration Phase III study of Yondelis® for the treatment of L-type sarcomas.

PharmaMar also completed patient enrolment for its Phase IIb trial of PM01183 in patientes with resistant-refractory ovarian cancer, allowing it to consider launching pivotal Phase IIb trials. PM01183 already showed clinical activity in this indication in the phase IIa study. PharmaMar also announced positive results in the Phase II study of PM01183 when compared with topotecan in patientes with resistant-refractory ovarian cancer.

In 2013 regulatory authorities in five countries have granted nine sales authorisations for Yondelis®, four are for the treatment of relapsed platinum-sensitive ovarian cancer (ROC), in combination with Caelyx® (pegylated liposomal doxorubicin), and 5 as monotherapy for treating soft tissue sarcoma (STS). The five countries that have granted these nine authorisations are UAE (United Arab Emirates), South Africa, Guatemala, Croatia and Turkey.

TCD Pharma developed TCD-717, a targeted cancer drug which offers significant advantages compared to chemotherapy and may in the future be specially useful for patients who cannot opt for other cancer treatments. It acts by inhibiting the choline kinase alpha enzyme (ChoKa) which is responsible for the involved in the creation and regulation of the cell membrane. The studies carried out by TCD Pharma showed that inhibiting the enzyme leads to the destruction of malignant cancer cells while also causing a temporary arrest of the proliferation of normal cells.

Plebiotic and Pharmacellion completed a research project in silico Molecular Modelling and Molecular Dynamics Model of Na K ATPase, a novel cancer target.

EC-70124, a kinase inhibitor developed by EntreChem, has shown efficacy when administered orally for prostate cancer with a malignant phenotype which requires ESE1/ ELF3 and NF-kB co-activation.

Lipopharma initiated a "Phasel/IIA" Study of Minerval for the treatment of advanced solid tumours including malignant glioma.

In order to promote and encourage innovation in the treatment of cancer, Merck Serono has established an immuno-oncology research and early-development platform integrating research, early development and biomarker strategies.

Amgen announced the approval of XGEVA® (denosumab) in Spain for the prevention of skeletal-related events in patients with bone metastases. It could make a big difference for cancer patients whose day to day life is affected by the consequences of bone metastases.

Seven Spanish hospitals participated in the international AVEX trial, a randomised Phase III study into the beneficial effects of a biological therapy in elderly patients with metastatic colorectal cancer. The treatment combined the angiogenesis inhibitor bevacizumab (Avastin®) with the oral chemotherapy agent capecitabine (Xeloda®), both are marketed by Roche. The findings showed that the treatment can extend progression-free survival (PFS) by an average of four months.

Eleven Spanish hospitals participated in the international Phase III TH3RESA study in patients with advanced HER2-positive breast cancer. The study made use the first antibody-drug conjugate for this type of cancer, bringing together a biological agent and a chemotherapy agent in a single molecule. Consequently, T-DM1, marketed in the US as 'Kadcyla,' combines biological properties of a very frequently used antibody in breast cancer due to its selective targeting, with a powerful chemotherapy agent, DM1, first directing second to the interior of the cancer cell and so limiting damage to healthy tissue.

Respiratory diseases

Almirall has launched Eklira® Genuair® in Spain. It is a bronchodilator medicine developed from its own research for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients. The active ingredient is aclidinium; a new inhaled and long-acting muscarinic antagonist, (LAMA), which is delivered through Genuair®, an innovative, patient friendly device.

Almirall and Forest Laboratories also announced positive results for the combination of aclidinium and formoterol for treatment of COPD.

Cardiovascular diseases

Researchers at the CSIC have successfully identified a new target potentially involved in the hardening of the arteries, a process that is a risk factor for the development of cardiovascular diseases and a prevailing phenomenon in hypertension, atherosclerosis and during ageing.

The 7th Framework Programme funded TRANSLINK project was launched by an international consortium made up of 13 private companies and research centres from 7 countries with an important contribution by the InKemia-IUCT group. The project aims

to find a technical and pharmacological treatment to avoid the autoimmune response to biological heart valve prostheses.

Oftalmology

Zeltia subsidiary, Sylentis, commenced Phase II clinical trials for its SYL040012 compound. The objective of the Phase II trial is to evaluate tolerance to the drug – as well as its effects - on 80 patients with ocular hypertension or glaucoma in three different countries. The SYL040012 compound is an example of interference RNA (RNAi) technology. Sylentis also initiated Phase II clinical trials for another RNAi compound, SYL1001 a new compound for the treatment of dry eye syndrome.

Neuroscience

VivaCell Biotechnology announced that it has entered into a research and marketing agreement with the US firm Aphios Corporation to develop a new range of therapeutic compounds for multiple sclerosis and other diseases of the central nervous system.

Vivacell Biotechnology, Bionaturis, Canvax Biotech, Vivia Biotech and Vivia Allosterics participated in the SNC_INTEGRA project as part of a consortium of private companies and public entities which aims to bring about an integration of platforms focused on the development of medications for diseases of the central nervous system.

Researchers from the Fundación Jiménez Díaz participated in the discovery of DEPDC5, a gene involved in focal epilepsy. The finding will allow the diagnosis of some types of familial partial epilepsy and the development of personalised treatments.

AB-Biotics has acquired the rights to a patent for technology which, using patients' DNA, can predict the side effects of antipsychotic drugs and the risk of developing extrapyramidal symptoms.

Neuron Bio patented NST0076 and NST0078, two new compounds which protect against neuronal death and which enter the brain more effectively, two essential characteristics for their use as treatments to slow down the onset of Alzheimer's and other neurodegenerative diseases.

Bionure announced that it would work with the US based Myelin Repair Foundation to develop its BN-201 therapeutic compound which could potentially be used as a treatment for acute optic neuritis and severe Multiple Sclerosis relapse.

A CSIC-led study revealed the role played by Erbb4, one of the genes involved in the development of schizophrenia. The gene encodes a family of receptor protein tyrosine kinases. Said gene is expressed at a very specific inhibitory neuron specific population and, therefore, is related to the connections to be produced between them.

Rare diseases

Digna Biotech launched a Phase I clinical trial in collaboration with CIMA and other centres within the framework of the European consortium AIPGENE to treat acute intermittent porphyria, a rare genetic disease that can cause significant neurological damage. The primary objective of the study is to evaluate the safety and obtain preliminary data on the efficacy of the gene therapy vector rAAV2/5-PBGD.

SOM Biotech announced that its SOM0226 compound for the treatment of Transthyretin Amyloidosis (ATTR) had received Orphan Drug Designation in the US from the FDA. ATTR is an orphan, irreversible and fatal disease caused by abnormal extracellular deposition of transthyretin (TTR), a transport protein carrying retinol and thyroxin (T4) in blood andcerebrospinal fluid.

Haematology

Oryzon initiated a research project with the Paterson Institute for Cancer Research (UK) to further study the inhibition of LSD1 as a stopper mechanism for the onset and progression of acute leukaemia. Also in 2013, Oryzon obtained orphan designation for ORY-1001, for the treatment of Acute Myeloid Leukemia, from the European Medicines Agency.

Scientists from the CIMA, the University of Navarre and the Centre for Genomic Regulation (CRG) in Barcelona successfully reprogrammed lymphoma and leukaemia cells in such a way that they are no longer

malignant. The cells maintain their new condition of benign cells even when they are not being treated, thereby reducing the possibilities of generating new tumours.

39 hospitals across Spain successfully trialled the new GA101 (Obinutuzumab) by Roche, an experimental therapy which in the Phase III CLL11 trial was shown to bring about a significant improvement in helping people with chronic lymphocytic leukaemia when combined with chemotherapy.

Digestive system diseases

Almirall and Ironwood Pharmaceuticals, Inc. announced the European launch of Constella®, the first approved prescription therapy in a new class of treatments for adults suffering from moderate to severe Irritable Bowel Syndrome Constipation (IBS-C).

The Instituto Internacional de Flebología unveiled the first treatment for haemorrhoidal disease without the need for surgery, thereby making it possible to avoid one of the most complicated postoperative recoveries.

Bioinformatics

Sistemas Genómicos launched GeneSys, an innovative tool for massive data analysis and interpretation, an innovative and useful platform that provides comprehensive analysis of data from resequencing studies.

Integromics released OmicsOffice 5, the latest version of its software for the statistical, biological and functional analysis and integration of genomic data with cross-platform validation tools and interactive visualization analytics of both internal and external workflows.

