











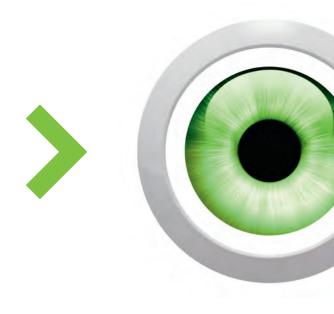


THE FAMILY

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OUR 150-YEAR HISTORY



IN OPHTHALMOLOGY

Written by | Lorraine Kaltenbach

The legacy of ophthalmology...

Destiny is chance given direction. Nothing prepared the CHIBRET family for becoming major players in the European pharmaceutical industry in the field of ophthalmology. But here we are! Paul CHIBRET, a young native of the Auvergne, born under the reign of Louis Philippe, contracted a serious eye disease. As a military doctor in eastern Kabylia, he was repatriated to France to be treated and trained by the great names of European ophthalmology, who practiced their art in Paris at the time. This visionary was present at the origins of an industrial saga that continues to this day.

Through 5 generations of the CHIBRET family and 6 portraits, this brochure retraces the company and its innovation, depicting strong personalities brimming with ideas and energy who shared the same entrepreneurial spirit and the same passion for research and ophthalmology.

It also reminds us of the strength of family companies, which rely both on innovation and on management with long-term vision.

Paul Chibret 1844-1911 Ophthalmologist -Founder of the French Society of Ophthalmology





Jean-Frédéric Chibret ¹⁹⁷⁵ MBA





Henri Chibret

Pharmacist Founder of Transphyto and Laboratoires THÉA, Chairman of the Board of THÉA Holding



Jacques Chibret 1941–1989 MBA Founder and CEO of Biophysic Medical (ophthalmic lasers and ultrasound)



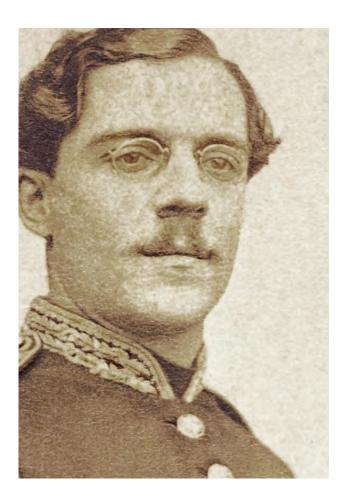
Jean Chibret

Pharmacist CEO of CHIBRET Laboratories



Henry Chibret 1876-1943

Pharmacist Founder of <u>Laboratoires CHIBRET</u>



1844–1911 • Ophthalmologist • Founder of the Société Française d'Ophtalmologie

French Society of Ophthalmology]

The destiny of the CHIBRET family in ophthalmology began with Paul CHIBRET, a military doctor, at the end of the Second Empire. While stationed in the region around Constantine, near the border with Tunisia, he became interested in trachoma, a pathology of the eye that would fascinate him all his life. Soon mobilized to participate in a campaign in eastern Kabylia, he was struck down in August 1871 by a bilateral chorio-retinitis, which left him almost blind. The following month, he was sent back to Europe.

On his return to France, he entrusted himself to the care of Professor GALEZOWSKY, visiting Professor DE WECKER and the major ophthalmological clinics in Paris. Ophthalmology rapidly became his true passion. In 1875, he left Paris and the ranks of the army and returned to his roots in the Auvergne. His family was originally from Cantal (Dienne, Vallée du Puy Mary). He settled in Clermont-Ferrand, becoming the only ophthalmologist in the Massif Central.

His clientele developed rapidly, but far from confining him to routine practice, it provided him with multiple subjects for observation and reflection that were beyond his imagination. Paul CHIBRET established himself as a doctor/surgeon, as well as researcher and inventor.

Scientific work

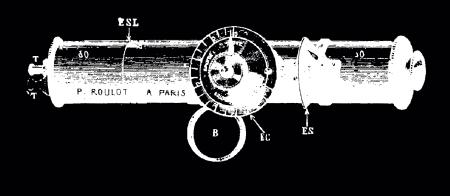
The scientific work of Paul CHIBRET was important and concerned various fields of ophthalmology. Among his inventions, the chromatophotoptometer used polarized light. This simple, inexpensive and small (20 cm) instrument could generate 2700 different shades of color and detect dyschromatopsia, such as color blindness.

He attempted to promote a method of measuring astigmatism, giving it the name skiascopy. He invented a syringe with simultaneous injection and aspiration of cortical masses in the posterior chamber after cataract surgery.

Infectious problems and asepsis were a lifelong interest of his. In 1891, he presented a report to the SFO on bacterial infections of the conjunctiva and in 1896, a report on trachoma. He recommended pre-, per- and post-operative precautions to reduce the risks of endophthalmitis.

With an original, creative and independent European mind, Paul CHIBRET would deeply influence the generations to come.

[Professors A. BRONNER and J. SAHEL edited an excellent bibliography on Paul CHIBRET in 1983.]

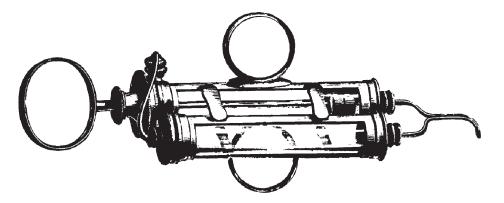




1 & 2 - With his colleagues IZARN and COLLARDEAU, Paul CHIBRET invented this "chromatophotoptometer" to detect failures in the perception of colors, like color blindness.

