ELLANSÉ®

An Expert's Guide

Ellansé® is the first, and currently the only, patented collagen stimulator that incorporates PCL microspheres, which contribute to its durable aesthetic enhancements. Ellansé's unique properties mean it is a desirable option for a range of soft-tissue procedures.

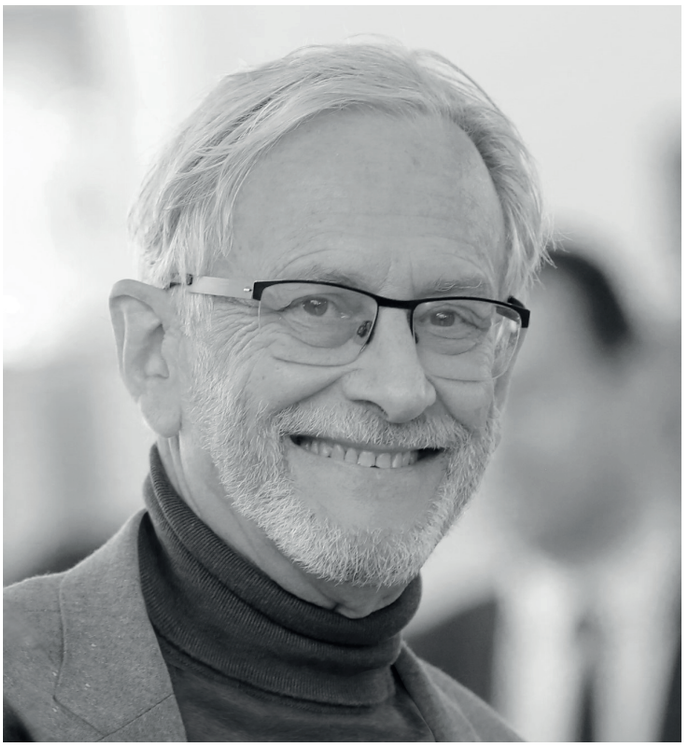
This book is intended to support clinicians who have completed Ellansé injection training in their clinical practice. The book will enhance your ongoing efforts to provide the optimal experience for patients seeking rejuvenation, prevention or beautification.

Certain sections throughout this book contain QR codes that, when scanned with your mobile device or tablet, will lead you to a 3D model of the face with relevant interactive and augmented reality content to enhance your learning and test your knowledge.

Date of Preparation: March 2022
UKBR-00665954-001-000

Ellansé®
An Expert's Guide

ELLANSÉ®



Seven years ago, we at Sinclair had the pleasure of meeting the great Pierre Nicolau. Already recognised by his peers as a plastic surgeon, a mentor and a teacher, Pierre had been involved with Ellansé and Silhouette Soft since their conception, working with the creators on development and clinical studies.

Today, more than 10 years since their launch, Ellansé and Silhouette Soft are still recognised as the most inspirational dermal fillers and threads on the market, and Pierre clearly contributed to this success. Pierre was dedicated to science, and dedicated to his patients. He was also an inspiration to many of his peers. He always wanted to learn more and to dive deeper. He was engaged and engaging, convinced and convincing, and sometimes unwilling to compromise. Most of our Ellansé and Silhouette Soft experts worldwide were initially trained by him, and today, we – as a family – all share the loss.

We are convinced that this book, one of his last projects with us, will be a game changer in convincing aesthetic practitioners to start using Ellansé in the most effective and safe way to achieve the best outcomes for their patients. For that reason and because “Spoken words fly away, written words remain” – "Verba volant, scripta manent” (Horace) - we would like to dedicate this Experts’ Guide to Pierre and to his family. May his passion for Ellansé keep inspiring the world through this book!

Dr Pierre Nicolau
1949 - 2022

Ellansé®
An Expert's Guide

EXPERT ADVISERS

Dr Francisco de Melo, UAE
Dr Shang-Li Lin, Taiwan
Dr Ingrid López-Gehrke, Mexico
Dr Pierre Nicolau, Spain
Dr Amanda Ong, Australia

Foreword

In the past 20 years, our understanding of one of the most complex areas of the human body – the face – has improved dramatically, with several new anatomical structures having been identified.

At the same time, a plethora of non-surgical procedures have become available for treating the signs of ageing and restoring the youthful appearance of the face. Ellansé® is the first, and currently the only, collagen stimulator that is made of polycaprolactone microspheres, which contribute to its durable aesthetic enhancements. Ellansé's unique properties mean it is a desirable option for a range of soft-tissue procedures.

In addition to independent and authoritative contributions from leading physicians in the field of aesthetics, this book incorporates the latest technology to deliver augmented reality assets that bring the Ellansé injection techniques to life. Facial anatomy and the consequences of ageing are covered, before recognised experts share best practice on patient preparation, injection technique and avoidance and management of complications and adverse events.

This book aims to support clinicians who have completed Ellansé injection training in their ongoing efforts to provide an optimal patient experience to those seeking to preserve their youthful appearance, balance or enhance facial features, or offset the effects of ageing.

Having read the book, you will be confident in the optimal use and benefits of Ellansé, becoming increasingly motivated to employ more advanced techniques and offer safer treatment to patients.

We at Sinclair hope you find this book rewarding and informative as it accompanies you on your Ellansé journey.