Biobanks

In 2013 the Biobanks Platform, an ISCIII initiative, came online with the participation of 52 institutions from across 14 autonomous communities. Amongst its objectives it aims to: provide a supportive scientific, technical and technological framework for R&D projects in Health Science and Technology, and efficiency for the management and transfer of biological samples and improved communication strategies in order to strengthen Spanish participation in international programmes and platforms.

VidaCord and Unilabs created Genebanking, the first DNA bank with a healthcare focus, its objective being to document and catalogue the original genetic map of patients for future diagnosis, either for them or their relatives.

Advanced therapies

Since 2013 Spain has had a Spanish advanced cell therapy product to treat knee cartilage lesions. Spain is also the third European country where the national health system has decided to reimburse this innovative product developed by TiGenix, the European leader in cell therapy. ChondroCelect® is a treatment which is aimed at patients of between 18 and 50 years of age

who suffer from knee lesions caused by microfractures, sports injuries or traffic accidents. The treatment is administered through a procedure involving autologous chondrocyte implantation. This innovative treatment has been shown to bring about long-term clinical benefits, particularly in patients with recent cartilage lesions.

TiGenix has also announced positive results in regard to the safety data of its Phase IIa study of Cx611 in rheumatoid arthritis. The multicenter, randomised, double blind, placebo-controlled Phase IIa trial enrolled 53 patients with active refractory rheumatoid arthritis who had failed to respond to at least two biologics. The study design was based on a three-cohort dose-escalating protocol.

The Institut Químic de Sarrià (IQS) presented a new patent for gene therapy based treatment of diseases such as a breast cancer, renal fibrosis and macular degeneration. The treatment uses a series of polymeric materials able to create nanoparticles with diverse genetic material. The patent has been licensed to Sagetis Biotech, an IQS spin-off.

Plasma Rich in Growth Factors has been recognised as a medicinal product for human use by the Spanish Agency of Medicine Products and Medical Devices (AEMPS). The resolution represents pioneering regulations at the international level and has had support from numerous scientific contributions including BTI Biotechnology Institute.

Vaccines

VLPbio presented Cervivax, an efficient vaccine for uterine cancer which makes use of particles similar to those of the human papillomavirus. It has achieved a 100% success rate in its first *in vivo* studies.

3P Biopharmaceuticals announced its participation in the European FLUTCORE project to develop a universal influenza virus vaccine.

06 Agrifood *Green biotechnology*

Agrifood - Green biotechnology

Functional food

Scientific research, technology innovation and the growth of health awareness have revolutionised the food industry through the new 'functional food' concept. It is a market which is experiencing fast growth.

In 2013 Biopolis developed a new probiotic called *Bifidobacterium longum* ES-1, which is aimed at people suffering from Coeliac disease. The probiotic has been shown to provide greater protection to the intestinal lining of celiacs, reduced inflammatory activity, and even inducing the synthesis of some compounds exerting anti-inflammatory activity.

Biopolis also developed a new *in vivo* model based on *Caenorhabditis elegans*, providing an efficient alternative to research using larger animals, which involves bigger regulatory and financial hurdles. The model was used to study ingredients to treat obesity and led to the discovery of a new ingredient a cocoa peptide, which showed antioxidant activity and can reduce the accumulation and toxicity of Amyloid β-peptides which play a critical in Alzheimer's disease.

Biosearch Life announced a patent application for probiotic bacteria loaded with metal nanoparticles for the diagnosis and treatment of tumors, which could also be used in the administration of mineral supplements in humans, improving their bioavailability and reducing side effects.

AB-Biotics was granted the European patent for its cholesterol-lowering probiotic AB-Life and another patent in China for AB-Fortis, its iron-fortified food product. The company also launched the first probiotic specifically designed to fight the oral pathogens causing caries, gingivitis and bad breath. The formula for AB-Dentis contains two bacterial strains (*Lactobacillus plantarum and Lactobacillus brevis*) which fight against the most common oral pathogens and preserve oral health.

The EU approved the use of Bioiberica's rooster comb extract in its dairy products. Rooster comb extract is rich in hyaluronic acid-when consumed regularly, hyaluronic acid is healthy for the joints. It is the first ever *Novel Food* approved and developed in Spain by a Spanish company.

The pharmaceutical company ESTEVE and the food company Grupo Leche Pascual brought together their experience in health and nutrition to create DiaBalance, the first brand offering products and services created exclusively to meet the needs of diabetic people and their environment. DiaBalance will market two product lines in pharmacies, supermarkets and large department stores.

Grupo Farmasierra launched Solvilit, a food supplement containing hidroxitirosol, a standardised concentrated olive (*Olea europaea L.)* extract, which can help to prevent coronary cardiovascular disease. This polifenol is the most potent natural antioxidant and is responsible for health benefits of olive oil because it protects cells from oxidative stress and cell ageing. Farmasierra has also developed Omedrai, a food supplement derived from fish oil rich in Omega-3.

NEIKER-Tecnalia has embarked on a project to produce flour with high levels of Omega 3 from marine plant sources.

A consortium made up of Iberdrola Engineering and Construction, Algae Biotech, the Instituto de la Grasa (CSIC) and Ainia, successfully extracted omega-3, 6 and 9 oil from microalgae using a technique based on supercritical fluids and ultrasound, which is more cost competitive and safer than conventional methods. These beneficial fatty acids could be used in the cosmetics and food industries

Product revalorisation

Neiker-Tecnalia and CEMITEC are exploring the use of rapeseed as a raw material to cover part of the diet of ruminants and to obtain biofuel for agricultural machinery. One of the aims of the project is to show that including rapeseed oil cake in the diet of ruminants can cut the production of methane created during the digestion process by over 10%. The project will also study the potential use of the oil extracted as fuel for agricultural vehicles as well as the effects of introducing rapeseed cultivation into the traditional rotation.

Neiker-Tecnalia and Guipuzkoa-based Ekonek will build a pilot plant to treat organic waste and convert it into high added value fertilisers. The plant will provide an efficient use for the organic matter from biogas plants generated during the anaerobic digestion process.

Neiker also studied the suitability of ash produced from the burning of tree biomass as a fertiliser for *pinus radiata* plantations.

The Centro de Edafología y Biología Aplicada del Segura (CEBAS-CSIC) developed new phytochemical-rich bioactive food product from pomegranate fruit (*Punica granatum L.*).

The Autonomous Community of La Rioja received European funding for the launch of an innovative project to investigate solutions through energy valorisation of agrifood industry by-products. The project, called PROVALUE, will be carried out in collaboration with national and international entities.

Technologies for quality and process control in the food industry

In regards to quality and process control in food, Neiker-Tecnalia, has developed a new method for the early detection of mildew, powdery mildew and botrytis, diseases common in vines. The new methodology based on molecular biology techniques makes it possible to detect the disease before the symptoms appear on the plant. That way it is possible to carry out the timely treatment of the plots or areas affected and thereby prevent the disease from spreading throughout a vineyard, and so reducing infective pressure.

Biomedal launched *AlerTox Sticks*, a product for milk and egg allergen detection in foodstuffs, drinks and surfaces. It also developed *AlerTox ELISA*, a sandwich type immunoabsorbent assay designed for the detection and quantification of allergens often found in food, and *AlerTox ELISA Specific for wine*, which detects egg and milk allergen residues in wine.

Through an INNTERCONECTA project, Biomedal also worked on the development of new technologies to improve milk quality as well as health and productive parameters in goat populations in Andalucia.

Ingenasa launched two new detection technologies: INGEZIM Beta-lactoglobulina crom, a rapid immunochromatic test for Beta-lactoglobulin in food, and INGEZIM caseína crom, a rapid immunochromatic test for the detection of casein in food.

Nanoimmunotech, through the INNOSABOR project, developed a line of innovative products for the meat canning sector, to increase food safety and organoleptic quality through the use of nanotechnology and artificial intelligence.

Instituto de Medicina Genómica (Imegen) has developed technology that can detect the presence of horse meat in DNA extracted from meat samples within 12 hours. The product is being marketed as RapidFinder Equine ID Kit.

Life Technologies will market the product among national food safety authorities and large biotechnology companies.