Instruments of Dr Paul Chibret

Presented by Moria - Dugast, Paris



1 - Double effect syringe



2 - Eyelid turning forceps



3 – Ophthalmoscope



4 - Lifter for newborns

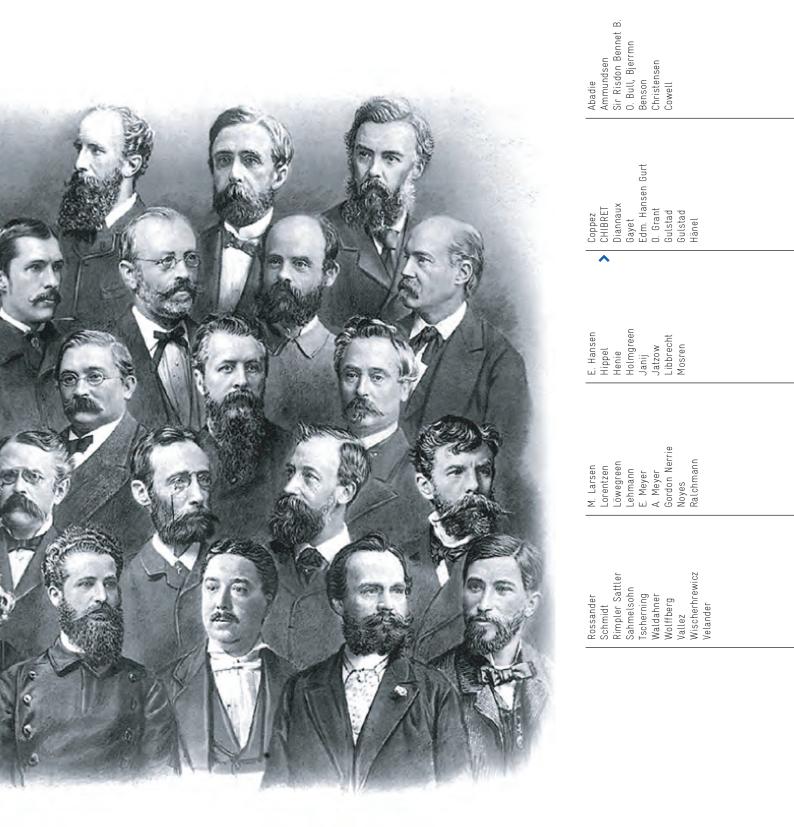


5 - Eye dislocation forceps

A European before his time

COPENHAGEN OPHTHALMOLOGY CONGRESS





The creation of the SFO

SOCIETE FRANÇAISE D'OPHTALMOLOGIE (SFO) [FRENCH OPHTHALMOLOGY SOCIETY]



Congress of the SFO in 1900

At the end of the 19th century, when science was triumphing, a tight network of congresses, professional societies and academies was created, linking an ever greater number of specialists throughout Europe. Paul CHIBRET then became one of these traveling scholars who criss-crossed Europe, participating in academies and congresses. He went to Russia and Poland to operate, maintaining extensive correspondence with his ophthalmologist colleagues. It is undoubtedly to Paul that his descendants in the CHIBRET family owe their closeness to French and foreign eye care professionals. Because of this, subsequent events would demonstrate an extraordinary permanence between the CHIBRET ancestors and new generations.

It was at the Amsterdam Congress in 1879 that the Doctors CHIBRET and MARTIN tried to create a French language scientific society of ophthalmology. This first attempt failed but a few years later, the project flowered. In September 1882, Paul CHIBRET published his new plan in the journal Clinique d'Oculistique du Sud-Ouest. The Société Française d'Ophtalmologie (SFO) was born in Paris on January 29, 1883.

He was the first Chairman of this new Society. The by-laws, which are still in effect today, specify that the Board of Directors will include a Chairman, who is always from the provinces and a Secretary General who is always Parisian. An annual report will be presented each year at the SFO congress without restriction as to nationality (AXENFELD was the first German reporter in 1906).

Paul CHIBRET reconciled the differences between French and foreigners, between liberal practitioners and professors, between Parisians and provincials. He insisted on the SFO being accessible to all and, in particular, to German ophthalmologists, who had been victims of ostracism since the annexation of Alsace Lorraine by Germany, following the French defeat of 1870. He chose the month of May for the annual congress, allowing German ophthalmologists to come to Paris and French ophthalmologists to go to the Heidelberg Society in the summer. Today, the Paul CHIBRET medal, which is awarded alternately by the SFO and the DOG (German Ophthalmological Society), celebrates this Franco-German friendship.



HOLDERS OF THE CHIBRET MEDAL, AWARDED ALTERNATIVELY BY THE SFO AND THE DOG (GERMAN OPHTHALMOLOGY

SOCIETY): 1974 - PROF. F. HOLLWICH, MÜNSTER (GERMANY) • 1976 - PROF. H. REMKY, MUNICH (GERMANY) • 1978 - PROF. A. BRONNER, STRASBOURG (FRANCE) • 1979 - PROF. W. STRAUB, MARBURG (GERMANY) • 1980 - PROF. H. SARAUX, PARIS (FRANCE) • 1981 - DR. P. AMALRIC, ALBI (FRANCE) • 1983 - PROF. E. KLOTI, ZÜRICH (SWITZERLAND) • 1984 - PROF. F. C. BLODI, IOWA (USA) • 1985 - PROF. J. ROYER, GENEUILLE (FRANCE) • 1986 - PROF. J. MICHIELS, LOUVAIN (BELGIUM) • 1989 - PROF. J. WOLLENSAK, BERLIN (GERMANY) • 1990 - PROF. M. BONNET, LYON (FRANCE) • 1991 - PROF. H. BAURMANN, KÖNIGSWINTER (GERMANY) • 1992 - DR. J. L. SEEGMULLER, STRASBOURG (FRANCE) • 1993 - DR. R. GREWE, MÜNSTER (GERMANY) • 1994 - PROF. H. HAMARD, PARIS (FRANCE) • 1995 - PROF. CHR. HARTMANN, BERLIN (GERMANY) • 1996 - PROF. H. BOURGEOIS, PARIS (FRANCE) • 1997 - PROF. H. NEUBAUER, COLOGNE (GERMANY) • 1998 - PROF. G. SOUBRANE, CRÉTEIL (FRANCE) • 1999 - DR. K. DILGER, INGOLSTADT (GERMANY) • 2000 -PROF. J. FLAMENT, STRASBOURG (FRANCE) • 2001 - PROF. H. BUSSE, MÜNSTER (GERMANY) • 2002 - PROF. J. P. ADENIS, LIMOGES (FRANCE) • 2003 - PROF. A. KAMPIK, MUNICH (GERMANY) • 2004 - PROF. J.-L. DUFIER, PARIS (FRANCE) • 2005 - PROF. P. RIECK, BERLIN (GERMANY) • 2006 - PROF. J.-L. ARNE, TOULOUSE (FRANCE) • 2007 - PROF. G. E. LANG, ULM (GERMANY) • 2008 - PROF. S. MORAX, NEUILLY (FRANCE) • 2009 - PROF. F. GREHN, WÜRZBURG (GERMANY) • 2010 - PROF. J.-A. BERNARD, PARIS (FRANCE) • 2011 - PROF. DR. K. G. KRIEGLSTEIN (GERMANY) • 2012 - PROF. PIERRE-YVES ROBERT, LIMOGES (FRANCE) • 2013 - PROF. THOMAS REINHARDT, MUNICH, (GERMANY) • 2014 : PROF. CARL ARNDT, REIMS (FRANCE) • 2015 - PROF. BERTHOLD SEITZ, ERLANGEN (GERMANY) 2016 - PROF. CLAUDE SPEEG SCHATZ, STRASBOURG (FRANCE) • 2017 - PROF FRANK HOLZ, BONN (GERMANY) • 2018 - DR. JEAN-MARC PERONE, METZ-THIONVILLE (FRANCE) • 2019 - PROF. CLAUS CURSIEFEN, ERLANGEN-NUREMBERG (GERMANY) • 2020 - PROF JOSÉ-ALAIN SAHEL, PARIS (FRANCE) 2021 - PROF. GEERLING, DÜSSELDORF (GERMANY) • 2022 - PROF. CREUZOT-GARCHER, DIJON (FRANCE).





With the encouragement of his uncle Paul, Henry CHIBRET, a pharmacist and son of a pharmacist, developed a passion for the design and manufacture of ophthalmic formulas. He preferred ointments, since eye drops presented problems of stability and sterility. In 1902, he founded Laboratoires CHIBRET, which developed modestly, like its French and foreign competitors, since the pharmacopoeia had few active drugs. It essentially consisted of mineral or organic salts and alkaloids. The pharmaceutical industry did not develop in ophthalmology until after the Second World War.

