ACTIP Animal Cell Technology Industrial Platform

ACTIP 1990 - 2010

1. ACTIP 20 years: an introduction

At this point in time, the year 2010, animal cell culture has become a viable platform for the development of treatments aimed at diseases with unmet medical needs. It is also the year in which ACTIP, the Animal Cell Technology Industrial Platform, celebrates its 20th anniversary. In those 20 years, animal cell technology for the production of biopharmaceuticals evolved from a minor technology to the technology of choice. But science went through great lengths before this came to be.






Over the years, the following have given their time and effort as ACTIP chairperson:

Dr. Michael Comer, Boehringer Mannheim (1990-1996)
Dr. Berthold Bödeker, Bayer (1996-2000)
Mr. Hans van den Berg, Akzo Nobel Pharma (2000-2004)
Dr. Avinoam Kadouri, Serono (2005-2006)
Dr. Christel Fenge, Astra Zeneca (2006-2008)
Dr. Luc Kupers, Genzyme (2008-....)






ACTIP

Networking is an important activity for ACTIP. Hence we try to make time for social activities after the meeting. On this and the following pages we present a selection of pictures from ACTIP meetings held in respectively Budapest (2000), Toulouse (2003), Berlin (2006), Dublin (2007) and Alicante (2010).

A first step was taken when salt solutions were used for tissue conservation. At the beginning of the previous century Ross Granville Harrison, professor of comparative anatomy at Yale University designed tissue-culture techniques thanks to his research on the amphibian embryo. Another pioneer on tissue culture was the French surgeon Carrel who was able to preserve chicken embryo cells for decades. It was the quest for viral vaccines, in particular for poliomyelitis, which elevated the development of animal cell culture to a new level. The Salk inactivated polio vaccine, for example, was one of the first treatments that was mass-produced using primary monkey kidney cells. In the early sixties Hayflick from the Wistar Institute developed a cell line from human embryonic tissue, the WI-38 (see also the tables at pages 38-41).
The cell line was freezable and could be reactivated with relative ease, making it the ideal base for the production of human viral vaccines.
The widely renowned CHO cell line was established by Professor Puck in the

Toulouse 2003






fifties and swiftly became the workhorse of biochemistry. In 1987, the first approval for the use of genetically modified CHO cells was granted to Genentech for the production of Tissue Plasminogen Activator (tPA) (see also the tables at pages 30-41).
Today, more than 65% of the available therapeutic proteins are produced in CHO cells. Modification of the CHO-cells, proper process development and optimization of cell culture strategies significantly increased the production rate per cell. From a regulatory point of view production of therapeutic proteins in CHO cells stood the test of time.

The use of animal cell cultures made it possible to develop new and innovative solutions for diseases previously untreatable. Rheumatoid arthritis, Crohn's

Berlin 2006

Inishturkbeg after Dublin meeting 1999

disease, intestinal cancer, breast cancer, psoriasis, genetic disease are but a few of the diseases that can now be treated with proteins produced thanks to animal cell technology. We have come a long way, but there is still tremendous potential in the use of animal cell cultures.

The development of stem cell technology provides revolutionary opportunities for regenerative medicine and the treatment of genetic diseases. At the same time, the reprogramming of somatic cells like skin fibroblasts (the induced pluripotent stem cells), shows great promise in creating therapies for previously unmet medical needs. Gene therapy, *in vitro* toxicology and nanobiotechnology are but a few of the fields where the use of animal cell culture technology can make a lasting difference.

The impact of animal cell culture on human health was, is and will be important. Advances in genomics, proteomics, metabolomics and system biology all contribute to an increasingly large number of products derived from human and animal cell culture that can lead to huge improvements in a patient's quality of life. It does not stop with rare and complicated diseases, as monoclonal antibodies will become available at large volumes, bringing protein therapies to large infectious diseases.

In November 1990 a group of people active in animal cell culture as applied in industry established the Animal Cell Technology Industrial Platform (ACTIP) to design a common strategy for the promotion of European R&D aimed at animal cell culture technology. The organization also functioned as an advisory organ to the European Community on related matters, as ACTIP published opinion letters to promote all kinds of research programmes in animal cell technology.

Originating as an advisory group, the platform evolved to a networking organization, providing members with ample opportunity for cooperation between SMEs and academics, benefiting the technology's advancement.

This year, we celebrate our 20th anniversary, and we are proud that our organization has remained active throughout this period. Biannual meetings are organized at different locations across Europe creating a platform for open and energetic discussions that strengthen our common resolve to promote animal cell culture technology. New members and visitors from invited companies or the academic world are taken in by the friendly and open atmosphere. Social events and the dinner are an ideal occasion for networking and allow us to form new bonds that can expand our organization. One of our members who is pivotal in our organization is Dr. Helma Hermans. As one of our founders, she continues to be the driving force behind ACTIP.

Like animal cell technology, ACTIP has come a long way over the past 20 years. Our journey does not end here however, as new and innovative therapeutic options are discovered every day. Just as the technology that ACTIP has chosen to promote, the organization itself continues to grow and expand. With the support from our professional staff and our members, I am certain that we will continue to have a lasting impact on the future development of animal cell culture technology as well as its promotion for the coming years.

Dr. Luc Kupers,
Chairman ACTIP

Alicante 2010






2. Objectives of ACTIP

In the mid and late 1980s, animal cell technology was a pioneering technology to produce viral vaccines and recombinant therapeutic proteins. The technology, however, was new, and the mechanistics of the processes involved poorly understood. There was poor understanding of the requirements for transcription, a poor understanding of translation, expensive and difficult fermentation, low yields, and a limited repertoire of cell lines, expression systems and possibilities for posttranslational modifications. Yet, the technology was widely seen as promising, and several industries took a keen interest in the development of animal cell culture processes. Academic research received a boost once the European Commission decided to make animal cell technology one of its spearhead technologies.

In June 1990, a Committee was formed to prepare for the official establishment of ACTIP. Its members were Dr. Michael Comer (then of Boehringer Mannheim, Germany), Dr. Jan Lupker of Sanofi Elf Biorecherches (France) and Dr. Helma Hermans, then of HOM Consultancy, the Netherlands. They organized and chaired the November 22, 1990 establishment meeting of ACTIP.

The initiative to establish an industrial platform in the area of animal cell technology was first discussed during the meeting of ESACT (European Society for Animal Cell Technology) in Avignon in May 1990. This was followed by an establishment meeting in Dublin in June 1990. At the Dublin meeting, hosted by BioResearch Ireland, the following reasons were cited as the basis for setting up such platform:

• as R&D activities of a European character in animal cell biotechnology are attracting increased

interest, new regulations and legislation developed in Europe are having a clear impact on the field;
- public interest (and concern) is increasing and the time is therefore ripe to organize a more active industrial role;
- the European Commission is organizing so-called tripartite (T-projects), one of these addressing animal cell technology. Such a project could well benefit from the existence of a European Industrial Platform.

Accordingly, a preparative Committee was formed to prepare the official establishment of ACTIP.

The official establishment meeting of ACTIP took place on November 22, 1990 in Brussels. During that meeting, it became clear that the Commission of the European Communities supported the establishment of ACTIP in relation to the CAN-BRIDGE T (targeted)-project on animal cell technology. The BRIDGE-programme, which ran from 1990-1994, was strongly focused on industrial interaction. As was written in the minutes of the Brussels meeting:
"The Services of the Commisison will participate in the elaboration of a platform of industries which have interest in this T-project, but do not wish to participate in contractual research. Such a platform will be closely involved in the implementation of the T-project."

And so ACTIP came to be. It set out to become an influential body with as members influential industries representing a cross section of European companies. It would exert its influence by establishing close contacts with the European Commission, providing expert opinions based on consensus of its members, informing its own network and sharing information, also with the public.