Animal health

Ingenasa launched several new animal health products: INGEZIM WEST NILE Ig, ELISA for the detection of IgM specific to West Nile virus in horse serum. INGEZIM SCHMALLENBERG COMPAC ELISA for the detection of antibodies specific to the Schmallenberg virus in the serum of ruminants, INGEZIM MAEDI SCREENING, ELISA for the detection of antibodies specific to ruminant lentivirus, and INGEZIM FVR, ELISA for the detection of antibodies specific to Rift Valley fever in the serum of ruminants.

Bionaturis is basing two new vaccines on its Flylifesystem, one of them for the agrifood industry. The company reached various agreements with companies from the veterinary industry which will be responsible for evaluating its efficacy and safety.

Vetgenomics is participating with other European entities in the POC4PETS project. The aim is to create and validate new diagnostic tools which are reliable, efficient, robust and useful for the detection of

DNA of pathogens that affect pets and can be used in the actual medical center (diagnostic point of care).

Bioiberica, in collaboration with IDEXX Laboratories, has marketed a tool that makes it possible to identify genetic predisposition to hip dysplasia in dogs of the Labrador breed globally.

Univet, Janus (now Spherium Biomed) and Histocell joined forces to create ArtinVet, the first Spanish company specialised in veterinary regenerative medicine in racing animals and pets.

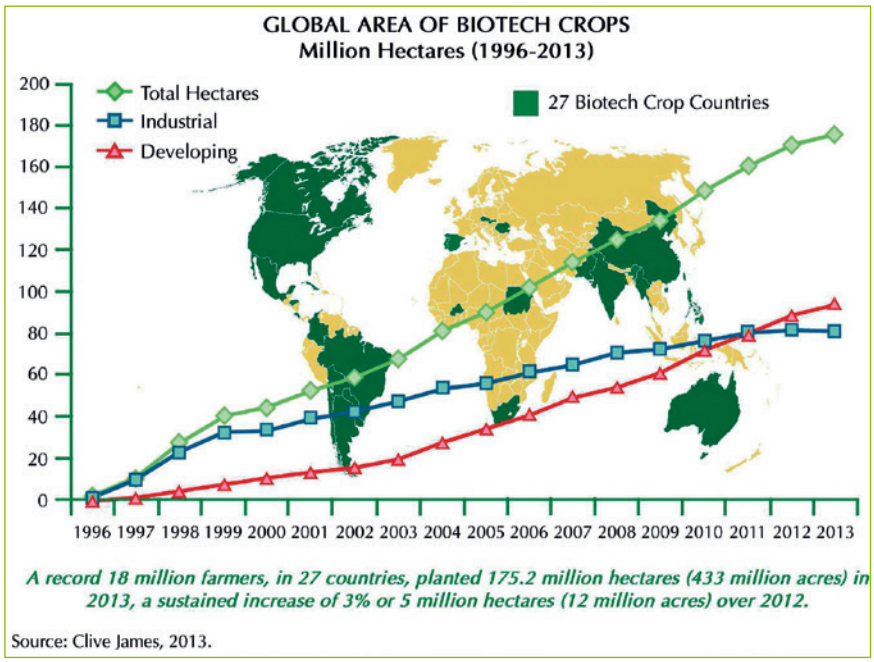


Figure 21. Global land use for agrobiotechnology. Source: ISAAA

Agriculture

According to the Annual report on the global status on the commercialisation of GM crops in 2013, published by the *International Service for the Acquisition of Agri-Biotech Applications* (ISAAA), in 2013 a total of 175,2 million hectares (ha) were grown globally, up from 170,3 million ha in 2012, an increase of 3%.

In 2013, 18 million farmers in 27 countries worldwide chose biotechnology crops. In these 18 years of GM crops, from 1996 to 2013, millions of farmers from around 30 countries decided to plant 1,6 billion hectares, equal to an area greater than the US or China.

Furthermore, a total of 36 countries have granted regulatory approvals for genetically modified (GM) crops for food and for environmental release. A total of 2,833 regulatory approvals involving 27 transgenic crops and 336 biotech events have been issued by the competent authorities, of which 1,321 are for food use (direct or processed), 918 for animal feed use and 599 for environmental release or planting. Japan has the most events approved (198), followed by the US (165 not including stacked events), Canada (146), Mexico (131), South Korea (103), Australia (93), New Zealand (83), European Union (71 including approvals that have expired or under renewal process), Philippines (68), Taiwan (65) and Colombia (59).

Maize has the largest number of approved events (130 events in 27 countries), followed by cotton (49 events in 22 countries), potato (31 events in 10 countries), canola (30 events in 12 countries) and soybean (27 events in 26 countries).

The two events that received the most approvals were the herbicide tolerant soybean event GTS-40-3-2 (51 approvals in 24 EU countries), followed by the insect resistant maize event MON810 (49 approvals in 22 countries EU countries).

The US led the 2013 rankings with a total of 69,5 billion hectares planted, followed by Brazil (40,3 million hectares), Argentina (24,4 million hectares), China (4,2 million hectares), Paraguay (3,6 million hectares) and Uruguay (1,5 million hectares).

According to the final data provided by the Ministry for Agriculture Food and Environment (MAGRAMA), a total of 136,962.45 hectares in Spain were planted with GM maize in 2013. This puts Spain in 16th place in the world with an increase of 20,655.85 hectares planted and an increase over the previous year of almost 18%. In the context of total maize production, genetically modified varieties accounted for 32% of the total planted country-wide, 2% more than in 2012.

With 54,451.15 hectares, Aragon is the autonomous community with the largest amount of land surface area planted with bt maize. It is followed by Catalonia and Extremadura with 33,995.95 and 16,979.12 respectively, an increase of 465.09 and 1,027.59 in each. The significant increase in Andalusia is very notable, there, 14,078.53 hectares have been planted, which means an increase of 35% compared to 2012. The provinces where most biotech maize has been planted are Huesca (33,228.82), Lerida (27,654.19), Zaragoza (21,055.86), Badajoz (10,459.71) and Seville (7,953.53).

The sustained grown in GM maize once again confirms the confidence of Spanish farmers in these varieties. These are seeds which increase crop sustainably and reduce use of resources per unit of production (less land, less water and less energy use). Such advantages mean more profits for farmers as their agricultural activity becomes more profitable and competitive.

The new developments in agriculture by Spanish entities were the following:

- The *Beauveria bassiana* fungus, a non chemical solution developed by Glen Biotech for the fight against the Red pal Weevil, was the basis for a proposal by a Valencia-based project as part of the EU LIFE+ programme. The aim is to reduce the volume of chemicals used to fight the insect in urban areas through a solution that can be used in a generalised manner.
- Plant Response Biotech joined the PATRIC project to investigate new methods for plant protection and treatment using natural products. Specifically, the consortium will make use of the inherent immunity of a plant by triggering resistance from the recognition of pathogen molecules. Plant Response will also work with its partners to identify new microbial immunity receptors and elicitors for a long term resistance in a wide variety of crops.
- Camelina España joined other entities on the NICAVA project to develop new exclusive camelina varieties, especially adapted to the agroclimatic conditions found in Spain.
- Neiker-Tecnalia carried out a controlled trial to assess the potential effectiveness on the *Vespa Velutina* of biocides tested in Chile on the *Vespula germanica*. This process will be carried out through the placing and controlled monitoring of baits in order to limit the effects on other insect populations, birds and vertebrates.
- CSIC scientists are seeking permission to plant a 1000 sqm plot of genetically modified wheat suitable for the consumption of people suffering from coeliac disease, a condition which currently has no cure and affects 1% of the world's population.
- CSIC researchers also developed plants, which without being pollinated, are able to produce highly nutritional seedless tomatoes.
- The Plant Breeding department at CEBAS-CSIC developed plums (*Prunus domestica L.*) with crown gall disease resistance.
- Bayer, under the brand Nunhems, will offer different crop seed varieties for specialised markets in Colombia.
- Neiker-Tecnalia has created two new potato varieties will be commercialised in 2014: the purple potato NK06130 and the yellow potato NK03100. The two varieties are characterised by their high antioxidant content, their good production both in size and number of tubers, as well as by their resistance to the usual diseases that affect these crops.

07 Industrial *White biotechnology*

Industrial White biotechnology

Biotechnology applications for the production of energy

Directive 2009/28/CE of the European Parliament and of the Council of Europe of April 23 2009 aims to promote the use of energy from renewable resources. The directive establishes a framework for the common and national objectives, as well as measures for the use of energy from renewable resources. Article 3 of the directive establishes that Member State must ensure that by 2020 the share of energy from renewable sources used in the transport sector accounts for at least 10% of final energy consumption in the sector.