Like his uncle Paul, Henry CHIBRET was a friend of many eye care professionals. In particular, he developed a very strong relationship with Albert BRONNER during the war, when the Strasbourg Faculty withdrew to Clermont-Ferrand. (A. BRONNER, an Alsatian, was arrested and deported in 1944. Liberated in 1945, he became Professor of Ophthalmology at the University of Strasbourg).



The first Laboratoires Chibret



The first successes of CHIBRET products allowed Henry to expand his establishment. After the First World War, his pharmacy and laboratory, opened in 1902, were transferred from the Place de l'Hôtel de Ville to 5, rue Saint-Hérem in Clermont-Ferrand, in a former furniture store.

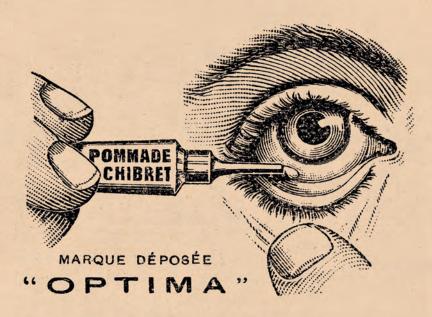
Initial packaging

Throughout history, packaging of medicines has been an eternal technical challenge. Suede bags for powder, stoneware and earthenware pots, wooden vases, glassware of various shapes and sizes, this packaging has evolved over the centuries to meet increasingly demanding standards in terms of hygiene and quality. The beginnings of Laboratoires CHIBRET were marked by an important use of flexible metal tubes in pure tin or lead. In agreement with his uncle Paul, Henry was a fervent advocate of ophthalmic ointments. Made from Vaseline, a petroleum jelly invented in 1872, the ointments were long-lasting, with very low viscosity, superior to eye drops and less prone to contamination, resulting in a clear improvement in "performance."









POMMADES OPHTALMIQUES "OPTIMA"

des Laboratoires CHIBRET, à Clermont-Ferrand

Prix spéciaux accordés à MM. les Docteurs, Hôpitaux et Cliniques.

1 ^{re} SÉRIE	2 ^{me} SÉRIE	3me SÉRIE
Oxyde jaune Violet de méthylène Bleu de méthylène Aristol Vioforme Iodoforme Rouge écarlate Cuivre (hémocuivre) Oxyde de zinc Zinc cadium Zinc tuménol Zinc ichtyol Calomel Iodo-Calcique Ichtyol Soufre Tannin Précipité blanc Bismuth-Hydroxyde Dermatol Extrait thyroldien Ecktogan	Collargol Argyrol Protargol Cocaine Stovaine Ethylhydrocupréine (Optochine) Rose Bengale Xéroforme Orthoforme Essence du Niaouli (Goménol) Airol	Esérine Euphtalmine Scopolamine Atropine Pilocarpine Adrénaline Dionine Homatropine

COFFRETS AMPOULES FONDANTES CHLORO-IODO.CALCIQUE (Bains d'yeux pour cataracte)

OEILLÈRE CHIBRET, à REBORD CAOUTCHOUTÉ (Marque déposée)

Les POMMADES "OPTIMA "FABRIQUÉES PAR H. CHIBRET, à CLERMONT-FERRAND sont livrées en tubes d'étain munis d'une canule dévissable et stérilisable sur laquelle s'adapte un capuchon. Cette canule facilite l'entrée de la pommade dans le cul de sac conjonctival sans l'intermédiaire d'accessoires (bâtonnets de verre, etc...) et n'en laisse sortir que strictement la quantité à employer, le reste est à l'abri de tout contact impur lorsque le capuchon est replacé.

Ces pommades sont faites d'après des procédés spéciaux de fabrication qui les rendent irréprochables.

Echantillons adressés gracieusement sur demande



Initial packaging



If the second part of the 20th century marked the golden age of glass for pharmaceutical use, at the time of Henry CHIBRET, this was still incipient. Pharmacy glassware was slowly expanding for eye drops. Bottles were still manufactured in a traditional way. The use of wood or cardboard for the packaging and the protection of the vials of eye drops developed in parallel.



915–1989 • Pharmacist • CEO of Laboratoires CHIBRET

After studying pharmacy in Clermont-Ferrand and Toulouse with his future wife, Marguerite DELCHER, and after the Second World War, Jean provided a national and then international dimension to Laboratoires CHIBRET, which soon became a leader in Europe, the Middle East and Africa. A visionary and tireless entrepreneur, Jean (with his brother René) established himself as an innovative industrialist who, in two decades, developed an entire range of eye drops and ophthalmic ointments. The AMM files are very well documented and Laboratoires CHIBRET moved to the forefront of most therapeutic classes of ophthalmology, notably antibiotics and corticoids. The research laboratories were then the most important at an international level and worked in close collaboration with the academic world, in particular, with the University of Clermont-Ferrand (Professors Pierre TRONCHE, François ROUHER, Roger CLUZEL, Pierre BASTIDE and Henri POURRAT).

In 1946, he visited MERCK Laboratories in the United States, with which he maintained increasingly close relations. He obtained their license for streptomycin and also for corticoids by 1950 for the launch of the first cortisone eye drops, followed by hydrocortisone and then dexamethasone. These would revolutionize the treatment of ocular inflammation.

In addition to research on molecules, Jean CHIBRET was interested in packaging. Scientific information was another of his hobbies. He was the first to understand the importance of audiovisual communication and initiated large-scale production of training films for eye care professionals. More than 200 films would be made with the great names in the field. He opened the world's largest documentation center (CHIBRET Institute), attended by entire classes of young specialists. He published the journal, Revue CHIBRET, which was circulated to 15,000 eye care professionals. He established ophthalmology symposiums, which brought together interns and centers of higher education every year in Clermont-Ferrand. The reputation of the name CHIBRET thus became synonymous with rigor, ethics and quality. Again, in the family tradition, he was interested in trachoma, subsidizing its international review, the gold medal and numerous research teams. Considering that he did not have the financial means to ensure worldwide distribution of his products, in 1969, he joined forces with the US firm MSD Laboratories, which would become the world's leading ophthalmic drug manufacturer. At the same time, MSD made the Clermont-Ferrand region its first research and production center.



René CHIBRET, Jean's younger brother, took part in the adventure and immediately after the Second World War, put his engineering talents at the service of the industrial development and investments of Laboratoires CHIBRET.

Laboratoires Chibret

During their visit to the United States in 1946, Jean and René CHIBRET were impressed by the American advances in the fields of standardization, mass production and quality control. On returning to France, they devoted themselves entirely to the modernization of the family laboratories. Their industrial dimension was fully achieved in the early 1960s with the inauguration of the new site at Avenue Clémentel in Clermont-Ferrand. Ultra-modern facilities were built with the latest equipment, which exceeded the quality standards required by the public authorities. The production unit of Laboratoires CHIBRET became one of the most modern and imposing in Europe.