Testimonials

"This book is the result of collective clinical experience. We intend to share our expertise and knowledge in when and how to incorporate Ellansé in clinical practice. I hope it will benefit the reader the same way it has worked for me for the past 10 years: offering safer treatments with a better outcome and long-lasting results. Ellansé is a fundamental tool in my practice and has made me a better injector!"

Dr Francisco de Melo
Plastic Surgeon, UAE

"Ellansé has been my favourite dermal filler for 7 years. This book will help you to master the use of Ellansé and you will fall in love with it."

Dr Shang-Li Lin
Dermatologist, Taiwan

“In daily clinical practice, we frequently need practical management guidelines to hand. This new book represents a simple and effective guide to best practice in the use of Ellansé. Since I learned about Ellansé several years ago, my clinical practice and the aesthetic results for my patients have developed considerably. The improvement in structure and skin quality resulting from Ellansé’s unique neocollagenesis is unmatched. Undoubtedly one of the best tools for clinics that want maximum efficacy and safety in an injectable product. Ellansé has the capacity to provide long-lasting lifting and enhanced facial structure with just a single session.”

Dr Ingrid López-Gehrke
Dermatologist, Mexico

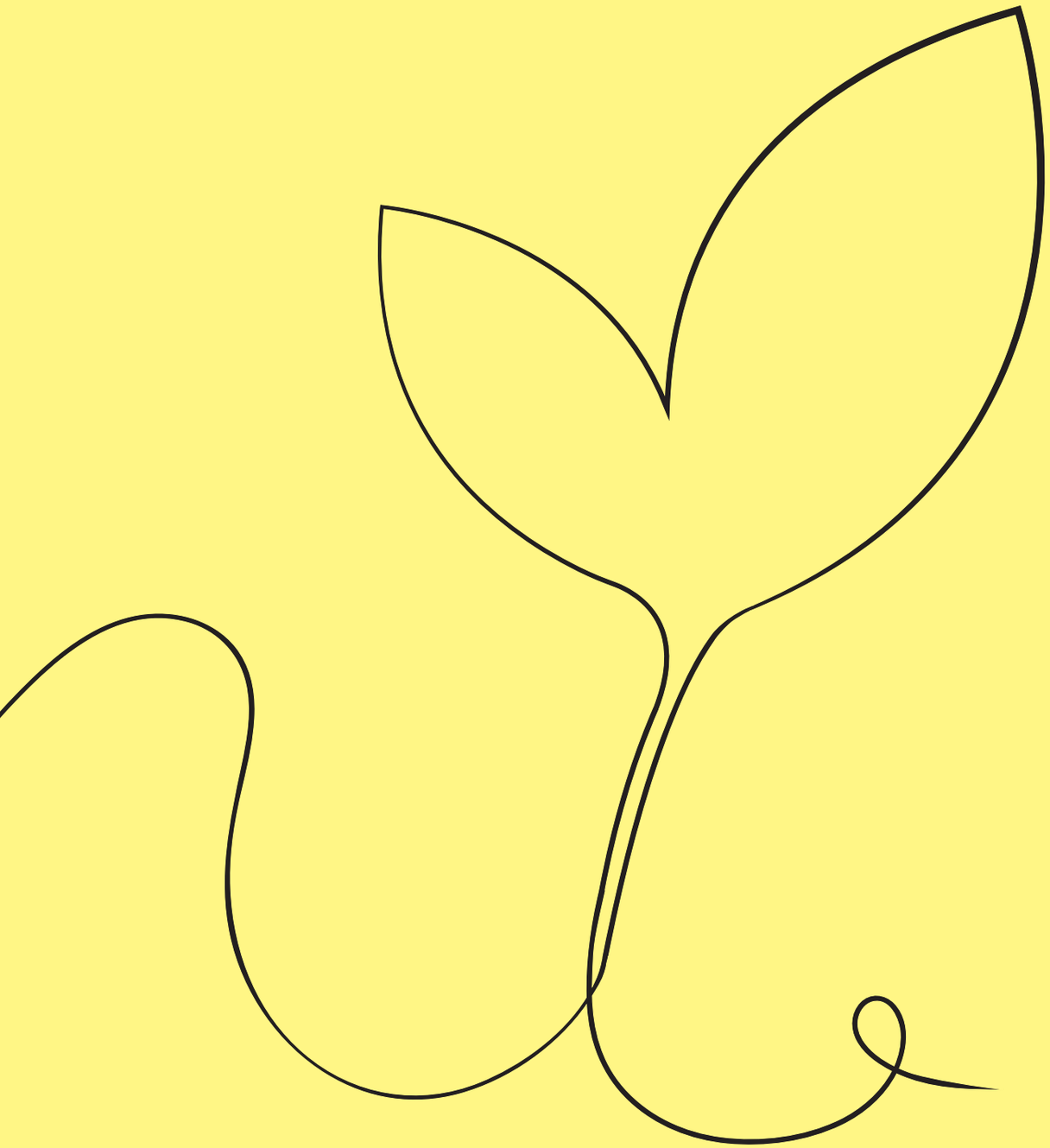
“I find great pleasure in using Ellansé due to its incredible volumising effect. This allows less product to be used, and through the real production of collagen type I, has a true capacity for skin regeneration. Many patients tell me: 'It is the first time I have something that lasts’, or 'Look at the quality of my skin’. Definitely my favourite filler.”