The Royal decree 459/2011 of 1 April 2011, which set the mandatory targets for biofuels in 2011, 2012 and 2013, established that regulated entities must certify annually that they have a minimum amount of biofuels in diesel certificates showing that the objectives have been met: 6.2% in 2011, 6.5% in 201 and 6.5% in 2013. Diesel biofuel targets for the same years are 6%, 7% and 7%, respectively.

On Friday 21 February 2013 the Government approved a battery of measures to promote competition in the hydrocarbon sector and thereby reduce oil and petrol prices. Consequently, since the 1st of January 2013 the exemption for biofuels mixed with hydrocarbons is no longer in force. The objective of these measures was to limit the impact of the end price on petrol and other oil-based products as well as provide some degree of stability to the sector. The Government decided to lower the minimum consumption of these 'green' fuels. So, according to the Ministry of Industry Energy and Tourism, for 2013 and the following years the proportion of biofuels as a share of total consumption will be reduced from 6.5% to 4.1%. In the case of petrol it will go from 4.1% to 3.9% and in oil from 7% to 4.1%.

The Ministry of Industry Energy and Tourism announced that these new standards will allow 'a limitation of the cost of fuel and an analysis of the necessary technological developments needed to reach the EU objectives for 2020', which establish, as noted above, that this year renewable energy must account for 10% of the energy used in transport.

Four years ago biofuel plants accounted for a total annual production capacity of over four million toe (tonne of oil equivalent). However, the Ministry of Industry Energy and Tourism noted in its 'Renewable Energy Plan 2011-2020' that 'growth in the production capacity had not been matched by a similar evolution in the consumption of biofuels'.

Argentina and Indonesia are the biggest exporters of biodiesel to Spain, accounting for a total of 80% of biodiesel sales in Spain in 2011. Since 2009 the two countries tax biodiesel at a lower rate than soy (the raw material used in the manufacture of biodiesel), making it cheaper to buy biodiesel than soy. Consequently, even though in 2011 biodiesel consumption in Spain grew by 21% compared to that of 2010, according to figures provided by APPA Biocarburantes, national Spanish production decreased by 46% compared to 2010.

In February 2013, the Secretary of State for Energy called an established a procedure through Orden IET/822/2012 for the assignment of diesel production quotas in order to meet the mandatory biofuel production targets for the following two years. The Government hopes the measure will lead to greater consumption of biodiesel and a reduction in CO_2 emissions of 5,46 tons annually between 2010 and 2011 (a total of 49 tonnes).

As published in November 2013 in the Official State Gazette, production allocations were shared for a maximum/total production of 5,5 annual tons between 42 production units owned by a number of different companies. Of the 42 units, 15 are located outside Spain.

Inkemia led a consortium of companies and research centres to win a EU public tender process called with the R&D project 'Glycerol Biorefinery Approach for the Production of High Quality Products of Industrial Value' (GRAIL).

Neol Biosolutions, patented its Neoleum™ microorganism which is fully developed and consolidated as part of the MicroBioil™ Platform. The microorganism converts hydrocarbonated residues into high value microbial oils which are mainly used in biofuels. It was the result of the selection of the optimal fermentation microorganism, which guarantees the highest productivity without the need to carry out any genetic modification by the company's researchers.

Algaenergy, the Regional Government of Andalucía and Iberdrola launched the CO2Algaefix programme. The initiative has received EU funding and aims to revalorise gases emitted from Iberdrola's Combined Cycle Power Plant using microalgae.

Abengoa joined the BIOFAT project to demonstrate the feasibility of industrial scale algae-based production of biofuels. The company is also participating in the LED project (Lignocellulosic Ethanol Demonstration) to design and build a biorefinery for the production of second-generation bioethanol from cereal straw to be ultimately used in public transport fleets, as well as the improvement of the enzymes involved in cellulose hydrolysis and the use of the lignin contained in the feedstock for high added value products.

Abengoa is also participating in the European Batteries2020 project to optimise batteries for electric

vehicles. Abengoa's role is to investigate the different factors that influence how batteries age and mechanism of degrade in order to identify the critical parameters that affect performance throughout the life of the battery.

The Institute of Catalysis and Petrochemistry at the CSIC along with other collaborating entities designed a method which utilises carrot waste to produce bioethanol, a chemical compound obtained from the fermentation of sugars which can be used as fuel.

Researchers at the Institute for Conservation and Improvement of Valentian Agrodiversity (COMAV) of the Polytechnic University of Valencia and from the Agrobiotechnology Institute (Public University of Navarra (UPNA), the Spanish National Research Council (CSIC), and the Government of Navarra) obtained tobacco plants able to produce up to seven times more starch than conventional plants, a characteristic which could be very valuable in the production of second generation biofuels.

Biopolymers and Bioplastics

According to European Commission (EC) data, over the last 50 years world-wide plastic production has increased from 1.5 million tons per year in 1950 to 245 million tons in 2008, a trend that is expected to continue. The marine environment is particularly vulnerable to plastic waste because as well as creating enormous waste patches, such waste can persist for hundreds of years. Up to 10 million tons of litter, mostly plastic, end up in the world's seas and oceans annually, turning them into the world's biggest plastic dump and causing sea species to suffer as a consequence of entanglement or ingestion.

Furthermore, conventional plastic contains a large number of chemical additives which can be carcinogenic, provoke other toxic reactions or act as endocrine disruptors through chemical substances foreing to the body which interrupt some physiological processes controlled by hormones.

That is why the EC has published the Green Paper on the management of plastic residues which aims to gather facts and views in order to assess the impacts of plastic waste and define a European strategy to mitigate them. A 26-questions consultation was launched in 2013 seeking to gather opinions on whether existing legislation should be adapted, and if so, how.

The following developments took place in the biopolymer sector:

- The Institut Químic de Sarriá commenced work on the Nano3Bio project, which aims to develop biotechnological production systems for nanoformulated chitosan polymers.
- Neiker joined other collaborating entities in the European BUGWORKERS project, a collaborative effort to develop bioplastics which uses sugar-eating bacteria which will naturally synthesise them.

- Gaiker-IK4 collaborated with Rafrinor on optimising the recycling of domestic cooking oil and associated plastic containers. Rafrinor collects cooking oil from nearly 80% of the municipalities in Bizkaia, treats it (humidity, acidity, sediments, and so on) and sells it for its subsequent use as a raw material in the production of biodiesel. With a growing volume of collected waste - currently about 400 tons annually - Rafrinor in collaboration with Gaiker-IK4 embarked on a project with a dual aim: to explore possible ways of recycling to obtain enhanced value from the tons of plastic container bottles left over after the used oil is extracted and to optimise the separation process oil and plastic at Rafrinor.