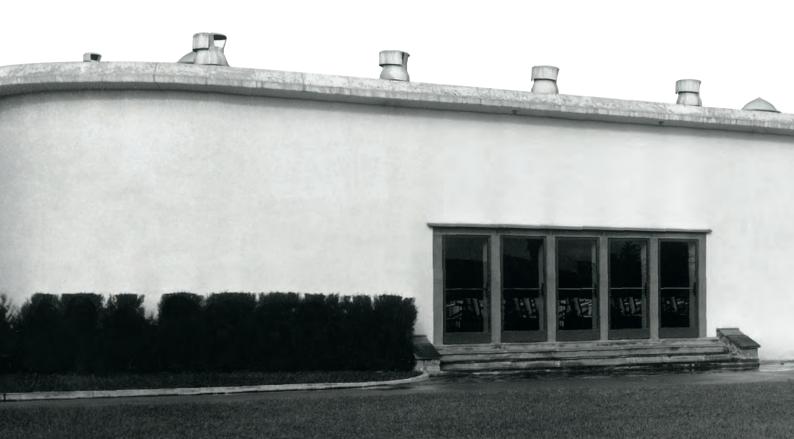


- Site at boulevard Etienne Clémentel (Clermont-Ferrand)
- 2 Jean CHIBRET and his staff
- **3** Sterile block for filling eye drops
- 4 Packaging line at the Avenue Clémentel site (Clermont-Ferrand) at the start of the 1960s



Institut Chibret

Jean CHIBRET was convinced that research and development had to spearhead the expansion of Laboratoires CHIBRET. He thus developed an internal R&D structure to create a "pipeline" of new products. He recruited a multidisciplinary team capable of studying all the new possibilities of physical, chemical and biological technologies for developing the pharmacopoeia. At the same time, he drew on every institutional research network. Finally, he opened the world's largest documentation center (books, theses, journals, photographs, films, etc.), the CHIBRET Institute, which was attended by entire classes of young specialists. This "Institute" published the Revue CHIBRET, which was circulated to 15,000 ophthalmologists. This structure also organized the ophthalmology symposiums each year in Clermont-Ferrand, which brought together interns and centers of higher education. The reputation of the CHIBRET name quickly became synonymous with rigor, ethics and quality.







- 2 Documentation center
- 3 Ocular electrophysiology center
- 4 Ophthalmology symposium of 1966



Bottles

In addition to research on molecules, Jean CHIBRET was interested in packaging.

After the Second World War, the quality of the glass and therefore of the bottles was improved by including additives as a function of their use. Manufacturing became fully automated and allowed for a strong increase in volumes and a decrease in production costs. The study of the stability of products packaged in containers led to the definition of several types of glass. At a later stage, these pharmaceutical glasses would be progressively challenged by plastics. At all of these stages, Laboratoires CHIBRET remained at the forefront of innovation: blown glass eye-dropper bottles, then treated glass with a sterile plastic pouring tip, plastic bottles, freeze-dried bottles, CHIBRET's packaging evolved in line with the latest scientific and technical discoveries for providing ever greater satisfaction to professionals and patients.

With a constant concern for the serious problem of contamination, Jean was also the first to introduce a preservative to the solutions and to impose a use-by date after opening the bottles. These two seemingly simple ideas were adopted by all public health administrative authorities.





FROM THE AGE OF GLASS ... TO THE AGE OF PLASTIC

The products

Jean CHIBRET was the first to supply practitioners with ophthalmic products based on penicillin and then cortisone. It should be noted that the three post-war decades marked a genuine therapeutic revolution. Antibiotics, corticoids, mydriatics, anesthetics, anti-glaucoma drugs, CHIBRET's range was expanded in line with the new discoveries which were constantly emerging and radically changed the eye care professional's daily routine. Numerous products, Novesine, Mydriaticum, Ryfamycin, Chibro-Cadron, Chibroxine (some of which are still available today) were developed at this time. The company became the "generalist" eye laboratory.

The presentation of the products underwent a spectacular evolution. Communications shifted from black and white to color; the visuals entrusted to communication professionals become more sophisticated. Laboratoires CHIBRET gave increasing space to medical information, anticipating that the public authorities would soon impose the inclusion of more and more mentions on boxes of medicines (name, form, active substance, classification, batch number for traceability, etc.) in order to ensure their quality and safety.



- Sample of the numerous products of Laboratoires CHIBRET
- $\mathbf 2$ Aureomycin advertising
- ${f 3}$ Chibro-Cadron advertising from the 60s







Stand of the Institute and Laboratoires CHIBRET at the SFO Congress in 1956

The SFO

CHIBRET FILS S.A. CLERMONT - P. - DARIS



Several decades after the creation of the Société Française d'Ophtalmologie by his ancestor Paul CHIBRET (1883), the annual congress of the SFO remained an exceptional opportunity for Jean CHIBRET to disseminate information on the family business. This congress, which was held over the years at the Marcelin Berthelot Center or at the large amphitheater of the Faculty of Medicine in Paris, took root in the post-war years at the Maison de la Chimie (Paris). The marketing departments of Laboratoires CHIBRET created stands presenting both the Laboratory and the Institute. The space created became, beyond a showcase for CHIBRET novelties, a place of welcome, meeting and exchange for all of the leaders in ophthalmology. Moreover, Jean CHIBRET and his teams participated in every world congress since that time. From Madrid to Berlin, from New York to Taiwan, from Manila to Rotterdam, they were in contact with the best specialists and guaranteed the international renown of the French company.



941–1989 • Holder of a MBA • Founder and CEO of Biophysic Medical (lasers and ophthalmic ultrasound scanners)

Jean CHIBRET passed on his passion for entrepreneurship, innovation and exporting to his two sons, Henri and Jacques. BIOPHYSIC MEDICAL arose in 1974. Jacques, the younger son, marketed an automatic electrophysiology device (the Pantops), with studies conducted in collaboration with the Ophthalmology Department of the University Hospital of Clermont-Ferrand (Profs. ROUHER, SOLE and ALFIERI). Prof. Jean HAUT, of the CHNO des Quinze-Vingts in Paris, and Dr. POUJOL would permit BIOPHYSIC MEDICAL to develop the emerging ultrasound technique. Jean HAUT and Florence PINON played a decisive role in the development of the first European ophthalmic Argon laser for the treatment of retinopathies.

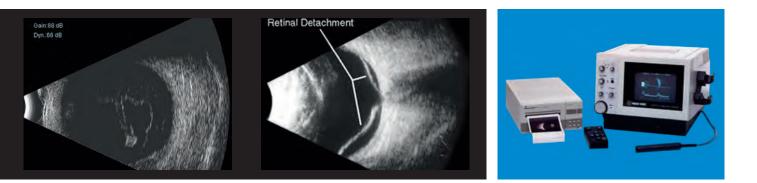
As with Laboratoires CHIBRET, BIOPHYSIC MEDICAL reached the critical threshold of a "big company that was too small" during the 1980s. In order to become a major player in the US market, which represented nearly 70% of the world market, BIOPHYSIC MEDICAL joined forces with the French group Synthelabo Biomedical* through its main shareholder l'Oréal. BIOPHYSIC MEDICAL USA was created in 1984 with Alain CHARMANT as director, experiencing rapid success.