Dr Pierre Nicolau
Plastic Surgeon, Spain

“Ellansé has become the principal filler treatment in my practice because it is a both a superior volumiser and a skin rejuvenator. The results are not only natural looking and long lasting, but also predictable. The Ellansé Expert’s Guide provides a detailed outline on everything you need to know about the product, including detailed protocols of all facial indications. This book will become your loyal best friend if you choose to embrace Ellansé as I do.”

Dr Amanda Ong
Aesthetic Physician, Australia

Contents



Introducing Ellansé®

01

Sinclair vision: Leading future change

Sinclair's vision is to use collagen-stimulation technology to harness the body's ability to regenerate itself, delivering natural-looking and age-appropriate enhancements that will lead the way in the aesthetics industry.

Sinclair's product portfolio is built around the belief that the shape of the face is the key to aesthetic beauty (Figure 1.1).

Ellansé resonates perfectly with Sinclair's vision: improving defects in facial contours, and restoring and treating signs of ageing – including the appearance of wrinkles and folds, and loss of facial volume.

Figure 1.1
Actual patient, results may vary.

Ellansé major milestones

Following extensive research and development, and clinical testing, Ellansé gained ISO 13485 Quality Management System certification in 2008[1] (Figure 1.2). In 2009, the European Conformity (CE) mark approval was granted, leading to the highly successful launch of the product in the UK, Germany and Spain. Other launches followed, with Ellansé being registered in more than 69 countries by 2018. By 2019, the 10-year anniversary of Ellansé, more than 1 million syringes had been sold worldwide. But the success story didn't stop there, with a new manufacturing site in the Netherlands starting production in 2020 and Ellansé launched in China in 2021.

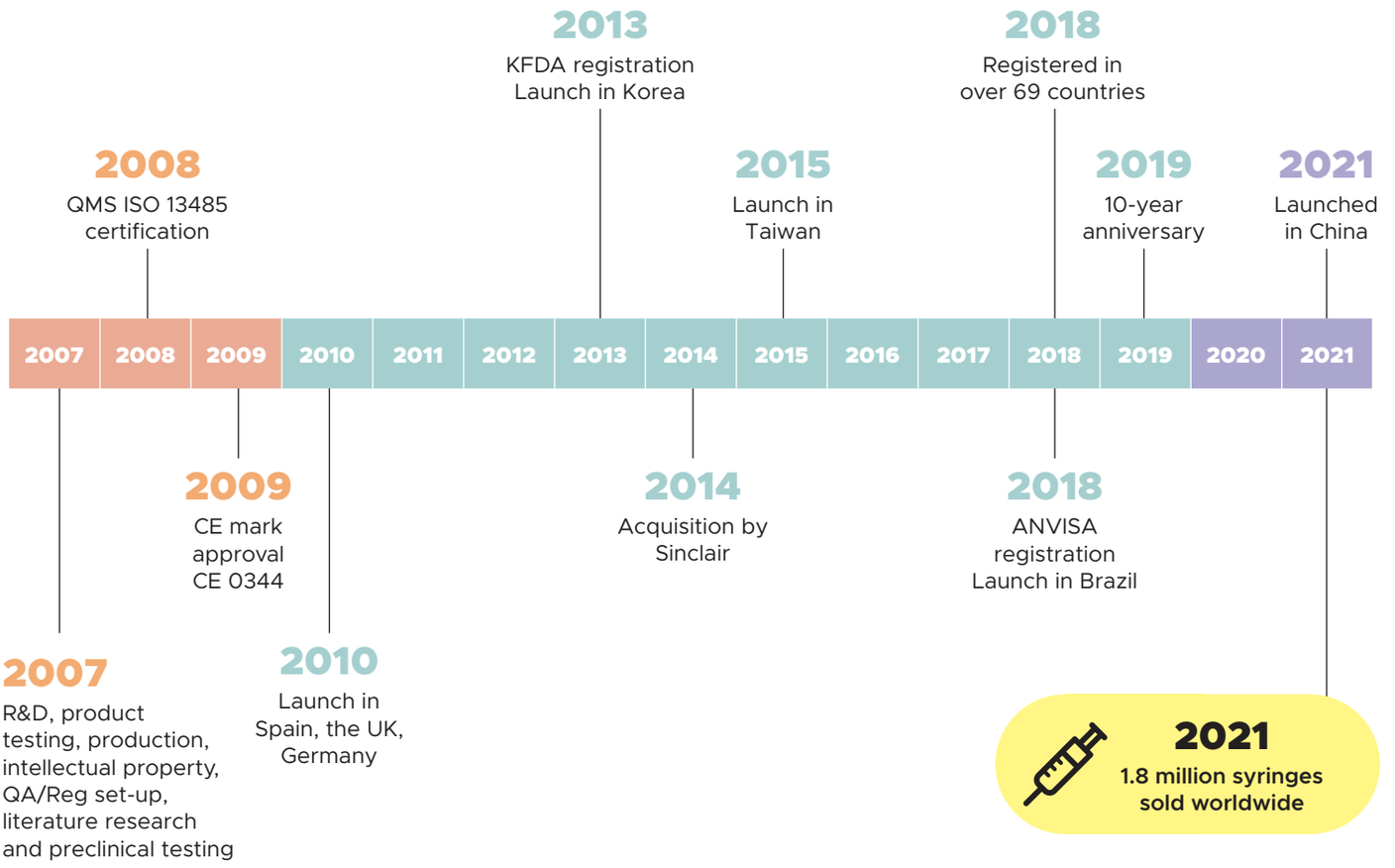


Figure 1.2
Ellansé major milestones

ANVISA, Brazilian Health Regulatory Agency; CE, European Conformity; KFDA, Korea Food and Drug Administration (now called Ministry of Food and Drug Safety [MFDS]); QA/Reg, quality assurance and regulation; R&D, research and development.