The initial objectives of ACTIP (1990) were:

1. Development of a common attitude in order to provide an industry perspective to publicly supported R&D in Europe as it concerns methodologies and technologies for animal cell culture;
2. Identification and development of solutions to problems and obstacles which (could) arise in the implementation of new methodologies and technologies of animal cell culture and the commercialization of its products;
3. Influencing of public opinion so that it recognizes the positive contributions biotechnology makes through animal cell culture.






It set out to respond fast and non-bureaucratic in an informal structure. To this day, ACTIP functions as an informal forum of European industries involved in animal cell technology.

Current objectives

Since 2004, its objectives are:

- networking among the member companies, with SMEs working in the field and with academics, notably those working on research projects sponsored by the European Commission;
- following new developments in R&D;
- maintaining a focus on mammalian cell technology;

For purposes of definition, mammalian cell technology is considered to include animal cells, human cells, primary cells, insect cells and stem cells.
New developments in other cell types are reported on regularly.

3. ACTIP member companies

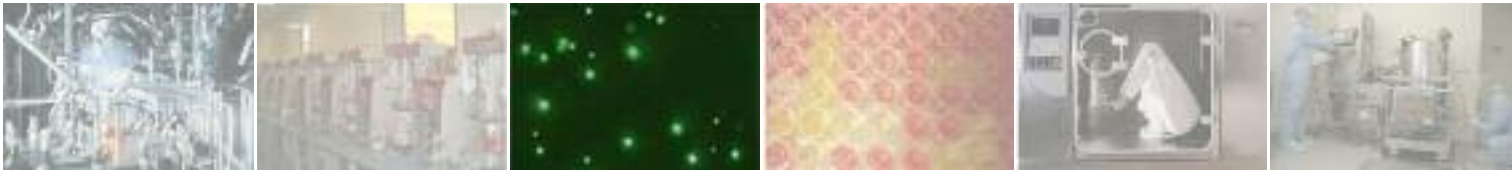
Right from the start, ACTIP membership was meant for Europe-based companies with significant activities in animal cell technology. As a consequence, ACTIP started to attract major European players involved in the production of vaccines, therapeutic proteins, as well as testing companies.

Early founding members included Schering, Boehringer Mannheim, Karl Thomae (later Boehringer Ingelheim), Sanofi Recherche, Celltech, SmithKline Biologicals, Merck, Wellcome Research Laboratories (later GSK), and Hungarian vaccine maker Phylaxia. In 1991 and 1992 such major players as Novo Nordisk, Behringwerke, Pasteur Mérieux, Pharmacia, Sandoz Pharma, Ciba-Geigy, Ares-Serono, Hoffmann-la Roche, Sartorius, Oxford Glycosystems and Protein Performance joined. Service providers (mostly testing houses) joined as well: Quality Biotech, Microbiological Associates, RBM, Hazleton Microtest and Inveresk Research. Facilitator Bioresearch Ireland joined as well, later through its spin-off company Archport.

The current (2010) membership criteria have hardly changed over the past 20 years;

- an applicant should have substantial activities in animal cell technology and being able to contribute actively and on content to ACTIP;
- an applicant should be based in Europe;
- an applicant should be more than just a sales organization (i.e. having own animal cell technology activities such as manufacturing, safety testing, R&D);
- in principle a holding company can hold only one membership of ACTIP; more

One of the early ACTIP meetings took place on April 6-7, 1992 at Loch Lomond, Glasgow (hosted by Quality Biotech). On the last row, 4th from left is Prof. Hervé Bazin of the Services of the European Commission. Prof. Bazin was one of the initiators of the T-project on animal cell technology and a staunch supporter of Industrial Platforms. First row center is ACTIP's founding father Prof. Michael Comer, flanked by co-founders Dr. Jan Lupker and Dr. Helma Hermans. Already representing their company in 1992 and still doing so in 2010 were Dr. Martin Wisher and Dr. Carl Martin (row 2, resp. 4th and 6th from the left), and Dr. Jarl Andersen and Dr. Zoltan Sümeghy (row 3, resp. far left and 7th from the left). On row 3, 2nd to the right, is one of ACTIP's founding members, Dr. William Werz of Karl Thomae/ Boehringer Ingelheim, who sadly died in 2002.



than one membership is only allowable when subsidiaries are diverse and independent, have a historic link to ACTIP or can offer unique expertise.

The most up-to-date membershiplist can be found on the ACTIP website: www.actip.org

This picture was taken during the May 11-12, 1995 meeting in Oxford, hosted by member company Oxford GlycoSystems. Between 1993-1997, ACTIP continued to attract major biopharmaceutical companies. New members included Bayer, Akzo Nobel Pharma, Solvay Duphar and Astra Biotech. These new member companies would supply later ACTIP chairpersons such as Dr. Hans van den Berg and Dr. Berthold Bödeker (on row 2, 4th and 8th left respectively). ACTIP also started to attract small- and medium sized companies, such as BioInvent, Biotest Pharma, Bio-Intermediair and Texcell. It was a time of intensive interactions with representatives of the European Parliament, the European Commission and various EU-funded projects in animal cell technology, represented in this meeting by respectively Mr. Armin Machmer (last row, 2nd right), Dr. Line Matthiessen (first row, 4th left) and Dr. Hansjörg Hauser (second row, 5th left). Since 1994, ties with ESACT strengthened, and since that date every ACTIP meeting has been attended by an ESACT Board member, mostly by its chairperson; shown here is Prof. Caroline MacDonald in her capacity as ESACT chairperson (first row, 3rd right).

In 2001, ACTIP decided to actively pursue the policy of inviting selected SMEs to its meetings. Invited SMEs either worked on a topic featuring in the meeting they were invited to, or they formed part of the network of the company hosting a particular meeting. Invited SMEs are always given the opportunity (but not obligation) to shortly present their company. For the ACTIP membership, the SMEs provided insight into new technologies and approaches; the SMEs gained the unique opportunity to present their company's core technology and to expand their network. No wonder that many invited SMEs decided to apply for membership. Thus, the early years into the new millennium saw an influx of new members, both small and large. New additions to the ACTIP membership between 2000-2010 were Innogenetics, Cambridge Antibody Technology (now MedImmune), 4C Biotech, Serologicals, Invitrogen, Genzyme, PharmAAware, Henogen, Morphosys, Berna Biotech (later Crucell), GenOWay, Centocor, Rentschler, Octapharma, Artelis, Pfizer, Wyeth, Eli Lilly and Merckle Biotech. This picture was taken during the May 28-29, 2009 meeting in Biberach an der Riss, Germany, hosted by member company Boehringer Ingelheim.






4. How ACTIP operates

ACTIP is an informal forum without official charter but with household rules, decided by its membership. This structure is reflected in its organization. Day to day business is taken care of by a Steering Committee, which is elected every two years from among the membership. The current Steering Committee has seven members. The Executive Secretary follows up actions, maintains contacts with European organizations, prepares meetings and is the first point of contact for infomation. The Executive Secretary, since ACTIP's foundation represented by Dr. Helma Hermans, is supported by the Secretariat, currently run by Mrs. Els van den Berg. Both work part-time for ACTIP on an hourly basis.

The ACTIP activities are financed exclusively through the annual membershipfees paid by the members. In 1991, membershipfee amounted to 1,800 ECU/year; in 2010, the amount had only sligthly risen, to 2,750 Euros/year.

Despite ACTIP's close links to the European Commission (especially in its early years), it has never received national or EU funding. This financial independence and its decision making by way of consensus ensure that ACTIP's opinions, positions and choice of meeting participants are valued highly in both academic, industrial and EU communities.