Jacques was a firm believer in the Excimer laser for refractive surgery of the cornea and, together with Dr. Philippe CROZAFON and the University of Nice, he developed the first prototype. Sadly, this project was interrupted by his tragic death in Africa. During a hunt in Cameroon in February 1989, he was mortally wounded. He had gone there to bring back the personal effects of Jean CHIBRET, who had died a few weeks earlier. 1989 will forever remain a black year in the history of the family.

^{*} Synthelabo Biomedical sold BIOPHYSIC MEDICAL to ALCON in 1989

Biophysic Medical

BIOPHYSIC MEDICAL rapidly became the world leader in the field of ophthalmic ultrasound and the world No. 2 in the field of lasers. This success was achieved through an in-depth analysis of the expectations of practitioners. The success was also the result of Jacques CHIBRET establishing a multidisciplinary team that allowed him to combine expertise and know-how. Leading researchers in the most varied fields (tubes, optical fibers, micro-mechanics, micro-electrics, etc.) agreed to work together. This joint effort resulted in revolutionary medical imaging machines manufactured in Clermont-Ferrand and sold throughout the world.



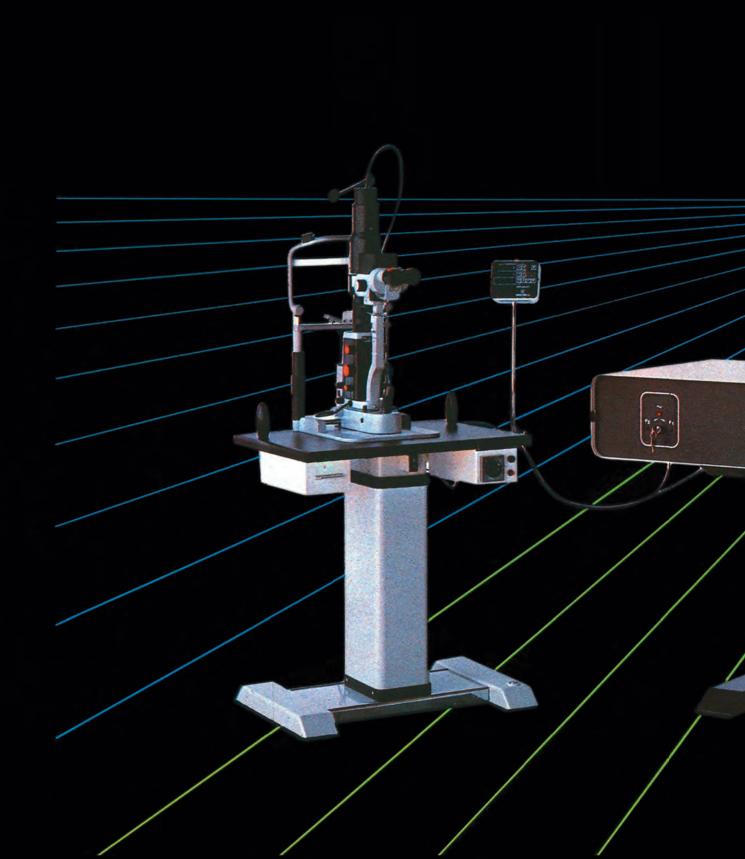


1 - Ultrasound

2 - BIOPHYSIC MEDICAL ophthalmic ultrasound

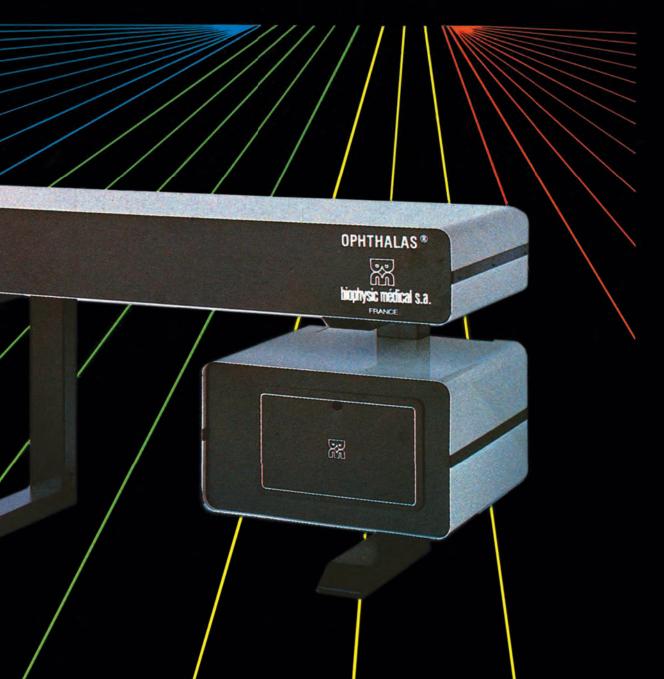
3 - BIOPHYSIC MEDICAL laser assembly line (Clermont-Ferrand)

Jacques CHIBRET constantly developed the BIOPHYSIC MEDICAL laser range: after Argon, he introduced Krypton and shortly afterwards YAG.

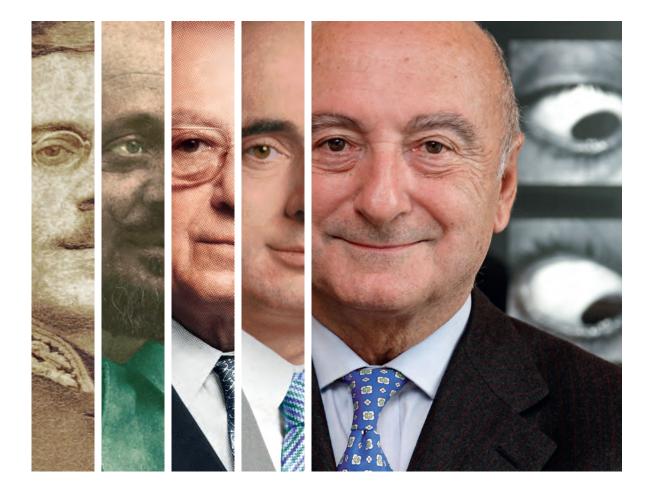




Argon and/or Krypton







940 • Pharmacist • Founder of Transphyto and THÉA Laboratories, Chairman of the Board of THÉA Holding

After studying pharmacy in Clermont-Ferrand and spending a year in North America, in New York State and Quebec, in 1965, Henri CHIBRET was entrusted with the management of all export activities of Laboratoires CHIBRET. One of his priorities was to establish the company in Germany (with Pierre CZAPINSKI, who worked for Franco-German reconciliation) and in the emerging countries of the Persian Gulf: Iran, Iraq and Saudi Arabia.