Sinclair Global Presence

Headquartered in London, UK, Sinclair is a global aesthetics company[2] (Figure 1.3) that manufactures a range of non-surgical aesthetic products, with a focus on stimulation of collagen.

Sinclair's portfolio of differentiated, complementary aesthetics technologies are increasingly in demand as they strive to satisfy the growing need for effective, high-quality, longer duration, natural-looking and minimally invasive aesthetic treatments.

Figure 1.3
Sinclair global presence


LONDON
Corporate head office, UK directly-owned affiliate and UK direct sales
AMSTERDAM
Direct sales
ALMERE
Manufacturing site
CHESTER
Global technical operations
LYON
Manufacturing site
MOSCOW
Directly - owned affiliate and direct sales
MANNHEIM
DACH directly-owned affiliate and direct sales (Germany, Austria and Switzerland)
DUBAI
UAE directly-owned affiliate and direct sales
SEOUL
South-Korean directly-owned affiliate and direct sales
HANGZHOU
Directly-owned affiliate and direct sales
SINGAPORE
Asian operations
MADRID
Spanish directly-owned affiliate and direct sales
PARIS
Global marketing, French directly-owned affiliate and direct sales

Unique composition

Ellansé is composed of a unique, patented blend of:

- 70% carboxymethyl cellulose (CMC)-based gel carrier
- 30% polycaprolactone (PCL) microspheres (Figure 1.4)[3,4,5]

The PCL microspheres are held in homogeneous suspension in the CMC-based gel carrier. PCL and CMC both have an excellent and proven biocompatibility profile.

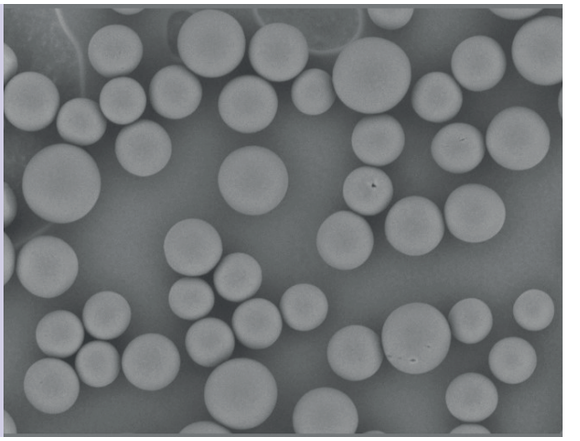
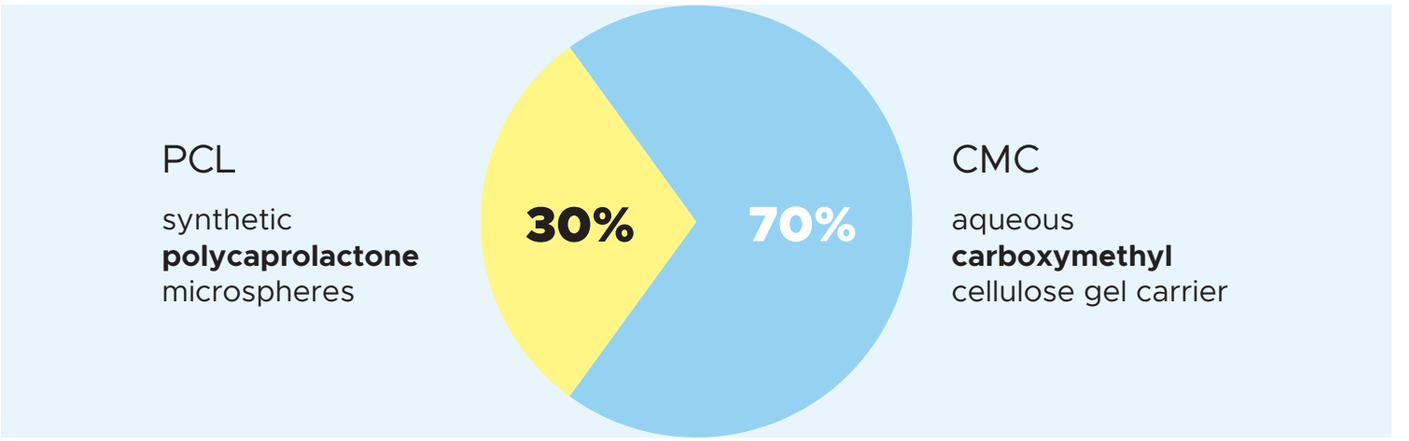