Over the years, many ACTIP member companies have provided representatives to serve in the ACTIP Steering Committee.
Here we present a nearly complete list:

Dr. Jan Lupker (1990-1996) and (2000-2002)
Dr. Elisabeth Lindner (1992-1994)
Dr. Zoltan Sümeghy (1992-1997)
Dr. Thomas Petri (1994-1998)
Mr. Hans van den Berg (1996-2006)
Dr. Carl Martin (1997-2006)
Mr. Malcolm Brattle (1997-2003)
Dr. Jarl Andersen (1999-2000)
Dr. Jürgen Vorlop (2000-2002)
Dr. Tim Clayton (2000-2003; 2006-2010)
Dr. Cristina Glad (2002-2010)
Dr. Etienne Boutry (2002 –2006)
Dr. Avinoam Kadouri (2003-2006)
Dr. Annie van Broekhoven (2004-....)
Dr. Aziz Cayli (2004-2005)
Dr. Christel Fenge (2006-2008)
Dr. Donnacha O'Driscoll (2006-2008)
Dr. Isabelle Knott (2006-2010)
Dr. Luc Kupers (2006-....)
Dr. Dieter Moosmayer (2006-2008)
Dr. Martin Wisher (2008-....)
Mr. Ralf Fehrenbach (2008-....)

ACTIP Secretariat, early days:

Diana Polder (1992-1997)
Annemarie de Heer (1997-2007)

ACTIP Secretariat, currently:

Augusta Thorbecke (1999-....): Meeting assistant. Graphic designer, responsible for ACTIP publications and website.
Els van den Berg (2008-....): ACTIP Secretary. Multilingual with international (embassies, industry) experience.

Executive Secretary:

Helma Hermans (1990-....): Endocrinologist. Head of Scientific Writing & Consultancy. Executive Secretary of ACTIP since 1990.

5. ACTIP's meetings

The by far most important activity of ACTIP is the twice yearly organization of a plenary meeting. Every meeting is hosted by a different member company and takes place in either this company's home town or even on the company premises. Often, a host company will organize a tour of its manufacturing and/or research facilities. Because of this arrangement, the past 20 years saw ACTIP meetings in many European countries.

These meetings are confidential and only open to ACTIP members, as well as to invited speakers and special guests. Since 2001, it has been ACTIP's policy to invite per meeting representatives of three to five SMEs; as a rule, these SMEs belong either to the network of the ACTIP host company, or they are specialized on the themes covered in that particular meeting. Since 2009, two ACTIP Fellows (see page 29) are invited as well to every meeting.

The organization of a meeting is in the hands of the ACTIP Secretariat and Executive Secretary, with local help and knowledge provided by the host company. The meeting programme is drafted by the members of the ACTIP Steering Committee and the regular representative of the host company.

After every meeting, extensive minutes are written, summarizing the presentations given. Over the course of 20 years, more than 950 pages of minutes have been written! These minutes are available on the secure part of the ACTIP website, as well as downloadable copies of the presentations given. Over the past 20 years we have come a long way: our early presentations consisted of overhead sheets or slides; by now we feature ever more sophisticated powerpoint presentations!

Prof. Frank Gannon used to be the overall co-ordinator of the EU-funded T-project on animal cell technology. As a rule, he presented the overall progress of the topics studied within the T-project. But his broad grasp of all issues related to animal cell technology made him an ideal reserve speaker: quite often he had to stand in for a speaker unable to attend a meeting due to airway strikes or other mishap. He would receive the overhead sheets of these presentations at night by fax in his hotel, consult with the original speaker and off he went! Thus giving someone else's presentation became an ACTIP-coined verb: 'to Gannonize a presentation'!

ACTIP

During its first 20 years, ACTIP has organized 39 meetings, to which it invited 355 speakers and guest companies. As an experiment, we organized only one meeting in 2001. All members agreed that one meeting per year was not enough to maintain contacts and keep up to date with new developments, so we quickly reverted to the twice yearly schedule.

ACTIP refunds the travel and accommodation costs of invited speakers from academia and accommodation costs of industrial invited speakers.
Member companies and invited guest companies pay their own expenses.

Amsterdam meeting 1996

20 years of meetings:

1990
ESACT meeting, Avignon, France, May (first discussion)
BioResearch Ireland, Dublin, Ireland, June 6. Establishment meeting; first discussion Task Force on BSE
HOM Consultancy, Brussels, Belgium, November 22

1991
Sanofi Elf Biorecherches, Labège/Toulouse, France, March 22-23
Ares Serono, Rome, Italy, November 11-12

1992
Quality Biotech, Glasgow, Scotland, April 6-7
Schering AG, Berlin, Germany, November 30

1993
Sandoz, Basel, Switzerland, June 4-5
Phylaxia, Budapest, Hungary, November 29-30

1994
Pharmacia, Stockholm, Sweden May 9-10
Boehringer Mannheim, Garmisch, Germany, November 24-25

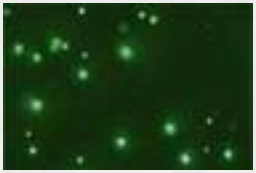
1995
Oxford Glycosystems, Oxford, UK, May 11-12
Pasteur Mérieux, Annecy, France, December 11-12

1996
ESACT, Vilamoura, Portugal, May 19-20
Akzo Nobel Pharma, Amsterdam, The Netherlands, December 9-10

Important topics covered in ACTIP meetings since 1990:

Cell and molecular biology:

Expression systems;
Glycosylation;
EC funded research projects;
BSE/scrapie;
Furry bioreactors/transgenic animals;
Tissue engineering;
Gene therapy;
Baculovirus-insect cell expression;
Apoptosis;
Stem cells;
Vaccines;
Monoclonal antibodies;
Genomics/Proteomics; Toxicogenomics
High producer expression systems;
Human cell lines;
Transient expression;



ACTIP

(topics, continued)

Technology issues

Safety;

Serum/protein cell culture free media;

Disposables;

High production strategies;

Upstream;

Downstream Processing;

Bioreactors; Scale-up;

Pilot plants;

Fed batch versus continuous processing;

Comparability/Biosimilars;

PAT/QBD;

CMO-client relationship;

Regulatory

Annual regulatory issues;

Harmonization/ICH;

FDA Points to consider;

EMA discussion papers;

Science and Society

BSE/scrapie;

Public relations;

Biotech in the European Parliament.

1997

Novo Nordisk, Copenhagen, Denmark, June 2-3

Bayer, Wuppertal, Germany, December 8-9 (start communication through website and e-mail)

1998

RBM, Ivrea, Italy, June 4-5

Glaxo-Wellcome, London, United Kingdom, December 3-4

1999

BioResearch Ireland, Dublin, Ireland, May 27-28

SmithKline Beecham Biologicals, Brussels, Belgium, November 29-30

2000

Novartis Pharma, Budapest, Hungary, May 22-23 (BioLinks proposal GBF, ESACT and ACTIP, linking contractors with industry. Not funded)

Texcell, Paris, France, November 27-28

2001

Covance, York, United Kingdom, September 20-21 (just after 9-11, many speakers and members unable to travel/attend)

2002

DSM Biologics, Amsterdam, The Netherlands, June 20-21

Innogenetics, Gent, Belgium, December 12-13

2003

Sanofi-Synthélabo, Toulouse, France, April 24-25 (application Research Training Network with ESACT, ACTIP)