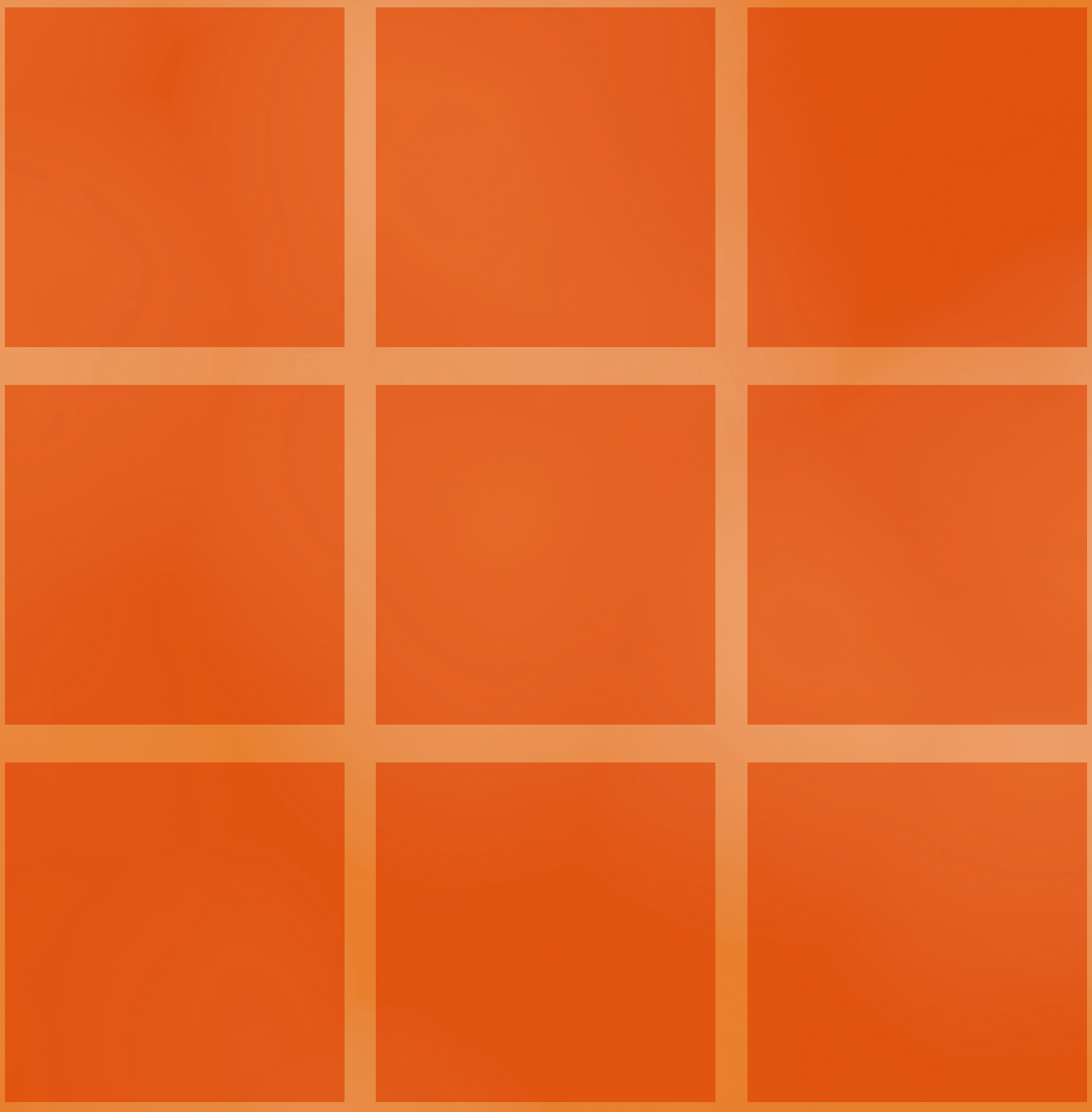
Bioprocesses and other bioproducts

Biochemize embarked on its participation in the BioConSepT project to obtain first and second generation building blocks using biomass and non edible oils and fats. Biochemize will focus on enzymatic and microbial processes to obtain hidroximetilfurfural (HMF) from fructose. It is also working on the LIQUION project which seeks investigate and generate knowledge in the area of in new ionic liquids and its technological applications through more environmentally friendly processes than those currently used – thereby meeting the great challenges of the transport, energy, environment and biomedicine sectors. Biochemize is also involved in the HOTDROPS project, which aims to obtain thermostable proteins for the design and up-scaling of biocatalytic processes in redox reactions and the generation of carbon-carbon bonds.

Entrechem initiated its participation in the European BIONEXGEN project with 16 international partners to develop new biocatalysts that will lead to a reduction in the emission of the greenhouse gases and toxic waste as well as energy saving in industrial processes. The project is funded by the European Union with 8 million euros for three years (January 2011-2014).

Gaiker-IK4 and Yflow collaborated in the INFINITEX project to develop functional textiles that incorporate active microcapsules during the manufacturing process. It is a CENIT project which has been allocated a budget of 29 million euros.

SYGNIS Biotech was granted a patent in the USP for QualiPhi® (an upgraded version of the Phi 29 polymerase), the polymerase for complete DNA amplification. It also launched the first two products of a series of kits based on QualiPhi®, marketed as SensiPhi®. The two kits, REPLI-g WTA Single Cell Kit and REPLI-g Cell WGA & WTA Kit, address key user challenges in new generation sequencing and other downstream applications, where DNA sequence analysis is limited by small amounts down to single cells of available sample material.



08 Financial *Environment*

Financial Environment

STAT Diagnostica, which was founded in 2010 and focuses on the development of Point of Care diagnostic solutions for clinical applications, leaded one of the biggest financing transactions in the biotechnology sector for 2013 with the closing of a financing round for a total of 17 million euros. Led by new investor Kurma Life Sciences Partners, the round also drew participation from Idinvest Partners, Boehringer Ingelheim Venture Fund, Caixa Capital Risc, Ysios Capital and Axis.

Tigenix also found itself in the limelight. On the one hand it raised 6.5 million in extra capital from a number of investors. Then it secured a structured debt refinancing agreement of up to 10 million euros from Europe's largest and leading provider of growth debt, Kreos Capital.

Minoryx Therapeutics, which specialises in developing new treatments for rare diseases, secured for 4.5 million euros in its first round of financing from Caixa Capital Risc, Inveready Biotech and the Business Angels Network de Catalunya. Public investors also participated - contributing to the total.

Palobiofarma closed its third round of financing for 4.5 million euros after obtaining backing from by Inveready, Fitalent and Sodena. Public funding sources also contributed to the total figure.

Digna Biotech secured over four million euros after a round of financing which included the participation of UNAV/FEUN, SODENA, Paramus, Pontegades, Caja Rural de Navarra, INFU-CAPITAL, CINAMAR, IEISA, SAINSA, CAIXA and Ciérvana S.L.

Inveready, the venture capital group, launched Inveready Biotech II SCR (IBII) with an initial 7 million euros. This is their fourth business created to invest in biotechnology sector companies and it will fund up to 20 projects in its first three years. The aim is to invest in companies focused on drug discovery, nutrition, and molecular and genetic diagnostics.

European venture capital firm, Ysios Capital, Ysios BioFund I, has successfully exited from Endosense, the US medical technology company, which was sold for 249 million euros. Ysios made 16.5 million from the sale of its 7% share in Endosense.

Towards the end of 2013 Avindia Capital announced that it would set up a 10 million euros fund that will be invested in 35 projects between 2014 and 2015. Avindia will primarily invest in newly launched firms from Andalusia working on new technologies and biotechnology.

At the end of 2013 Ferrer announced the takeover of Janus Developments, a biotechnology company specialised in the management of transition phases of biomedical projects. Ferrer bought 75% of Spherium and the two

companies and the remaining 25% is still held by Janus partners. The two companies merged under the name Spherium Biomed. The objective of the transaction was to set up Spherium as the R&D platform for the development of Ferrer's new pharmaceutical products.

Grifols acquired 60% of Progenika Biopharma, a company specialised in the development of technology for personalised medicine. BBVA Corporate Finance provided financial advice for the 37 million euros transaction. The sale involved a combination of cash for 50% of the purchase price, with the remaining 50% being paid in the form of non-voting (Class B) Grifols shares.

As well as the purchase of Progenika, Grifols acquired 35% of the US firm Aradigm Corporation, which specialises in the development and marketing of drugs delivered by inhalation for the treatment and prevention of severe respiratory disease. The transaction involved a 25.7 million US dollars (20.6 million euros) cash injection as part of a total capital investment of 40.7 million dollars and a broader strategic agreement.

Gri-Cel, part of Grifols, acquired 21.3% of the biotechnology firm TiGenix through the subscription of a capital increase for a value of 12.4 million euros. The acquisition was financed using own funds as part of a drive to invest and manage companies engaged in advanced therapies and personalised medicine.

Amadix, a company specialising in the development and marketing of innovative oncology diagnostics technology merged with Transbiomed, a Vall d'Hebron Research Institute (VHIR) spin-off which works in the field of *in vitro* molecular diagnostics through the use of genomic and proteomic technologies for hormone based tumours.

Amadix closed a two million euros capital increase with CRB Bio II and Inveready which invested 1.5 million euros and 500.000 euros respectively. The acquisition, involving a share swap, means Amadix now owns 100% of Transbiomed in a merger creating a leading company with expertise in range of prevalent types of cancer.

Inibsa, the pharmaceutical group, acquired 100% of Biotools B & M Labs SA, a leading biotechnology company focused on research, development and the manufacture of recombinant enzymes and other molecular biology tools.

09 *Internationalisation*

Internationalisation

Spain in the international context

In spite of the recent economic crisis, Spain has the fourth biggest economy in the European Union and the 13th in the world, according to the World Bank GDP Ranking (2012). This means that, even though we lag behind other countries in terms of the percentage of our GDP that we reinvest in R&D, Spain still invests a significant amount of money in absolute terms when it comes to those indicators that measure scientific and technological potential.