After the sale of the family firm to MERCK in 1969, Henri CHIBRET pursued his career for a few years with Merck in Brussels and then with Ferlux in Clermont-Ferrand.

Seeking to focus exclusively on free and independent research activities, in the mid-1970s, he created TRANSPHYTO, the first French start-up dedicated to pharmaceutical research. Its innovations were produced and marketed by French and foreign laboratories, with its revenues being guaranteed by royalties and the sale of patented raw materials. This resolutely innovative strategy was combined with another original feature: TRANSPHYTO outsourced the majority of its research activities to subcontractors, drawing on the best research institutes. The collaboration with Prof. Philippe LAPALUS of the Faculty of Nice and then with Pierre-Paul ELENA (IRIS-PHARMA), for example, would prove invaluable in the fields of toxicology and ocular pharmacology.

These innovations included several major contributions. At a time when the therapeutic arsenal in the field of dry eye was still limited to aqueous solutions, Transphyto introduced the first carbomer-based gel, permitting an important reduction of the number of instillations and increased patient comfort. TRANSPHYTO also developed one of the very first anti-allergic mast cell stabilizing agents (NAAGA) and a gel for the treatment of herpes, etc.



Laboratoires Théa

The main partners of TRANSPHYTO were: ALLERGAN, CIBAVISION, ZYMA, MSD-CHIBRET, CUSI. This was a success in scientific and financial terms, but Henri CHIBRET was frustrated not only to see his innovations passing from hand to hand in line with mergers and acquisitions, but also by the fact that he did not control their commercial future and was deprived of contact with eye care professionals. He thus decided to market his products himself. He nevertheless did not intend to return to the market with a banal range, or yet another anti-allergic, or beta-blocker, but with a breakthrough innovation. The name of CHIBRET has always been associated with research; this return had to be achieved through the front door.

The development of THÉA would thus be based (like that of Laboratoires CHIBRET and BIOPHYSIC MEDICAL) on the absolute priority given to innovation.

It was in this way, for example, that in the early days of THÉA, the World Health Organization's Alliance for the Global Elimination of Trachoma by 2020, sent an urgent request to the pharmaceutical industry for the development of a topical form of antibiotic, with a short duration treatment. Henri CHIBRET heard this appeal and took up the challenge. He began a long development program for new azithromycin-based eye drops, which would last for 8 years due to technical difficulties, notably relating to galenics. Today, the rate of incidents of trachoma is falling wherever this treatment is administered: entire populations have been saved from blindness.

"But even before this major innovation, with a single step, Henri CHIBRET had made his young company a key player in European ophthalmology, by making accessible what seemed to be out of reach."

THE PIONEER AND WORLD LEADER IN PRESERVATIVE-FREE PRODUCTS

44

At that point, still in the mid-1990s, the scientific community was starting to become aware of the harmfulness of preservatives to the eye. At the same time, all attempts by the pharmaceutical industry to develop a preservative-free multi-dose "eye drop" bottle were unsuccessful. After ten years of research, Henri CHIBRET developed the ABAK® bottle, which provided the solution. With it, THÉA was genuinely created, since on that day, it was not just a simple pharmaceutical laboratory that was born, but the pioneer and world leader in preservative-free ophthalmic treatments; a position that would continue to be consolidated due to the involvement of his nephew, Jean-Frédéric CHIBRET.



Launched in the mid-1990s, ABAK[®] was the first multi-dose eye drop bottle capable of delivering preservative-free drops. Its filtering membrane kept the contents of the bottle sterile for a period of 2-3 months. The harmful effects of preservatives such as benzalkonium chloride were avoided. Ironically, Henri CHIBRET eliminated the use of preservatives that his father had introduced.

With this global first, Henri CHIBRET contributed a breakthrough innovation. Millions of patients rapidly benefited from a range of ophthalmic treatments that finally respected the integrity of the eye. Henri CHIBRET and his nephew Jean-Frédéric have aimed at the constant improvement of the ABAK[®]. It has become smaller, more manageable and more efficient, with an increasingly long shelf life.



Reservoir containing up to 300 sterile drops (for a 10 ml bottle) ABBA

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Flexible and ergonomic wall made of low-density polyethylene

Notching system for tamper-proof ring

Neutral microporous swab

Bifunctional hydrophilic/hydrophobic 0.2 µm PES membrane

Rounded protective tip

Calibrated drops (30 $\mu l)$ without preservative

Easy-Grip[®] A SECOND PRESERVATIVE-FREE BOTTLE

Alongside ABAK[®], a second bottle was developed, using EASY-GRIP[®] technology, suitable for certain molecules, notably in the field of glaucoma. The CHIBRET "duo" then tackled contamination of gels, particularly for eyelid hygiene, by launching the STERI-FREE[®] tube, which delivers sterile gels for the periphery of the eye throughout the use of the product.

With Laboratoires THÉA, the "preservative-free" revolution was underway.





Steri-Free

THE TUBE WITH STERILE GEL-STERILE BEFORE AND AFTER OPENING

Laboratoires THÉA's Italian site, which produces the ABAK® bottle, has been restructured to produce a tube with revolutionary technology capable of dispensing sterile gels which remain sterile throughout the use of the product. Behind this major innovation was an airless pump tube, but above all, a state-of-the-art production line allowing the product to be packaged in a sterile way ("STERI-FREE" technology). This new technology made it possible to offer gels containing only the essentials, i.e. no pseudo-preservatives or other irritant agents. By virtue of this invention, Laboratoires THÉA consolidated its image as a pioneer and leader in the fight against the harmful effects of preservatives in ophthalmic products.



Tube containing 30 g of gel -> 65 applications

Flexible and ergonomic tube -> Comfortable application

Polyfoil® tube with an aluminum wall -> Hermetic

Hermetic membrane located inside the airless pump -> Hygienic, protection against bacterial contamination

Airless pump (MEGA Airless® pump) - Easy to use -> Simple and easy application - No residues -> over 96% product return

Calibrated dosing - Accurate and consistent - Reduced risk of misuse and overconsumption



STERT FREE

Preservative-free products make their mark in the world

In 1994, when Henri CHIBRET created ABAK[®], the first multidose eye drop bottle capable of delivering preservative-free drops, no-one suspected that this world first would usher in the preservative-free era in ophthalmics.

Very few doctors then were aware of the harmful effects of preservatives. Fortunately, the work of Prof. Christophe BAUDOUIN (Paris) during the 1990s, confirmed by numerous teams around the world, clearly demonstrated the role of preservatives in the phenomena of irritation, dryness and inflammation. From then on, it became evident that an attempt was needed to reduce or completely eliminate the quantity of preservatives ophthalmic treatments. The need for preservative-free treatment first arose in patients suffering from ocular surface pathology, in particular, in those who had developed hypersensitivity, or even severe intolerance to preservatives; then in patients suffering from chronic diseases, such as glaucoma. Little by little, eye care professionals became accustomed to prescribing preservativefree treatments to all of their patients.