Serono, Montreux, Switzerland, December 11-12






2004
Chiron Vaccines, Marburg, Germany, June 3-4
Genzyme Flanders, Antwerp, Belgium, December 9-10

2005
BioInvent International, Lund, Sweden, June 16-17
Sartorius, Göttingen, Germany, December 8-9

2006
Schering, Berlin, Germany, May 15-16
BioReliance/Invitrogen, Edinburgh, Scotland, December 7-8

2007
NICB/Archport, Dublin, Ireland, May 10-11
RBM MerckSerono, Ivrea, Italy, November 29-30

2008
GlaxoSmithKline Biologicals, Brussels, Belgium, May 22-23
MedImmune, Cambridge, United Kingdom, November 17-18

2009
Boehringer Ingelheim, Biberach an der Riss, Germany, May 28-29
DSM Biologics, Leiden, The Netherlands, November 19-20

2010
ACTIP Secretariat, Alicante, Spain, May 26-28
Roche Diagnostics, Penzberg, Germany, December 2-3

Dublin meeting

Alicante meeting

6. Our output over the years

In addition to the twice-yearly meetings, ACTIP's activities include the writing of newsletters, leaflets, booklets, and position papers. The latter reflect consensus views of the members, and have been influential papers, submitted to national or international bodies such as the FDA, EMA or the European Commission.
On an ad-hoc basis, ACTIP has also organized Working Parties, composed of representatives of member companies. Often, the work of these Working Parties has resulted in special thematic sessions at meetings, in position papers or in member-only informative documents.
Furthermore, ACTIP occasionally delegates one or two members as an Interested Party to international meetings of regulatory authorities.
On an ad-hoc basis, Working Parties composed of representatives of member companies can be formed. Over the years we had the following:

Topical Working Parties:

1992: WP Biological Standards
WP Public Relations
WP Regulatory Affairs
WP Science
WP In-vitro Toxicology (led to the establishment of the In Vitro Testing Industrial Platform in 1993)
1995: WP Insect cell technology
1997: WP TSE/BSE

Position papers and publications:

1992: ACTIP proposal on future lines of research
1992: ACTIP position paper on unconventional agents of spongiform encephalopathies



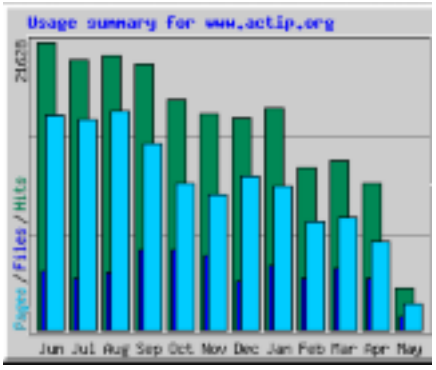



1993: ACTIP proposal on future lines of research in animal cell technology
1994: Fate ACTIP proposal on BSE
1994: Joint policy statement of ACTIP and EWGT on somatic gene therapy
1994: ACTIP policy statement on somatic gene therapy
1994: Publication Beneficial Effects of Animal Cell Technology (authors Dr. Anke-Peggy Holtorf, Dr. Thomas Petri, Dr. Helma Hermans)
1995: Comments on PTC 'Cell lines to produce biologicals'
1995: The what and why of patents in biotechnology
1996: ACTIP position paper on unconventional agents of spongiform encephalopathies
1996: Proposal for funding by the European Union of research in the field of animal cell technology and related areas within the 5th Framework Programme (FP5)
1996: Leaflet on the Animal Cell Technology Industrial Platform
1997: ACTIP's position paper on key figures of the European Biotech industry
1998: Poster on ACTIP and projects followed during FP4
1998: ACTIP letter to DGXII: ACTIP calls for basing assessments on quality of research and creating a strong scientific basis in the Life Sciences
2000: ACTIP comments on implementation FP5
2000: ACTIP position paper: Back to basics – balancing fundamental and applied research for the future of health and life sciences (input for FP6)
2001: Comment on Communication from the Commission: Towards a Strategic vision of Life Sciences and Biotechnology
2002: Internal ACTIP paper: The baculoviurus/insect cell system: an inventory of current knowledge of the risks associated with the system for commercial production of therapeutic proteins
2002: Input ACTIP into Work Programme FP6
2010: ACTIP Position Paper on Future Areas of Research: to be developed.






7. Our website



ACTIP website statistics for 2009-2010. The statistics shown here detail per month the number of hits received (green bars), the number of pages visited (blue bars) and the number of files downloaded (purple bars). On average, the website receives 20,000 hits per month.

Since 1997, ACTIP has established a website, publicly available at www.actip.org. The website attracts between 10,000-20,000 visitors per month, and functions as an important source of information to those interested in animal cell technology.

Of course, the website provides information on ACTIP itself, such as our objectives, its organization, and special activities.

Of much value to visitors is the sharing of ACTIP's network, by listing both its own member companies as well as providing useful links to organizations and non-member companies active in the field of animal cell technology. Equally valuable are monographs on topics related to the practice of animal cell technology, as well as tables with products made using animal cell technology. There is also a library with documents of interest.

Also freely downloadable is ACTIP's regular Newsletter, which appears at least two times per year. The Newsletter covers News from the European Commission, Business News, Research News, News on Mergers and Acquisitions, Regulatory News, feature articles and an up to date agenda of interesting events. It was started in 1995, and had been available on the web since 1998. Up until the end of 2010, 60 Newsletters have been written, totaling more than 1,000 pages of text.

Finally, the website also features a password protected members only area. Here ACTIP members can consult contact details of ACTIP member companies, of invited speakers and of guests. The secure area also contains the full minutes written after every meeting, as well as pdf-files of all the presentations given.

8. ACTIP's network

Networking is an important objective of an ACTIP meeting. Our network includes first and foremost our own members. Therefore, at each meeting we allocate sufficient time for informal talks and get-togethers. As a rule we have a joint dinner (mostly courtesy of the host company), often preceded by an informal reception. But we also engage in other social activities, such as guided tours of a city (did you ever do sightseeing after 23.00 hrs in snow or rain?), boat rides or steam trains bringing us to special dinner locations and late night dancing into the wee hours of the morning (one of us danced in Stockholm with a broken leg in a plaster cast). Very memorable was the 1992 meeting in Berlin,

Following the Dublin meeting in May 1999, a group of ACTIP members visited Inishturkbeg, the island home of its Executive Secretary, in Clew Bay, Western Ireland. Landing was a bit wet and primitive.

ACTIP members and guests enjoying the Santa Barbara castle view in Alicante, May 2010.

where the ACTIP group visited a puppet-rendition of Mozart's Zauberflöte in just-opened East-Berlin, followed by a midnight supper. Equally memorable were the 1999 weekend visit by boat to Inishturkbeg, the Clew Bay island home of its Executive Secretary in Northwest Ireland, and the 20th Anniversary meeting in Alicante, where we met in a seacliff hotel with entertainment in an on-site amphitheater.

ESACT

Our network also includes the ESACT membership and its Board of Directors. After all, ESACT stands for the European Society of Animal Cell Technology and therefore represents individual scientists working in academia and industry. To ensure close links, since 1994 ESACT is a permanent observer of ACTIP, delegating its current chairperson (or another member of the ESACT Board) to each and every ACTIP meeting, where a slot is reserved for a presentation on 'News from ESACT'. In addition, over the years, ACTIP and ESACT have teamed up to write joint project proposals seeking European funding. Thus, ACTIP and ESACT are ensuring that the animal cell technology community speaks with one voice.

ESACT observers to ACTIP:

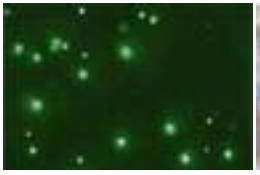
Prof. Caroline MacDonald (1994-1997)
Prof. Manuel Carrondo (1997-2000)
Dr. Otto Wilhelm Merten (1999-2004)
Prof. Florian Wurm (2005-2009)
Dr. Martin Fussenegger (2010 until present day)












European Commission

Another important element of the ACTIP network is the European Commission. After all, ACTIP was established with strong encouragement from the Commission in the person of Prof. Hervé Bazin!