Figure 1.4
Unique composition of microspheres

Image courtesy of Dr Kim Jong-Seo, South Korea



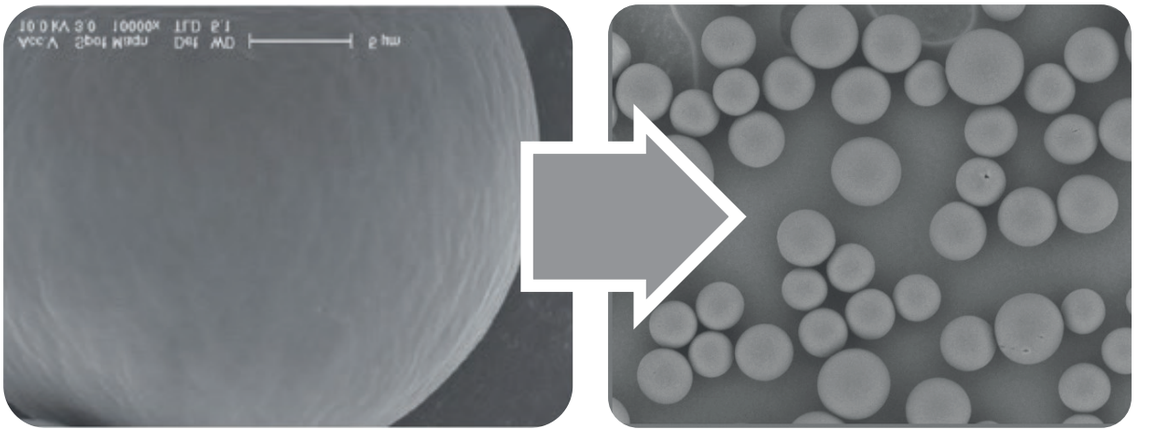


Figure 1.5
Scanning electron microscope and light microscope images of polycaprolactone spheres[5]

PCL MICROSPHERES

PCL is a non-toxic medical polyester, first synthesised in the early 1930s[4], that is attractive for use in dermal fillers because of its ease of bioresorption; it is naturally hydrolysed into carbon dioxide and water within the body[5].

The PCL microspheres used in Ellansé are designed to offer optimal biocompatibility[6]. They have a smooth surface, a spherical shape and a size of approximately 25–50 μm (Figure 1.5)[2,3,4].

PCL has an excellent safety profile[3] and has been used in the biomedical field for more than 70 years for a range of applications, from sutures to tissue and organ replacements by 3D printing (Figure 1.6)[4]. It is also used in CE-marked and US Food and Drug Administration (FDA)-approved products.

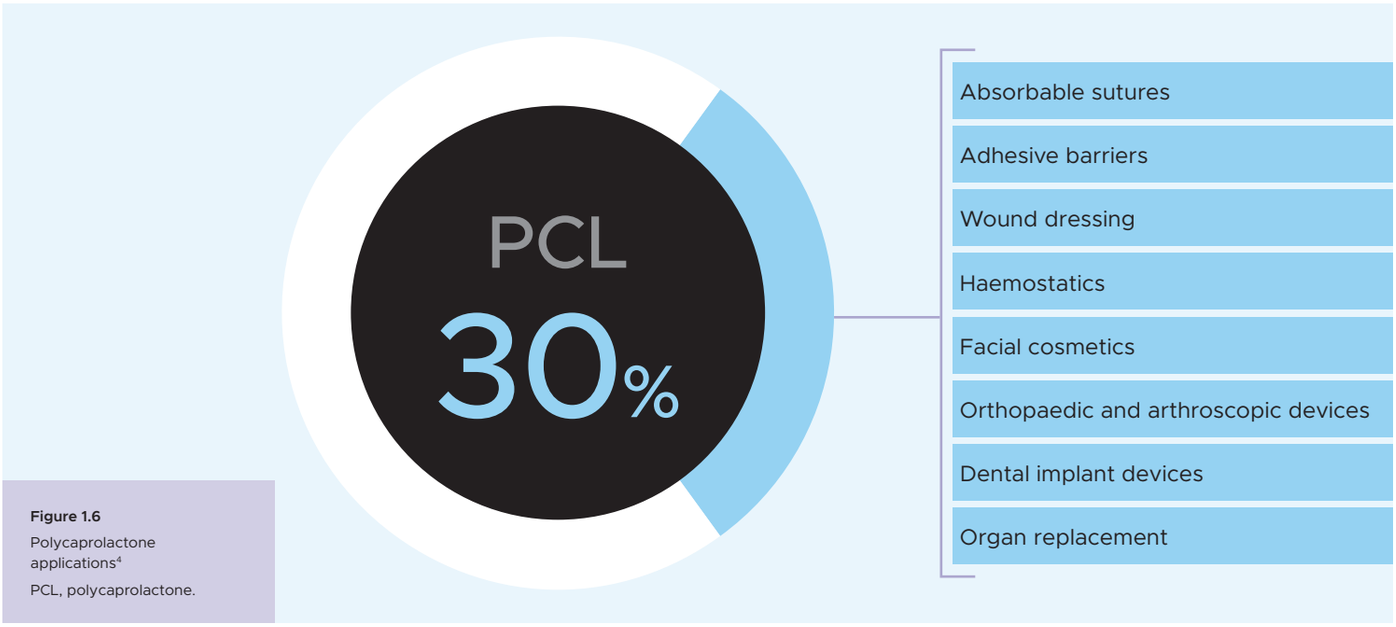


Figure 1.6
Polycaprolactone applications[4]
PCL, polycaprolactone.