One thing is certain, more than a quarter of a century after the invention of ABAK[®], "preservative-free" has become a "standard", and doctors and patients are unanimous in noting improved tolerance and compliance. Henri CHIBRET and THÉA have converted the world market, and more importantly, the medical authorities. One after the other, these authorities, like the professional societies, have recommended that preservativefree eye drops be used to maintain the integrity of the eye.





975 • MBA • Chairman of the THEA group

The next generation

In the 2000s, Henri CHIBRET set himself three objectives: accelerating research efforts, pursuing the Europeanization of the company and placing his nephew in the saddle.

After a two-year apprenticeship with the Spanish subsidiary (2000-2001), Jean-Frédéric CHIBRET, who had a commercial background, returned to Clermont-Ferrand and successfully adapted to the various activities of the company. As a result, in 2008, Henri CHIBRET entrusted him with the reins of the Laboratories so that he could take over the management beside him. From then on, Jean-Frédéric would take charge of the destiny of the company by accelerating its international expansion, its research efforts, the modernization of its production sites and the deployment of knowledge sharing, not to mention the launch of FONDATION THÉA. His uncle Henri remains at the head of THÉA Holding and now focuses on the group's scientific and financial strategy.

This new family team clearly continues to prioritize innovation.



INNOVATION CONTINUES...

A complete range of ophthalmic treatments



THÉA'S R&D would generate some 25 innovations in 25 years in most therapeutic classes, offering practitioners and their patients the most modern range of ophthalmic treatments. It would produce major advances in areas such as glaucoma, allergy, infection, inflammation and dry eye. It would also contribute to the creation of new markets and new concepts, not only with "preservative-free" products, but also for eyelid hygiene, ocular nutrition, antibiotic therapy and intracameral mydriasis.

INNOVATION CONTINUES...

Contraction Théa Open Innovation

Since the key to success lies in adding and multiplying innovation, in 2019, Jean-Frédéric CHIBRET launched "THÉA OPEN INNOVATION" (TOI), a new "tool" which will serve as a pipeline for tomorrow's treatments. This new structure had the objective of identifying, assessing and promoting the best innovative solutions from start-ups, university teams and researchers. By implementing licensing agreements and equity investments on behalf of the Clermont Group, TOI provides its partners with the ophthalmic development expertise and financing needed to reach proof of concept in humans, with the capacity of Laboratoires THÉA to then conduct the regulatory development and marketing phases of the products.





An international presence

Even before his arrival as Chairman of THÉA, Jean-Frédéric CHIBRET began with the assumption that the company required a presence in a number of key European countries. In his view, Italy, Spain, Germany and England were strategic countries. He was thus the one who would gradually direct and structure the international activity of THÉA by creating new subsidiaries. This international expansion, often preceded and facilitated by strategic acquisitions in the host countries, was driven by an observation: research knows neither borders, or more compellingly, established discipline and knowledge. Only an increased territorial presence will permit a pharmaceutical company to rub shoulders with new scientific communities, to support and strengthen the dynamics of decompartmentalization of its research and accelerate its development.

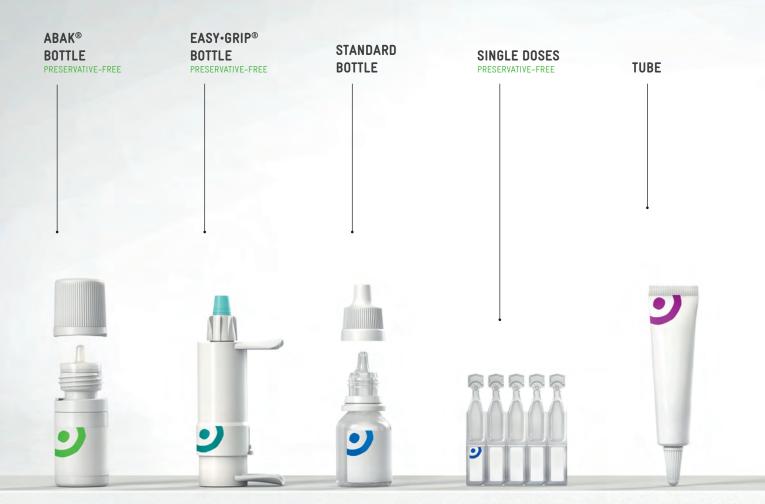
With the completion of this first deployment in 2008, Jean-Frédéric CHIBRET presided over the acquisition of several products that opened the door to new countries, such as Russia, Sweden, Norway, Finland, Denmark, Austria and Turkey. A sequence of openings of subsidiaries followed, allowing THÉA to enter the closed circle of the French pharmaceutical companies which have subsidiaries in the four pivotal corners of the European continent.

After Europe, Jean-Frédéric CHIBRET set out to conquer sub-Saharan Africa, the Maghreb, the Middle East, but also the American continent, by opening subsidiaries in South America, Central America and in Canada but also in the United States, while continuing the dissemination of THÉA products in 75 countries throughout the world.





THÉA is present on all five continents through its network of subsidiaries and distributors.



European quality

A COMPLETE RANGE OF PHARMACEUTICAL FORMS



With THÉA, it is European excellence that is exported daily and acclaimed throughout the world.

Laboratoires THÉA ensure their supplies of raw materials and active substances within the European Union. In parallel, for production in the strict sense of the word, they have joined forces with the best manufacturers on the continent by product category. In the past, eye drops and ointments were the main products used for eye care. Nowadays, the range of eye care products available to the eye care professional has grown considerably: single-dose or bottle eye drops, ointments, gels, wipes, injectables, ophthalmic inserts, etc. Our company, which is 100% dedicated toeye care professionals, offers more than twenty galenic forms, all of which require specific know-how, skills and equipment, whence Jean-Frédéric CHIBRET's decision to outsource part of the manufacturing process, via long-term partnerships, in order to offer practitioners and patients treatments which meet the highest quality standards.

Development of our production sites

Being at the cutting edge of progress means not only drawing on the best in Europe, but also keeping a firm grip on our strategic technologies. In this way, our ophthalmic insert for cataract surgery or certain ophthalmic diagnostics is produced by us near La Rochelle (Charente-Maritime). In the same way, the ABAK[®] bottle (for preservative-free eye drops) and the STERI-FREE TECHNOLOGY tube (for preservative-free gels) are filled in our Farmila plant near Milan, Italy; a site that has recently increased its capacity and can now produce up to 60 million units of ABAK® treatments each year. The entire challenge for THÉA is to maintain, beyond our alliances with external partners, a certain control over our production, and to avoid what are called supply constraints, i.e. tensions on the production apparatus. In short, THÉA has equipped itself with the means to keep pace with its growth.