During the EC-funded CAN-BRIDGE programme (1990-1994), which was created for industry, the Commission initiated the so-called T-projects, which were large, transnational networks of competence, creating opportunities for precompetitive research and involvement of industry. The T did not only stand for 'Targeted', but also for Tripartite: Academia, the European Commission, and Industry. As Prof. Hervé Bazin told the potential ACTIP members gathered in Brussels in 1990:

"DG XII (Research) needs for its T-project Animal Cell Biotechnology an independent, industrial platform like ACTIP to actively promote input for future research programmes since these are specially designed to provide a basis for European industry".

Thus started a long-lasting, fruitful relationship. Over the years, several scientific officers attended the ACTIP meetings, and if they were absent, at least they could

Joint research proposals ACTIP-ESACT:

- *FP5, February 2000: Accompanying measure, BioLink: linking industry and academia in Cell-factory-related projects of FP5*
- *FP6, March 2002: Expression of Interest for AC Training: Dedicated training activities in animal cell culture technology*

The following Scientific Officers of the Services of the European Commission were regularly present at the ACTIP meetings:
Prof. Hervé Bazin (1990-1994),
Dr. Line Matthiessen (1994-1998) and
Dr. Jürgen Sautter (2006 until present day).

be reached for information on its various Framework Programmes, Calls for Proposals, funded projects and EC-policy in the life sciences. In return, ACTIP provided input for the various Framework Programmes in the form of position papers, and sent invited representatives to meetings in Brussels to evaluate research projects funded by the EC. In addition, each and every ACTIP meeting features a presentation called 'News from the Commission'.
In total, ACTIP learned about the CAN-BRIDGE programme (1990-1994) with the large T-project on animal cell technology; the Supplement Programme (FP2) 1994-1996, with seven G (generic) projects; and the various Framework Programmes. These included FP4 (1994-1998, with many projects in animal cell technology, gene therapy, vaccines and stem cells); FP5 (1998-2002, which was a break with the past, featuring problem solving Key Actions and a break with the special status of Industrial Platforms); FP6 (2002-2007, emphasis on European Research Area and many projects in immunology and stem cell technology), and the current FP7 programme (2007-2013), with of special interest to the ACTIP members immunology, infectious diseases, vaccinology, stem cell technology, gene therapy and tissue engineering.

Prof. Frank Gannon was the co-ordinator of the Commisison's publicly funded T-project on animal cell technology.

Co-ordinators EU-funded projects

The 1990-1994 T-project on animal cell technology was tripartite: ACTIP, the European Commission and Academia. This large, integrated project focused on:

* genetic elements such as DNA constructs with improved expression possibilities, and systems to induce expression, select the best clones and amplify genes;
* safety aspects, focused on predictability: development of extrachromosomal vectors or targeted integration into the chromosome;
* product quality as a consequence of the focus on genetic elements and safety.

At the time, the topics given below were specifically excluded. It is a sign of evolution of the field that the topics then excluded now often are the focus of ACTIP meetings:

* selection of new host cells;
* study of host cell physiology per se;
* media optimization or replacements;
* fermentation technology;
* downstream processing.

The overall co-ordinator of the T-project on animal cell technology, Prof. Frank Gannon of Galway University, happily attended every ACTIP meeting between 1990 and 1994, reporting on the overall scientific progress of the project and suggesting that we invite as speakers academics working on specific parts of the project. This led to the tradition that every meeting features invited speakers from academic or industrial research projects. This greatly expanded the ACTIP network, with more than 100 scientists attending our meetings over the past 20 years.

The T-project on animal cell technology was followed by a G-project on animal cell technology, part of a special Supplement Programme which ran from 1994-1998. The co-ordinator of those projects, Dr. Hansjörg Hauser of GBF Braunschweig, became the regular scientific advisor of ACTIP in 1994 and anno 2010 he still serves as a permanent observer to ACTIP.
Co-ordinators of other EU-funded projects regularly attended the ACTIP meetings as well, with Dr. Finn Skou Pedersen of Copenhagen being the special co-ordinator of gene therapy projects from 1996-1998.

Dr. Hansjörg Hauser of GBF Braunschweig joined ACTIP in 1994 as the overall co-ordinator of the G-projects on animal cell technology. Sixteen years later he is still a permanent observer of ACTIP and one of our most important scientific contacts. He was also the initiator behind the joint project proposals of ESACT and ACTIP, always working to improve education and training of animal cell technologists.





Over the years, a wide variety of invited speakers attended our meetings, greatly extending our network. On average, a meeting has 5-7 invited speakers. These can be academics working on a research project, representatives of start-up companies or SMEs, specialists of ACTIP member companies, industrialists, consultants, and representatives of governments, science parks or regulatory bodies. Shown here is Prof. Wei Shou Hu of the University of Minnesota, USA, presenting at an ACTIP meeting in Stockholm, 1994. He would again present at the 2010 meeting in Penzberg.

Invited SMEs

In 2000, at our 10th anniversary, the ACTIP membership discussed the future of ACTIP. Although seen as highly successful, it was felt that we should not become 'an old boy's network', but keep the organization open and focused on the future. This initiated a new policy based on two pillars. Pillar one was to devise meetings centered around two themes, one theme representing the technology or business interests of the ACTIP members and the other theme looking forward to the future, being oriented towards research with a potential impact on the practice of animal cell technology. The second pillar sets out to invite, to every meeting, SMEs working on the themes covered by the meeting, whereby the SMEs were given the chance to present their company's core technology to the ACTIP membership. Needless to say that all SMEs invited over the years seized the chance to expand their network, while the ACTIP membership benefited from the SME's specialist know-how and expertise in certain fields. Quite a few collaborations between SMEs and ACTIP member companies were the result of this new policy. Another result was that a number of the invited SMEs later applied for ACTIP membership.

9. ACTIP Fellowship Awards

In 2008, ACTIP decided to open up its meetings to young scientists working on a project in biomanufacturing or related activity of industrial interest, i.e. development of new expression systems, new mammalian cell lines, test development etc. ACTIP wanted to offer young scientists the floor to present their project and personal expertise to our community.
In order to be selected for such an invitation, ACTIP decided to establish the ACTIP Fellowship Awards, consisting of all costs paid to attend a two-day meeting of ACTIP. To qualify, the young scientists have to send in an application, which is reviewed by experts of ACTIP member companies. Annually, four Fellows are selected to attend our meetings. See the ACTIP website (www.actip.org) for up to date information on the Fellows and their projects.






Human biopharmaceuticals produced

Trade Name	Generic Name	Target	Protein Class
Abbokinase®	Urokinase	Serine protease	Enzyme
Activase	Alteplase	tPA	Enzyme
Epogen®/Procrit®	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor
Recombinate®/Bioclate®	Antihemophilic factor	Factor VIII	Blood factor
Pulmozyme®	Dornase-α	Deoxyribonuclease	Enzyme
ReoPro®	Abciximab	GPIIb/IIa receptor	Chimeric MAB
ProstaScint®	Capromab Pendetide	PSMA	Murine MAB
Serostim LQ®	Somatropin	hGH	Hormone
Verluma®	Nofetumomab Merpentan	CD20	Murine MAB
Simulect®	Basiliximab	IL-2Rα	Murine MAB
Rebif®	Interferon β-1a glycoprotein	Interferon β-1a	Cytokine/receptor antagonist/growth factor
HumaSPECT®	Votumumab	CTAA16.88 (or CTA#1) cytokeratin tumor-associated complex of antigens	Humanized MAB
Zenapax®	Daclizumab	IL-2Rα	Murine MAB
CEA-Scan®	Arcitumomab	CEA	Murine MAB
Remicade®	Infliximab	TNF	Chimeric MAB
Synagis®	Palivizumab	RSV	Chimeric MAB
Eprex®	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor

For Abbreviations see page 42

with animal cell technology (status 2010)

Therapeutic Area	Company	First EMA Approval	First FDA Approval	Cell Line	Notes
Pulmonary embolism	ImaRx		1978	Primary Human Neonatal Kidney cells	
Acute myocardial infection	Genentech	2002	1987	CHO	
Anaemia	Amgen		1989	CHO	
Hemophilia A	Baxter Healthcare	1992	1992	CHO	
Cystic fibrosis	Genentech	1994	1993	CHO	
Cardiovascular disease	Eli Lilly	1995	1994	Sp2/0	
Detection of prostate cancer	EUSA Pharma		1996	Hybridoma	
AIDS cachexia-related indications	Merck Serono		1996	C-127	
Detection of small cell lung cancer	NeoRX		1996	Hybridoma	Discontinued
Transplant rejection	Novartis/Cerimon Pharmaceuticals	1998	1998	NS0	
Multiple sclerosis	Serono	1998	2002	CHO	
Radiodiagnosis of colorectal cancer	Bioreactor Technology	1998		A human lympho-blastoid cell line transformed with Epstein-Barr virus (EBV)	
Transplant rejection	Hoffmann-La Roche	1999	1997	Sp2/0	
Detection of colorectal carcinoma	Immunomedics	1999	1998	Hybridoma	Discontinued
Crohn's disease/ rheumatoid arthritis	Centocor/J&J	1999	1998	Sp2/0	
RSV disease	AstraZenec/MedImmune	1999	1998	NS0	
Anaemia	Ortho Biotech/J&J	1999	1999	CHO	

Human biopharmaceuticals produced

Trade Name	Generic Name	Target	Protein Class
Mylotarg®	Gemtuzumab Ozogamicin	CD33 Receptor with Cytotoxin	Murine MAB
Kogenate®/Helixate®	Octocog α	Factor VIII	Blood factor
Herceptin®	Trastuzumab	HER2 Receptor	Chimeric MAB
Thyrogen®	Thyrotropin α	TSH	Hormone
Ovidrel®	Choriogonadotropin-α	HCG	Hormone
TNKase®	Tenecteplase	Modified Human TPA	Enzyme
Aranesp®	Darbepoetin-α	EPO	Cytokine/receptor antagonist/growth factor
Fabrazyme®	Agalsidase-β	Human α-galactosidase	Enzyme
Replagal®	Agalsidase-α	Human α-galactosidase	Enzyme
Activase®	Alteplase	Human r-tPA	Enzyme
Campath®/MabCampath®	Alemtuzumab	CD52	Humanized MAB
OP-1 Implant®	Eptotermin-α	BMP-7	Cytokine/receptor antagonist/growth factor
Opgenra®	Eptotermin α	OP-1	Osteogenic protein
Xigris®	Drotrecogin α (activated)	Human activated Protein C	Blood factor
INFUSE® bone graph	Dibotermin-α	BMP-2	Cytokine/receptor antagonist/growth factor
Dynepo®	Epoetin-δ	EPO	Hormone
Aldurazyme®	Iduronidase	α-L-Iduronidase	Enzyme
Amevive®	Alefacept	Leukocyte antigen-3/IgG	Fusion protein
Bexxar®	Tositumomab	CD20 with Iodine -131	Murine MAB
Zorbtive®	Somatropin	hGH	Hormone
Raptiva®	Efalizumab	CD11a	Humanized MAB

For Abbreviations see page 42

with animal cell technology (status 2010)

Therapeutic Area	Company	First EMA Approval	First FDA Approval	Cell Line	Notes
Acute myeloid leukemia	Wyeth		2000	NS0	
Hemophilia A	Bayer	2000	1993	BHK	
Breast cancer	Genentech	2000	1998	CHO	
Thyroid cancer	Genzyme	2000	1998	CHO	
Infertility	Serono	2001	2000	CHO	
Thrombolysis	Genentech	2001	2000	CHO	
Anaemia	Amgen	2001	2001	CHO	
Fabry disease	Genzyme	2001	2003	CHO	
Fabry disease	Shire	2001		Human HT-1080 cell line	
Acute myocardial infarction	Genentech	2002	1996	CHO	
CLL	Genzyme	2002	2001	CHO	
Alternative to autograft	Stryker Biotech	2002	2001	CHO	
Alternative to autograft	Stryker Biotech	2002	2001	CHO	
Sepsis	Eli Lilly	2002	2001	HEK 293	
Tibial shaft fractures	Wyeth	2002	2002	CHO	
Anemia associated with CRF	Shire/Sanofi Aventis	2002		Human HT-1080 cell line	
MPS I	Genzyme/BioMarin	2003	2003	CHO	
Chronic plaque psoriasis	Astellas Pharma/Biogen Idec		2003	CHO	
Non-Hodgkin's lymphoma	GSK		2003	Hybridoma	
Short bowel syndrome	Merck Serono		2003	Murine tumor cell line C-127	
Psoriasis	Genentech/Xoma	2004	2003	CHO	FDA & EMA approval withdrawn

Human biopharmaceuticals produced

Trade Name	Generic Name	Target	Protein Class
Erbitux®	Cetuximab	EGF Receptor	Chimeric MAB
NeutroSpec®	Fanolesomab	CD15	Murine MAB
Xolair®	Omalizumab	IgE	Humanized MAB
Avastin®	Bevacizumab	Vascular endothelial growth factor	Humanized MAB
Proxinium®	Catumaxomab	EpCAM	Humanized MAB
Hylenex®	Hyaluronidase	PH-20	Glycoprotein
iPlex®	Mecasermin rinfibate	IGFBO-3	Cytokine/receptor antagonist/growth factor
Myozyme®/Lumizyme®	Alglucosidase α	α-glucosidase	Enzyme
Atryn®	Antithrombin-III	AT-III	Glycoprotein
LeukoScan®	Sulesomab	Human granulocytes	Murine MAB
Orencia®	Abatacept	CTLA4 Receptor	Chimeric protein
Elaprase®	Idursulfase	L-iduronate 2-sulfate	Enzyme
Vectibix®	Panitumumab	EGF Receptor	Humanized MAB
Mircera® (pegylated version of NeoRecormon)	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor
Soliris®	Eculizumab	C5	Humanized MAB
Abseamed®	Epoeietin-α	Red blood cell progenitor	Hormone
Benecrit® (biosimilar)	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor
Hexal® (biosimilar)	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor
Stada® (biosimilar)	Epoeietin-α	EPO	Cytokine/receptor antagonist/growth factor
Recothrom®	rhThrombin	Thrombin	Blood factor

For Abbreviations see page 42

with animal cell technology (status 2010)

Therapeutic Area	Company	First EMA Approval	First FDA Approval	Cell Line	Notes
Squamous cell carcinoma/ colorectal cancer	Eli Lilly	2004	2004	Hybridoma	
Scintigraphic imaging for appendicitis	Palatin Technologies		2004	Hybridoma	FDA approval withdrawn
Asthma	Genentech/Novartis/Tanox	2005	2003	CHO	
Colorectal cancer	Genentech/Hoffmann-La Roche	2005	2004	CHO	
Head and neck cancer	Viventia Biotech	2005	2005	CHO	
IVF	Haloyme Therapeutics		2005	CHO	
IGF-1 deficiency	Insmed		2005	E.coli/CHO	
Pompe disease	Genzyme	2006	2006	CHO	
Congenital AT-III deficiency	Genzyme	2006	2008	Transgenic goat milk	
Radiodiagnosis of osteomyelitis	Immunomedics/Eli Lilly	2006		NS0	
Rheumatoid arthritis	Bristol-Myers Squibb	2007	2005	CHO	
Hunter syndrome (MPS II)	Shire	2007	2006	Human HT-1080 cell line	
Colorectal cancer	Amgen	2007	2006	CHO	
Anaemia	Hoffmann-La Roche	2007	2007	CHO	
Paroxysmal nocturnal hemoglobinuria	Alexion Pharmaceuticals	2007	2007	NS0	
Anaemia	Medice Arzneimittel Putter	2007		CHO	
Anaemia	Sandoz/Novartis	2007		CHO	
Anaemia	Hexal Biotech/Novartis	2007		CHO	
Anaemia	Stada Arzneimittel AG	2007		CHO CHO	
Hemostasis	Zymogenetics/Bayer		2008	CHO	