PROPERTIES OF CMC

CMC is a natural material derived from cellulose; it is not cross-linked, and is non-toxic. Its other properties include (Figure 1.7)[4]:

- It is a recognised pharmaceutical excipient
- It is hygroscopic
- It has been designated by the FDA as generally recognised as safe (GRAS)
- Resorption occurs in 2–3 months

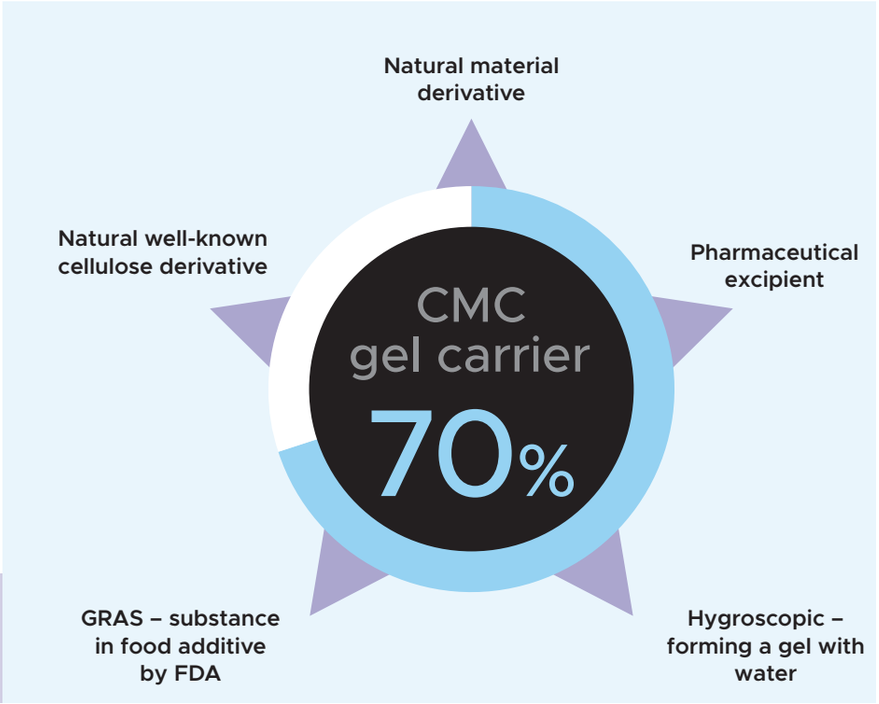
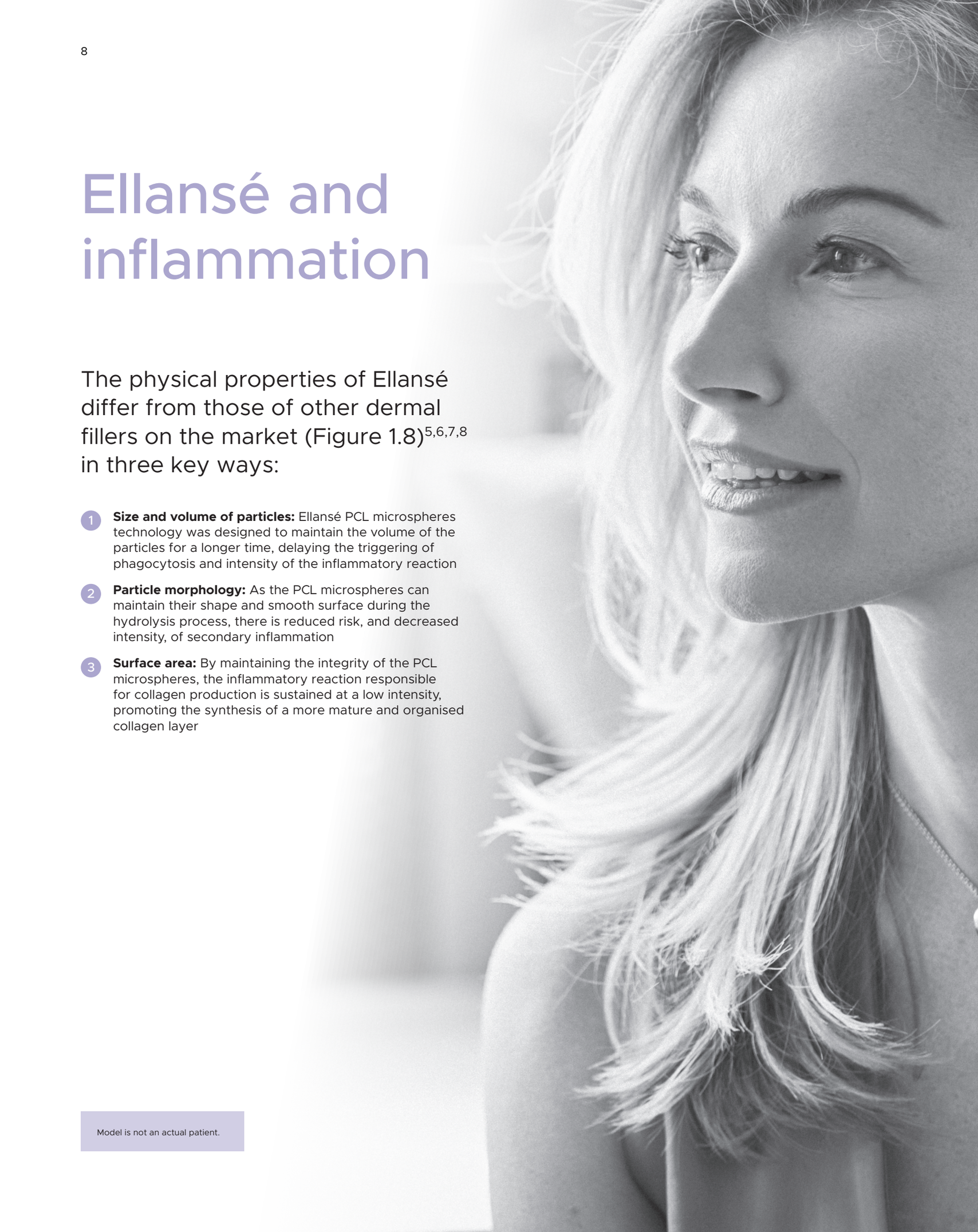


Figure 1.7
Properties of carboxymethyl cellulose
GRAS, generally recognised as safe.