In the World Bank Ranking for knowledge-based economies, the Knowledge Economy Index (KEI) 2013, Spain 16th in the world ahead of countries including Austria, Japan, France, Singapore and Israel. Spain particularly stands out in the categories for Education where it is positioned in 10th place, on Innovation it is in 15th place, and in terms of economic incentives for which it is 21st. On the other hand, its less impressive 34th place for Information and Communication Technology highlights an area that needs improvement.

Being well placed amongst the knowledge-based economies makes it possible for Spain's scientific output to shine in almost all areas of knowledge. According to SCImago Country Rank, Spain was placed 9th in the world in terms of scientific productivity from 1996 to 2012 and 10th in 2012.

Although the size of the Spanish economy as a proportion of the global economy has decreased (prior to the crisis Spain's economy was the 8th biggest in the world), it has managed to keep it place amongst the top ten in scientific productivity.

Spain is amongst the top ten in practically all biotechnology-related areas, 8th when it comes to Applied Microbiology and Biotechnology, 9th in terms of biotechnology-related publications.

The Spanish National Research Council (CSIC) is also amongst the top ten institutions in the world in terms of scientific productivity. It is currently in 8th place, steadily climbing positions every year (in the period 2003-2007 it was positioned 15th).

Although when we refer to these rankings we are not strictly speaking about biotechnology, Spain's positive performance position in these indicators directly impacts its development in biotechnology. If we look at the growth of the pipeline for molecules in all phases of development, we can see that Spain has experienced the biggest growth in percentage terms (+160%) in the period 2007-2012 with the exception of Israel (+192%). According to data cited in the 'Beyond Borders' report, which is published annually by the consultancy firm Ernst & Young, Spain has the 8th biggest biotechnology pipeline in the world, ahead of countries including Italy, Austria, and Belgium – and close behind Denmark.

Internationalisation Survey

This section details the main conclusions drawn from the survey on internationalisation amongst biotechnology companies over 2013, a survey ASEBIO has conducted amongst its members for the six consecutive year.

As in 2012, 100% of respondents considered that internationalising their activities was essential or very important, showing that the sector's commitment for this aspect of its business activities is not a temporary trend.

Of those companies which are not internationally active yet, 78% feel that it is one of their short-term high priority objectives. Furthermore, 92% of companies currently not internationally active say that it is because they are too new and prefer to consolidate their activities in Spain before expanding abroad.

According to the internationalisation survey, 85% of ASEBIO member companies are involved in some sort of international activity. This figure is slightly lower than in 2012, although we must bear in mind that over the last year the total number of ASEBIO members has grown as many start-ups not yet engaged in any international activities have joined ASEBIO.

Research alliance/collaboration	63.16%
Exporting products/services	61.84%
7th Framework Programme	39.47%
Licensing Out	39.47%
Licensing In	22.37%
Trade Agency	19.74%
Representation Office	15.79%
Eureka/Canadeka/Iberoeka programme	9.21%
Manufacturing plant	9.21%

Table 7. Main international activities by ASEBIO members in 2013

The business activities that ASEBIO members have engaged in during 2013 reflect similar patterns to 2012, according to the internationalisation survey, although alliances and collaborations are now in first place – ahead of exporting products and services.

53.3% of companies have a specific department for international relationships, a figure which is practically the same as in 2012. In 2009, the first year the survey was carried out, the number was only at 31%.

For the first time since we started conducting the survey, the market which ASEBIO members consider to be the top priority for their internationalisation strategy is the Latin American market, particularly those of Mexico (96.67%) and Colombia (95.83%).

The EU (93.24%), Switzerland (90.48%) and the US (88.41%) continue to be high priority markets for the sector. Other important markets for our companies include the Middle East (87.50%), Japan (85%), Chile (81.25%) and Brazil 80%).

It is worth noting that geographical locations and priorities have changed considerably over the years. In 2009, the only high priority market was the EU, followed by the US with the rest of countries a long way behind. The fact that in 2013 such a variety of markets are in the sights of our companies shows their degree of consolidation, maturity and global vision when it comes to internationalising their activities.

A lack of economic resources continues to be the main barrier to engaging in effective internationalisation processes for 85.51% of companies. The percentage is lower than in 2012 (91%) and back in 2009 it stood at 100%. Other barriers include the lack of specific information on internationalisation (31.88%), language barriers (13.04%) and a lack of entrepreneurial culture (8.70%).

We should also point out that over the years the language barrier and lack of entrepreneurial culture have stopped being impediments for the majority of companies and that there is constantly growing demand for knowledge and training in international business.

To finish, ASEBIO members judge participation in partnerings and commercial fairs to be the best tool in the identification of potential clients and partners for their internationalisation processes. 96% of respondents felt this type of activity to be the most effective.

Our members were also very satisfied with the two events organised by ASEBIO: Biospain (84%) and Biolatam (73%).

Overseas Expansion

One of the main characteristics of biotechnology companies is the wide variety of them out there – their heterogeneity- and the broad range of very different business models. That is why internationalisation strategies must also be different, however, something they do have in common which differentiates the biotechnology sector from other sectors is their capability for fast overseas expansion through the establishment of a direct presence in other countries.

The reasons for this fast ability to expand overseas are, beyond simple commercial strategy, about the need to be in the great international clusters where the presence of big pharmaceutical companies and capital is also greater, which facilitates the process of finding investors and strategic collaborations with other companies.

The number of subsidiaries, branches and representation offices remains stable compared to 2012, partly due to the consolidation of investment and expansion carried out by biotechnology companies over recent years. In 2009 ASEBIO members accounted for barely 20 companies with a presence in 22 countries, compared with 43 companies in 39 countries in 2013.

60% of subsidiaries belonging to ASEBIO members are in the US (18.1% of the total); Portugal (8.3%);

Germany (7.5%); Italy (6%); France (5.26%); the UK (5.26%); Mexico and China (4.5%).

In terms of geographical area, Europe continues to account for nearly half of overseas subsidiaries with 47% of the total, followed by Latin America (24%), the US/Canada (20%), and Asia-Pacific (9%).

The table below shows the number of biotechnology companies that are ASEBIO members with subsidiaries, branches or some other form of representation, in each country.

USA	24
PORTUGAL	11
GERMANY	10
ITALY	8
FRANCE	7
UK	7
MEXICO	6
CHINA	6
BRAZIL	5
COLOMBIA	4
SWISS	4
CHILE	3
NETHERLANDS	3
POLAND	3
CANADA	2
ARGENTINA	2
BELGIUM	2
SWITZERLAND	2
HONDURAS	1
DOMINICAN REPUBLIC	1
PANAMA	1
BOLIVIA	1
PARAGUAY	1
GUATEMALA	1
EL SALVADOR	1
COSTA RICA	1
VENEZUELA	1
ECUADOR	1
PERU	1
URUGUAY	1
DENMARK	1

Table 8. International presence of ASEBIO members by number of subsidiaris/branchess/representation offices. Source: ASEBIO

The list below shows the ASEBIO member biotechs and the countries in which they have an established direct presence.

Company	*Countries with a direct presence*
ABENGOA BIOENERGÍA	US, France, Netherlands and Brazil
ALMIRALL	Canada, US, Mexico, Portugal, UK, France, Italy, Switzerland, Belgium, Netherlands, Germany, Denmark, Austria and Poland
ASPHALION	Germany
BIOIBERICA	Poland, Brazil, US and Italy
BIOMEDAL	US
BIONCOTECH THERAPEUTICS	US
BIONURE	US
Biotools B&M Labs	Brazil
BTI BIOTECHNOLOGY INSTITUTE	Germany, Italy, Portugal, UK, Mexico and US
CYTOGNOS	Netherlands
DIGNA BIOTECH	US
Era7 Information Technologies	US
ESTEVE	Germany, China, US, Italy, Mexico, Portugal, Sweden and Turkey
FERRER INTERNACIONAL	France, Germany, Belgium, Greece, Portugal, US, Mexico, Honduras, Dominican Republic, Panama, Bolivia, Paraguay, Guatemala, El Salvador, Costa Rica, Colombia, Venezuela, Ecuador, Peru, Brazil, Uruguay, Argentina and Chile
GADEA BIOPHARMA	Malta and China
GENETADI BIOTECH	Mexico
GENETRIX	Sweden
GENNOVA SCIENTIFIC	Sweden, China
Grifols	Czech Republic, France, Germany, Italy, Poland, Portugal, Slovakia, Switzerland, Sweden, UK, Canada, Mexico, US, Argentina, Brazil, Chile, Colombia, Australia, Japan, China, Malaysia, Singapore y Thailand
GRUPO FARMASIERRA	Portugal
INGENIATRICS	US
Insights in Life Sciences	US and China
INTEGROMICS	US
INTELLIGENT PHARMA	UK, Germany and US
LABORATORIOS LETI	Germany and Portugal
LABORATORIOS RUBIÓ	Portugal
LIFE SCIENCE PRAXIS	US
LIPOPHARMA THERAPEUTICS	US
n-life Therapeutics	Portugal
NATAC BIOTECH	US and Chile
NEURON BIO	US
Neuroscience Technologies	UK
NORAYBIO	France, UK and Italy
OSTEOPHOENIX	Colombia
PHARMAMAR	US, Italy and Germany
PIVOTAL	Portugal, Italy, France and UK
PRAXIS PHARMACEUTICALS	Portugal, France and Colombia
Progenika Biopharma	US and UAE
SINOPTIA	US and China
SYGNIS	Germany
Thrombotargets Europe	US