Human biopharmaceuticals produced

Trade Name	Generic Name	Target	Protein Class
Xyntha® (formerly ReFactor®)	Moro-octocog α	Factor VIII	Blood factor
Ilaris®	Canakinumab	IL-1β Receptor	Chimeric MAB
Simponi®	Golimumab	TNF α	Chimeric MAB
Stelara®	Usetekinumab	IL-12/23	Humanized MAB
Chondrocelect®	Chondrocytes	Femoral condyle	Chondrocytes
Removab®	Catumaxomab	EpCAM/CD3	Chimeric MAB
Scintimun®	Besilesomab	CEA	Murine MAB
Arzerra®	Ofatumumab	CD20	Humanized MAB
Vpriv	Velaglucurase-α	Glucocerebrosidase	Enzyme
FSH-CTP®	Corifollitropin α	FSH	Hormone
Actemra®	Atlizumab	IL-6 receptor	Humanized MAB
Prolia	Denosumab	EGF Receptor	Humanized MAB
Rhucin®	C1 Esterase	C1-Inhibitor	Esterase inhibitor
Abthrax®	Raxibacumab	Macrophage cells	Murine MAB
Bosatria®	Mepolizumab	IL-5 Receptor	Humanized MAB
Medi-524® (NuMax®)	Motavizumab	RSV	Chimeric MAB
	Belatacept	IG1Fc-CTLA4 fragment	Fusion protein

This list of human biopharmaceuticals produced with animal cell technology is regularly updated on our website: www.actip.org/pages/products. Our website also gives a list of biopharmaceuticals produced from tissues or organs.

For Abbreviations see page 42

with animal cell technology (status 2010)

Therapeutic Area	Company	First EMA Approval	First FDA Approval	Cell Line	Notes
Hemophilia A	Wyeth	2009	2008	CHO	
Cryopyrin-associated periodic syndromes	Novartis	2009	2009	Sp2/0	
Rheumatoid arthritis	Centocor	2009	2009	Sp2/0	
Psoriasis	Centocor/J&J	2009	2009	CHO	
Cartilage defects	TiGenix	2009		Autologous chondrocytes	
Epithelial cancers	Fresenius Biotech	2009		Rat-mouse hybrid hybridoma cell line	
Detection of lesions and metastases	CIS Bio International	2009			
CLL	GSK	2010	2009	CHO	
Gaucher disease (type 1)	Shire	2010	2010	Human HT-1080 cell line	
IVF	Merck/Organon Teknika	2010	Pending	CHO	
Rheumatoid arthritis	Hoffmann-La Roche/Chugai		2010		
Postmenopausal osteoporosis	Amgen		2010	CHO	
C1 inhibitor deficiency	Pharming	Pending		Transgenic rabbit milk	
Inhalation anthrax	Human Genome Sciences		Pending	NS0	
Hypereosinophilic syndrome	GSK		Pending	CHO	
RSV disease	AstraZeneca/MedImmune		Pending	NS0	
Transplant rejection	Bristol-Myers Squibb		Pending	CHO	

Human vaccines produced with animal

Prophylactic vaccines

Virus/Infectious disease due to	Cells	Notes
Measles	Primary Chicken embryo fibroblasts	live attenuated vaccine strain Ender Edmonston or Schwarz
Rubella	MRC-5 diploïd cell line	live attenuated vaccine strain WI RA 27/3
Mumps	Primary Chicken embryo fibroblasts	live attenuated vaccine strain Jeryl Lynn
Varicella / Chicken Pox	MRC-5 diploïd cell line	live attenuated vaccine strain Oka/Merck
Zooster Herpesvirus	MRC-5 diploïd cell line	live attenuated vaccine strain Oka/Merck
Rotavirus	Vero cells (African green monkey kidney cell line)	live attenuated vaccine strains G1, G2, G3, G4, and G6 capsid proteins live attenuated vaccine strain 89-12 G1P[8] RIX 4414
Smallpox	Vero cells (African green monkey kidney cell line)	live attenuated vaccine strain Dryvax
Human papilloma virus	Baculovirus expression system - insect cell line derived from trichoplusia	Virus-like particle, adjuvanted vaccine strains type 16, 18
Japanese encephalitis	Vero cells (African green monkey kidney cells)	inactivated vaccine strain S14-14-12

For Abbreviations see page 42

cell technology (status 2010)

Company	FDA Approval	EMA Approval	Trade Name	Remarks
Sanofi-Pasteur		1986	ROUVAX	and in combination with Measles, Mumps
Merck		2006	MMR VaxPro	and in combination with Measles, Mumps and Varicella
	X?		ATTENUVAX	and in combination with Rubella, Mumps and Varicella
GSK		X	PRIORIX	and in combination with Mumps, Rubella
Crucell		X	TRIVITAREN	
Sanofi-Pasteur		1988	RUDIVAX	and in combination with Measles and Mumps
Merck		2006	MMR VaxPro	and in combination with Measles, Mumps and Varicella
	X?		MERUVAX II	and in combination with Rubella, Mumps and Varicella
GSK		X	PRIORIX	and in combination with Measles and Mumps
Crucell			TRIVITAREN	
Sanofi-Pasteur		1985	MMR vaccine	and in combination with Measles, Rubella
Merck	X?	2006	MUMPSVAX	and in combination with Rubella, Mumps and Varicella
GSK		X	PRIORIX	and in combination with Measles, Rubella
Crucell		X	TRIVITAREN	
Merck	1996	2001	VARIVAX	and in combination with Measles, Mumps and Rubella
GSK		X	VARILIX	
Merck		2006	ZOSTAVAX	
Merck	2006	2006	ROTATEQ	
GSK	2008	2006	ROTARIX	
Acambis / Sanofi Pasteur	2007		ACAM2000	
GSK	2009	2007	CERVARIX	
Intercell/Novartis	2009	2009	IXIARO	

Human vaccines produced with animal

Prophylactic vaccines

Virus/Infectious disease due to	Cells	Notes
Influenza	Vero cells (African green monkey kidney cells)	Inactivated vaccine strain A H1N1
		Inactivated vaccine strain A H5N1
	Madine darby canine kidney cells	Inactivated vaccine strains A H1N1, A H3N2 and B
Poliomyelitis	Primary monkey kidney cells	inactivated vaccine strains type 1 Mahoney, type 2 MEF-2 and type 3 Sauket
	MRC-5 diploïd cell line	inactivated vaccine strains type 1 Mahoney, type 2 MEF-2 and type 3 Sauket
		live attenuated vaccine strains type 1, 2, 3
	Vero cell line (African green monkey kidney cells)	inactivated vaccine strains type 1 Mahoney, type 2 MEF-2 and type 3 Sauket
		inactivated vaccine strains type 1 Mahoney, type 2 MEF-2 and type 3 Sauket
		live attenuated vaccine strains type 1, 2, 3
		inactivated vaccine strains type 1 Mahoney, type 2 MEF-2 and type 3 Sauket
Rabies	MRC-5 diploïd cell line	inactivated vaccine strain PM
	Vero cells (African green monkey kidney cells)	inactivated vaccine strain PM
		inactivated vaccine strain PM-1503-3M
Hepatitis A	MRC-5 diploïd cell line	inactivated vaccine

A table listing veterinary vaccines produced with animal cell technology is available on our website: www.actip.org/pages/products.