Ellansé and inflammation

The physical properties of Ellansé differ from those of other dermal fillers on the market (Figure 1.8)[5,6,7,8] in three key ways:

1. **Size and volume of particles:** Ellansé PCL microspheres technology was designed to maintain the volume of the particles for a longer time, delaying the triggering of phagocytosis and intensity of the inflammatory reaction
2. **Particle morphology:** As the PCL microspheres can maintain their shape and smooth surface during the hydrolysis process, there is reduced risk, and decreased intensity, of secondary inflammation
3. **Surface area:** By maintaining the integrity of the PCL microspheres, the inflammatory reaction responsible for collagen production is sustained at a low intensity, promoting the synthesis of a more mature and organised collagen layer



Model is not an actual patient.

DURATION OF INFLAMMATION

The human body is capable of differentially responding to the total contact surface area of foreign material within the tissues. A gradual increase in the surface area will reach a tipping point where an acute inflammatory reaction is initiated by the body in an attempt to eradicate what it considers to be a tumoural process[8]. This explains the majority of late inflammatory reactions seen in daily practice following dermal filler use[5].

Ellansé maintains its integrity over time, with the PCL microspheres triggering a low-intensity inflammatory reaction that induces neocollagenesis, which favours the more lasting type I collagen[4]. The end result is the long-lasting aesthetic improvement seen with Ellansé of up to 24 months[4,9,10].

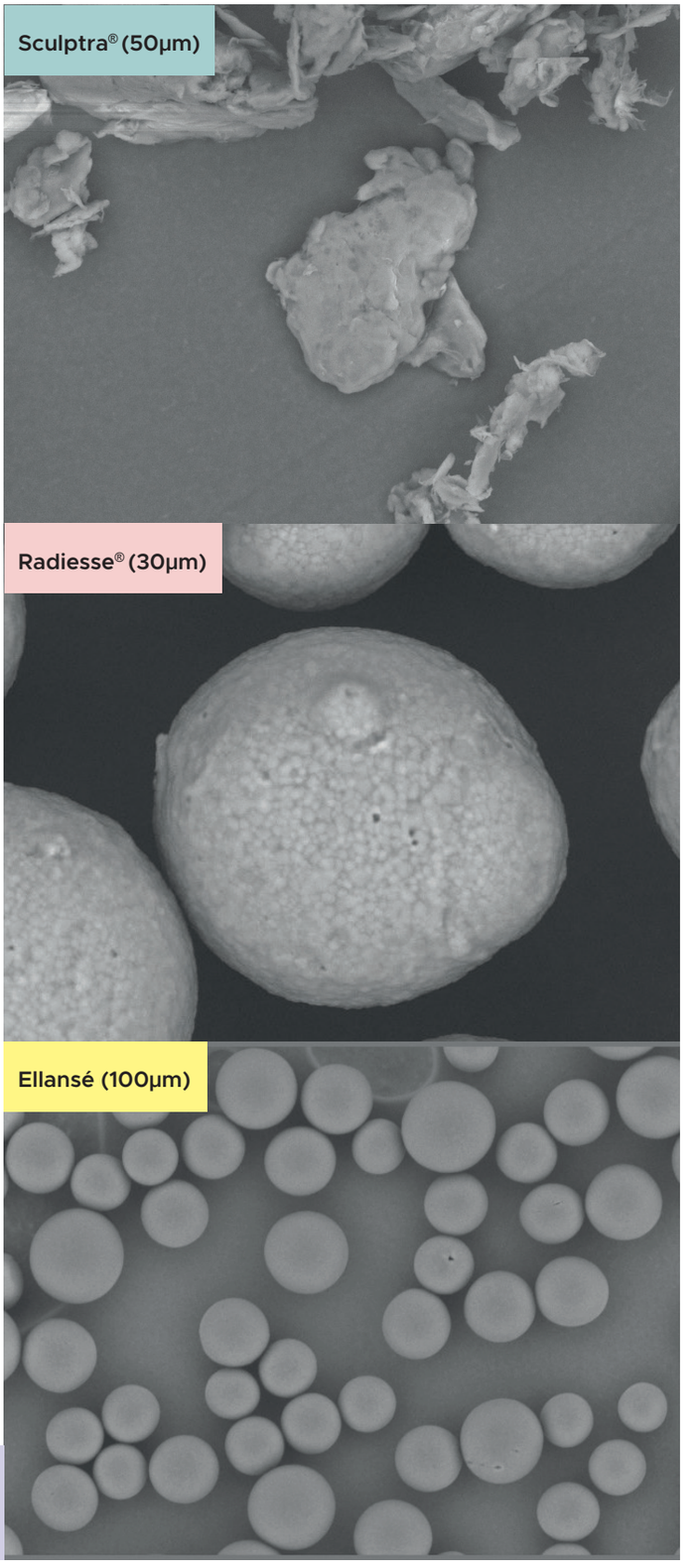


Figure 1.8
Physical composition of different fillers[1]

Ellansé mechanism of action

Ellansé has two distinct phases of activity (Figure 1.9)[1,4]:

- **Step 1:** Immediately after injection, the CMC component provides temporary volume, which gradually decreases over 2–3 months
- **Step 2:** The PCL microspheres induce neocollagenesis of types I and III collagen, with more persistent type I collagen structure gradually increasing over 1–3 months and the PCL microspheres becoming embedded in the type I collagen scaffold. The resulting collagen volume replaces the initial volume increase caused by the CMC gel

The collagen scaffold stimulated by the PCL microspheres persists after they have been resorbed, leading to the durable volume increase seen with Ellansé (Figure 1.10)[3].