Table 9. Biotechnology companies which are members of ASEBIO and countries in which they have a direct presence. Source: ASEBIO

International Alliances

During 2013, 57 Spanish biotechnology companies and entities (+39% compared to 2012) signed a total of 108 international alliances (+42%), the second most significant increase since ASEBIO started keeping records on this type of international partnership.

In regards to geographical distribution the pattern is similar to other years, although we should note that the number of alliances with Asian and Latin American countries has doubled. Since 2009 the number of international alliances has increased by 170%.

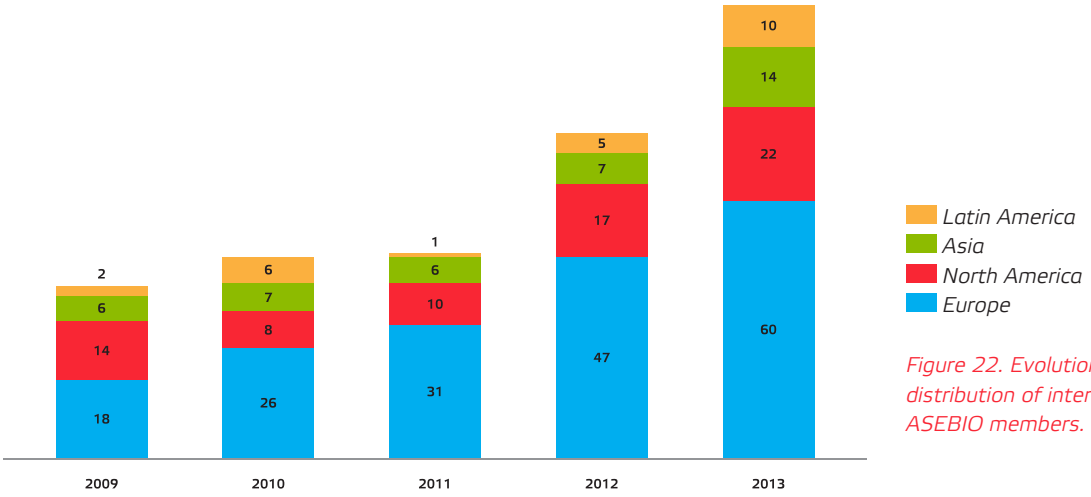


Figure 22. Evolution of geographical distribution of international alliances by ASEBIO members. Source: ASEBIO

This statistic includes any type of formal agreement between at least one Spanish biotechnology company or institution and any other international entity involving an explicit commitment to achieve a shared objective or objectives of any given nature (R&D, production, sales, etc).

Examples of success in the internationalisation of Spanish biotechnology companies

The internationalisation of companies may involve a whole range of strategies, always depending on the profile of the company in question and the product or service offered. A company can undertake the internationalisation process via non commercial formulas (such as licences, production contracts, manufacturing plants, etc); by establishing presence or direct sales (through an overseas office or subsidiary or internationalisation department); international alliances (consortia for international projects, and other R&D collaborations) or via indirect sales through a distributor or representative.

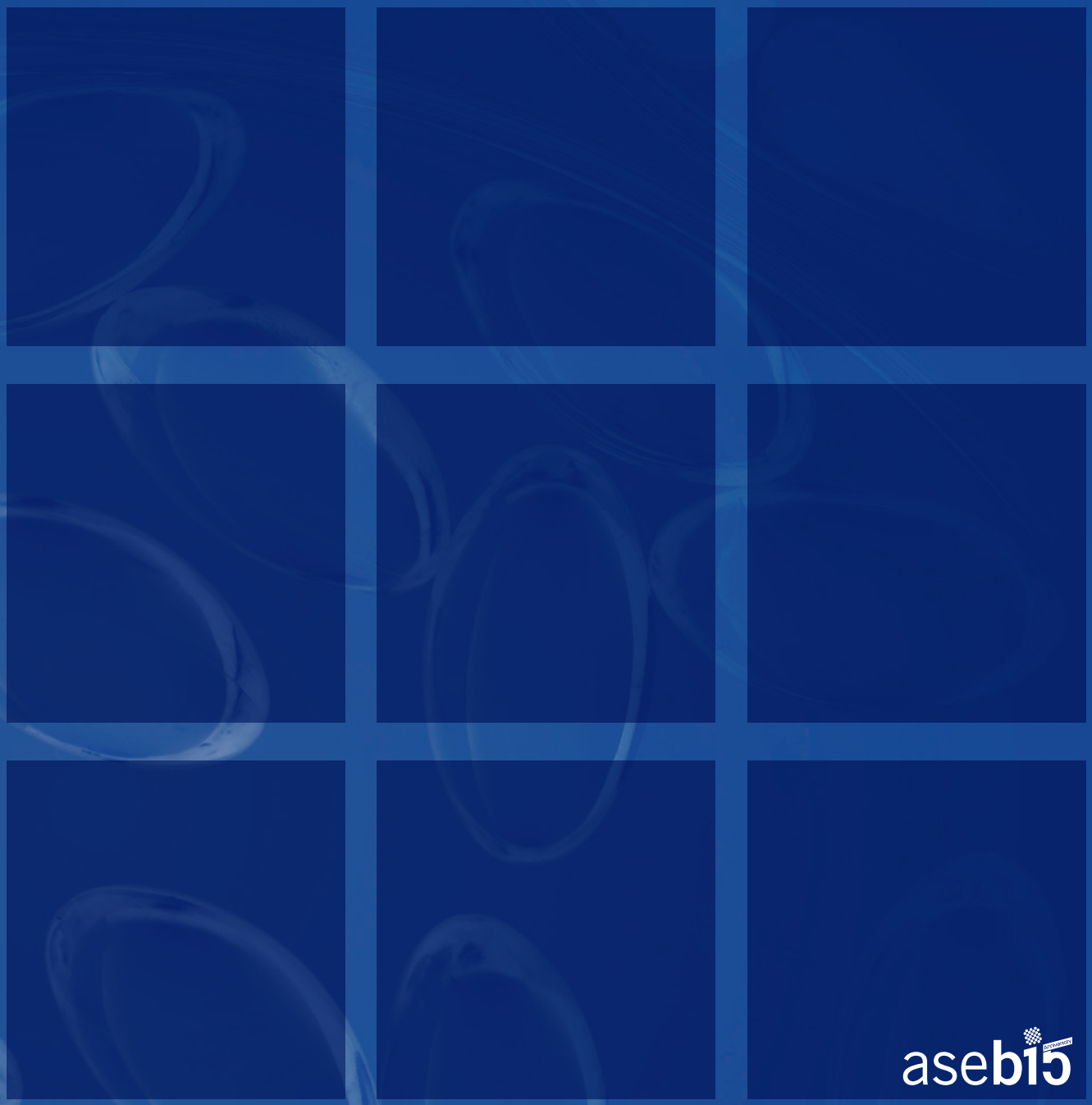
All these possible strategies for the international development of a company have been successfully applied at some point by biotechnology companies who are members of ASEBIO. Some, such as Grifols, Abengoa and Repsol, who have subsidiaries and production plants around the world, find themselves in positions of international leadership amongst the most important multinational in the world, according to the FORBES world ranking.