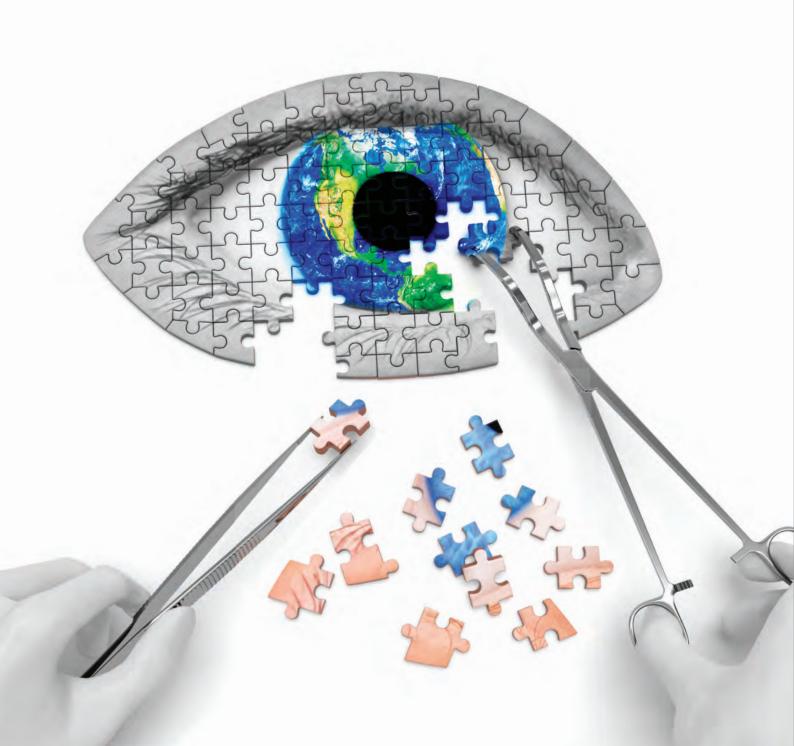
 View of the Théa Farmila plant in Settimo Milanese 20019 (MI) in Italy

> 2 - Sterile fabrication plant for the ABAK® bottle





#NeverStopLearning



Théa Education

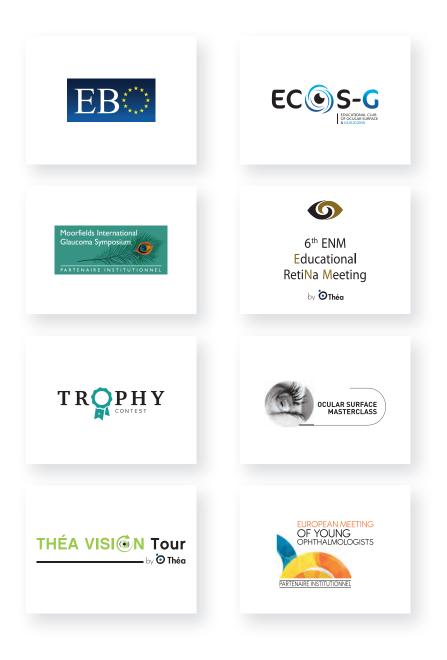
Under the aegis of THÉA or FONDATION THÉA, programs are multiplying to disseminate knowledge. These initiatives are assembled under a single banner: Théacadémy.

In a world in which scientific progress is changing the field of possibilities every day, THÉA is at the service of eye care professionals from interns to senior practitioners, who aspire to regular training in order to maintain the quality of their practices. THÉA accompanies the specialists of tomorrow by supporting initiatives designed by young people for young eye care professional during the EMYO "Young Ophthalmologists" /"institutional partner" (EMYO) congresses; by enabling surgeons who are just starting out in their careers to perfect their skills on a simulator, Dry or Wet Lab; or also by inviting young interns and heads of clinics to participate, in a spirit of emulation, in the TROPHY, an international competition of clinical cases which offers the winners the opportunity to present their work at renowned congresses (ARVO or EVER).

Events

This dynamic of sharing and disseminating knowledge is not limited to young people, but is aimed at all practitioners, beginners and seasoned professionals. It also takes the form of numerous events dedicated to different pathologies. A calendar of international meetings coupled with an editorial activity, within the framework of the "Librairie Médicale Théa" collection, which deals with various subjects or pathologies in collaboration with recognized international eye care professionals.

Throughout the year, THÉA accompanies young practitioners towards success while meeting the aspirations of experienced practitioners.





Fondation Théa



- **1** Jean-Baptiste Huynh
- **2** Auscultation session in Kolofata
- **3** DryLab
- **4** E-Learning

FONDATION THÉA supports the long distance learning program of the Collège des Ophtalmologistes Universitaires de France (COUF), and promotes its deployment among young African practitioners, including those of the IOTA. At present, 1400 students, in some twenty African countries, are improving their skills in ophthalmology through this online program in support of the official program of the WAHO (West African Health Organization). In 2012, Jean-Frédéric CHIBRET created FONDATION THÉA to further the work of his ancestors in the fight against blindness and the improvement of eye health. For greater efficiency, he chose to concentrate on the fight against trachoma and in the field of training in Frenchand Portuguese-speaking Africa. In just a few years of existence, the geographical impact of the FONDATION THÉA has continued to grow to include some fifteen countries: Algeria, Benin, Burkina, Cameroon, Guinea, Mali, Morocco, Mozambique, Niger, Central African Republic, Chad, Tunisia, etc.

In the field of trachoma, the FONDATION has quickly become an important player on account of the excellent results of the new topical form of antibiotic in short duration treatment, developed by Laboratoires THÉA at the request of the WHO. By virtue of these new eye drops, the elimination of this blinding disease, which has mobilized five generations of CHIBRET, is finally within reach.

In parallel, and because human resources for health are a major issue in Africa, the FONDATION finances all or part of primary or specialized training. Attentive to specifically African "solutions" to the staffing crisis, it supports training centers such as MICEI in Cameroon, IONA in Angola, and IOTA in Mali. Lastly, it invests massively in new technologies, technical surgical training (simulator, Dry and Wet Lab), but above all, online courses, facilitating the dissemination of E-Ophta, a tool developed by the Collège des Ophtalmologistes Universitaires de France (COUF), which offers high-level distance learning in ophthalmology to hundreds of students from Frenchspeaking sub-Saharan Africa and the Maghreb.













In the future, THÉA will continue to expand around the world, relying on its two strategic axes:

• Staying at the forefront of innovation. Tomorrow's challenges are immense. Recent advances in pathophysiology, biotechnology and genetics are opening the way to new therapeutic perspectives in ophthalmology. The turning point of gene therapy will make it possible to respond specifically to the needs of patients in the treatment of many diseases. With connected health and artificial intelligence (AI), the digital metamorphosis also promises us much more preventive, predictive and personalized medicine. THÉA will continue to invest in making breakthrough innovations and the treatments of tomorrow accessible to patients.

• **Developing new territories**: after Europe, Africa and the Middle East, South America, Central America, Canada and the United States, the company will continue its worldwide expansion.

We would like to thank Lorraine Kaltenbach, whose initiative this work was, as well as the entire team around her: EDITORIAL: Lorraine Kaltenbach DESIGN - CREATION: Jean Michel Istre GRAPHIC DESIGNERS: Marina Glavanovic, Nathalie Navarre, Damien Marcos 3D: Pixel de Lune, Tous les trois PHOTOGRAVING: Labo Photo Pro PHOTOGRAPHERS: François Berrué PRINTING: PRINT CONSEIL