For Abbreviations see page 42

cell technology (status 2010)

Company	FDA Approval	EMA Approval	Trade Name	Remarks
Baxter		2009	CELVAPAN	
		2009	Pandemic Influenza Vaccine Baxter	
Novartis		2007	OPTAFLU	
Sanofi-Pasteur		1966	DTPolio	
Sanofi-Pasteur	1987	1987	POLIOVAX	
GSK			OPV oral Polio vaccine	
Sanofi-Pasteur		1982	IMOVAX Polio	
Sanofi-Pasteur	1990		IPOL	
Sanofi-Pasteur		1988	OPV oral Polio vaccine	
GSK	2002	X	POLIORIX and part of Infanrix hexa, Infanrix penta and Pediatrix	
Sanofi-Pasteur	1980		IMOVAX Rabies	
Sanofi-Pasteur		1985	VERORAB	
Novartis	X?		RABAVERT	
Sanofi Pasteur		1996	AVAXIM	
Merck	1996	1997	VAQTA	
GSK	1995	1993	HAVRIX	and part of Ambirix, Twinrix, Hepatyrix combo

Abbreviations

ADA	Adenosine deaminase
AT-III	Antithrombin-III
BAFF	B-cell activating factor
BHK	Baby hamster kidney cells
BMP	Bone morphogenetic protein
C-127	Murine mammary tumor derived cell line
CA-125	Cancer antigen 125
CD	Cluster of differentiation
CEA	Carcinoembryonic antigen
CHO	Chinese Hamster Ovary
CLL	Chronic Lymphocytic Leukemia
CTAA	Colon tumor-associated antigen
CTLA-4	Cytotoxic T-Lymphocyte Antigen 4
E.coli	Escherichia coli (bacterium)
EGF	Epidermal growth factor
EMA	European Medicine Agency
EpCAM	Epithelial cell adhesion molecule
EPO	Erythropoeietin
FDA	Food and Drug Administration
FSH	Follicle stimulating hormone
GAG	Glycosaminoglycans
GPIIb/IIa receptor	Glycoprotein IIb/IIa receptor
HCG	Human chorionic gonadotrophin
HEK 293	Human embryonic kidney cell line
HER2 Receptor	Human epidermal growth factor receptor 2
HGH	Human Growth Hormone
HT-1080	Human fibrosarcoma cell line
IgE	Immunoglobulin E
IGFBP3	Insulin-like growth factor binding protein 3
IL-1 Receptor	Interleukin-1 Receptor
IL-X	Interleukin-X
MAB	Monoclonal Antibody
MPS I	Mucopolysaccharidose I
MRC-5	Medical Research Council 5 human fetal cells
NS0	Mouse myeloma cell line (lymphoblast)
OP-1	Osteogenic protein 1
PSMA	Prostate Specific Membrane Antigen
r-tPA	Recombinant tissue plasminogen activator
RSV	Respiratory syncytial virus
Sp2/0	Mouse myeloma cell line
TAG-72	Tumor-associated glycoprotein 72
TNF	Tumor necrosis factor
WI-38	Wistar Institute 38 human fetal lung tissue






Fed-batch fermentation using animal cells for the production of biopharmaceuticals at one of the ACTIP member companies (Genzyme).

Colophon:

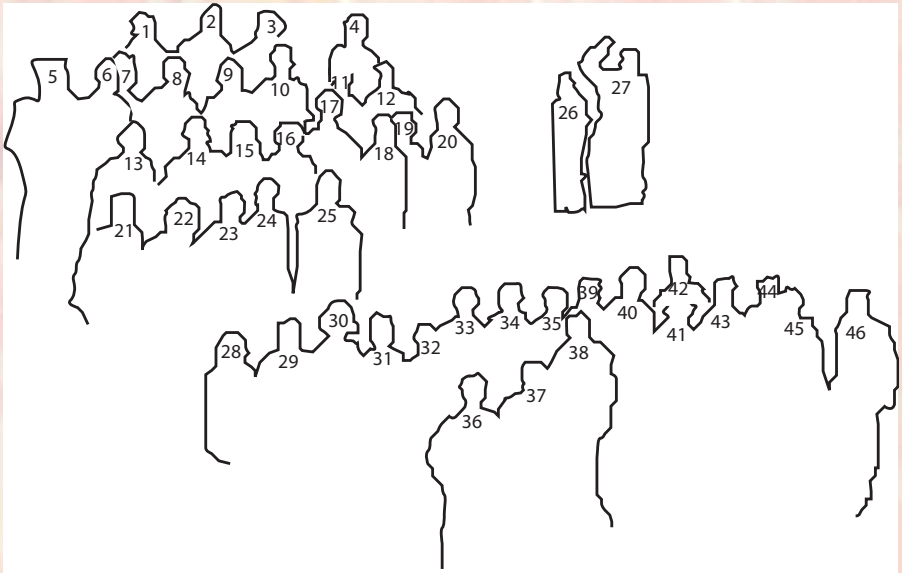
Text: Dr. Luc Kupers, Genzyme, Belgium and Dr. Helma Hermans, Executive Secretary ACTIP, Spain
Product table: Peter Kupers, Belgium
Graphs and Figures: Augusta Thorbecke, Amsterdam, The Netherlands
Lay-out: Augusta Thorbecke, Amsterdam, The Netherlands
Print: Zona Creativa, Alfaz del Pi, Spain
Photography: The photos depicting scenes from the biomanufacturing process (in bar at the bottom of pages, and on page 43) were kindly provided by Artelis, DSM Biologics, Genzyme, MedImmune, Pfizer, Rentschler, Hoffmann La-Roche. Also available on the ACTIP website.
Other photos: Ton Out, Relleu; personal archives of Annie van Broekhoven, Michael Comer, Frans Dubois, Christel Fenge, Martin Fussenegger, Helma Hermans, Elisabeth Lindner, Jan Lupker, Jürgen Sautter, Augusta Thorbecke

The ACTIP organization has done its utmost to contact representatives of ACTIP member companies, guests and speakers at meetings for permission to use his/her picture.

Printed in Spain, December 2010

ACTIP website: www.ACTIP.org

Cover info:



On group photo at ACTIP's 20th anniversary meeting in Pueblo Acantilado, Spain:

1. Geert Deschamps
2. David Birch
3. Patrick Gammell
4. Jürgen Sautter
5. Augusta Thorbecke
6. Ralf Fehrenbach
7. Tobias May
8. Otto Merten
9. Luc Kupers
10. Nicolas Havelange
11. Thomas Petri
12. Alberto D'Avino
13. Malcolm Brattle
14. Thomas Link
15. Roland Wagner
16. Avinoam Kadouri
17. Ruud Brands
18. Ciska Dalm
19. Jan Lupker
20. Hansjörg Hauser
21. Frans Dubois
22. Martin Wisher
23. Alexander Bulloch
24. Emiliano Toso
25. Jean-François Bouquet
26. Kristina Martinelle
27. Tim Clayton
28. Christel Fenge
29. Michael Comer
30. Cristina Glad
31. Markus Heine
32. Aziz Cayli
33. Andreas Castan
34. Jürgen Wieland
35. Holger Lübben
36. Greg Dean
37. Andreas Popp
38. Helma Hermans
39. Marc Bastiaansen
40. Jürgen Vorlop
41. Els van den Berg
42. Helge Neidhardt
43. Manuel Carrondo
44. Ralph Kempken
45. Jarl Regner Andersen
46. Donnacha O'Driscoll