But not only large companies have had success in their internationalisation processes. Companies which only recently considered themselves to be biotechnology SMEs - companies such as NorayBio, Pharmamar, Praxis Pharmaceuticals, BTI Biotechnology Institute and Intelligente Pharma, to name just a few – today have subsidiaries across a number of countries.

Even ASEBIO, as the trade association for such an internally dynamic sector, has not only grown to become the third biggest trade association for biotechnology companies in Europe, but it has also made its main event, Biospain, one of the most attended biotechnology events in Europe just as it has internationalised its actives, organising the first edition of Biolatam, the biggest biotechnology event to date in Latin America.

This year, as an example of a big success story in the sector because of the many challenges it involved, we will talk about 3P Biopharmaceuticals, who through its efforts to consolidate its international position has created a client portfolio from a wide range of countries including France, Italy, the UK, Norway, the US, Mexico, Argentina and Australia. In the US the company has two projects underway, one of them with a large multinational.

10 *Biolatam 2013*



Biolatam 2013

Biolatam 2013 took place in Bogotá, Colomia, on the 9th and 10th of December.

On its first edition, the objective was for Biolatam to become a showcase and meeting point for the Latin American biotechnology sector. The event also included biotechnology user companies: pharmaceuticals, food industry firms, cosmetics companies, veterinary industry firms, chemicals industry actors, energy companies and others. It also attracted international investors (particularly capital venture funds). As such, it was conceived as a meeting point for global biotechnology with interests in Latin America.

An event of these characteristics brings about mutual benefits for Latin American and European companies and institutions, fostering technological collaborations, opening up key potential markets such as that of the EU and Latin America, encouraging bilateral investment in biotechnology, contributing to economic development and generating highly skilled employment.

Biolatam was organised by the Spanish Bioindustry Association (ASEBIO) and Invest in Bogota, with the institutional support of the Bogota Chamber of Commerce, iNNpulsa, Bogota City Hall (Department of Economic Development) and the Gobernación de (Department of) Cundinamarca (Department of Science, Technology and Innovation).

From Spain, the event received the support of ICEX, the Spanish Foreign Trade Institute, and CDTI, the Centre for Industrial Technological Development. The organization of American States (OAE) also provided institutional support for the event, as well as many sectoral associations from various countries across the America and Europe.

For its first edition Biolatam was structured in such a way as to meet the commercial and information related demands of the sector, providing the necessary tools for its development, both at the local and international level. The event combined a partnering *(*with *one-to-one meetings),* a programme of conferences and networking events all with the objective of facilitating the development of relationships between international companies, investors, institutions and research centres from the biotechnology field and related areas of study.

The results from this first edition of the event reveal some important numbers for its consolidation. A total of 720 delegates from 29 countries attended the event, 500 delegates representing almost 300 different entities took part in the partnering, where 839 one-to-one meetings took place. During the course of the event many collaboration agreements were announced.

Also, amongst the delegates were representatives from 17 international investment funds,

one of the objectives being to increase the presence of specialised biotechnology investors from Spain, Europe and Latin America. The event, which took place in the Bogotá Chamber of Commerce, also hosted a small trade fair with 23 exhibitors.

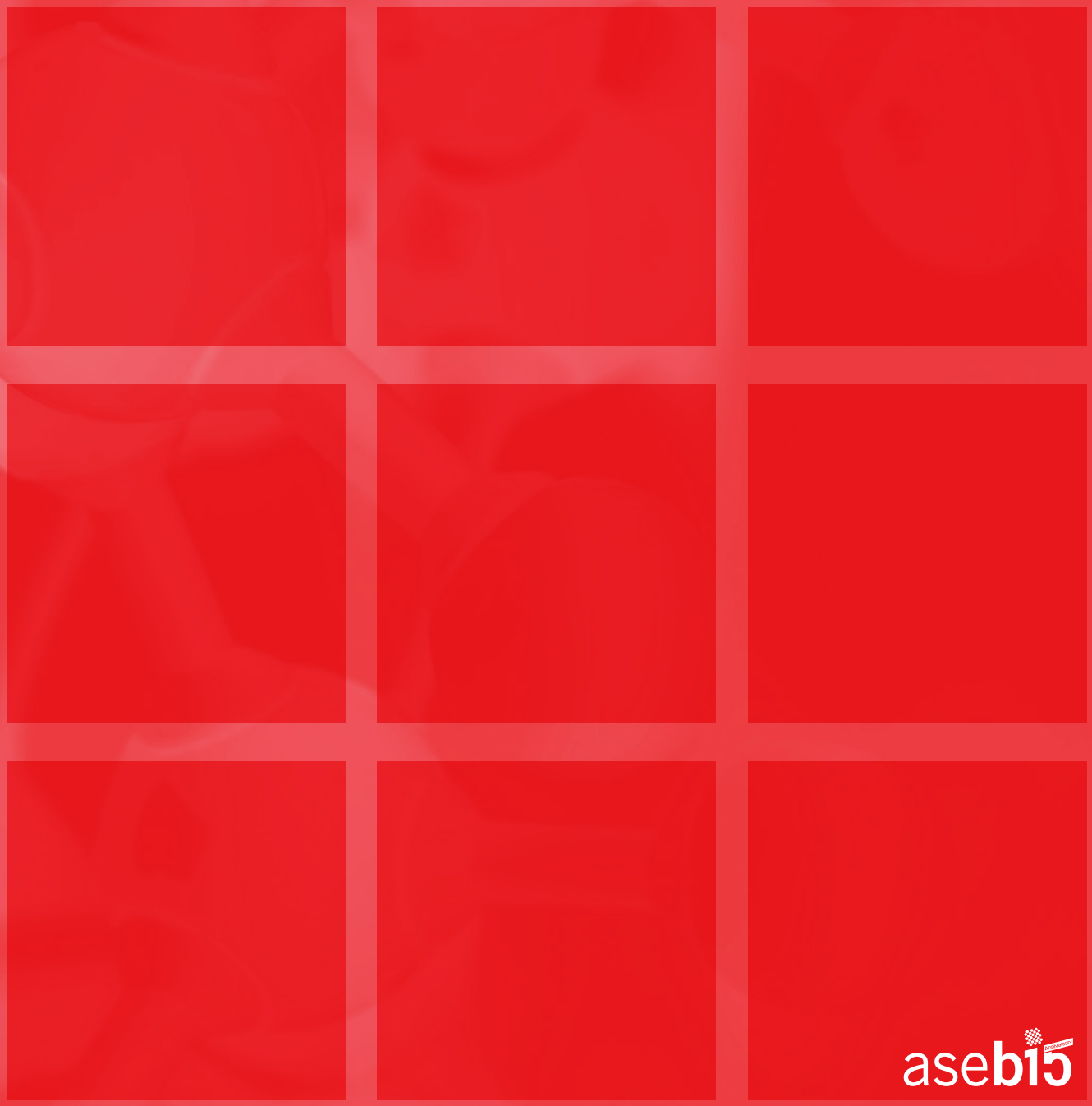
Regarding the geographical distribution of the participating delegates, Colombian entities accounted for 41.8% (at 125) of the total, followed by Spanish companies whose delegation included over 70 companies (24.1%). Behind them, entities from the US (6%), Brazil (4.7%), Mexico (4.3%), and Chile (3.7%) had the most representatives. Other countries including China, India, Finland, Germany, the UK and Holland, among others.

Breaking it down by sector, the pharmaceutical industry had the biggest presence accounting for 25.7% of representatives. Representatives from clusters and other public entities made up the second largest group, at 15%, and the agrifood sector, with 13.6%, was the third most represented. There were also delegates present from entities associated with medical devices, cosmetics, the veterinary industry, bioinformatics, the chemicals industry, the energy sector, as well as investment funds, universities, hospitals and others.

Up to six countries from Latin American regions showed interest in providing a venue for the 2015 event, the next edition. In the framework of Biospain 2014 (24-26 September 2014, Santiago de Compostela), the Biolatam showcase will take place, bringing Latin American biotechnology to Spain.

In its first edition, Biolatam became the main partnering event in the Latin American biotechnology sector for business development between biotechnology firms and user sectors from all around the world that see the opportunities in Latin America.

A1 Who Is Who *ASEBIO Members*



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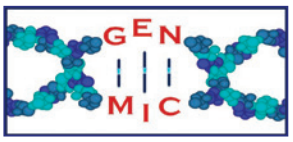
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