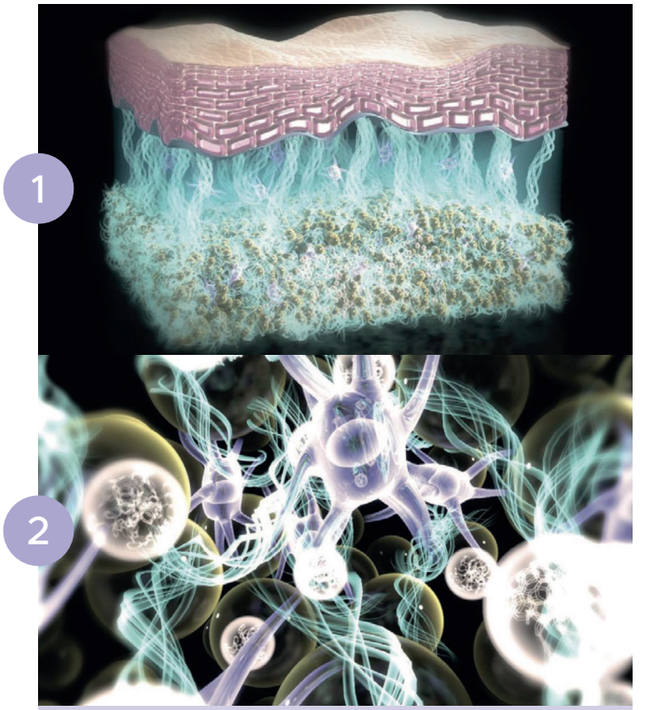


Figure 1.9
Ellansé dual mode of action[3]

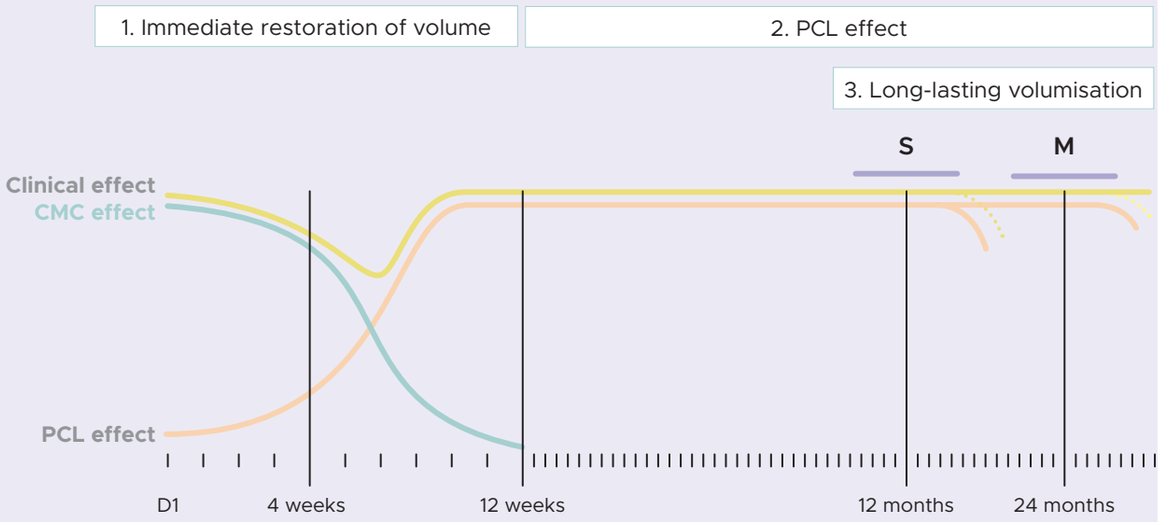


Figure 1.10
Ellansé dual mode of action[1,4]
D1, day 1.

Collagen stimulation by Ellansé: Scientific evidence

Ellansé has been tested in an animal model where rabbits were injected with either Ellansé S (PCL-1) or Ellansé M (PCL-2) to investigate neocollagenesis[5].

Nine months after injection of PCL-1, neocollagenesis had occurred and the PCL microspheres of PCL-1 had been completely resorbed (Figure 1.11)[5]. Meanwhile, with PCL-2 at 9 months, there was evidence of formation of type I and type III collagen around PCL microspheres. At 21 months post-injection, PCL-2 microspheres were still present in the injected tissue[5].

In a pilot study of Ellansé in humans, patients were enrolled to receive Ellansé injected intradermally into the temple region[9]. Histological analysis of tissue obtained from the biopsies revealed collagen formation around the injected PCL particles (Figure 1.12)[9], supporting similar findings previously shown in rabbit tissue[5].

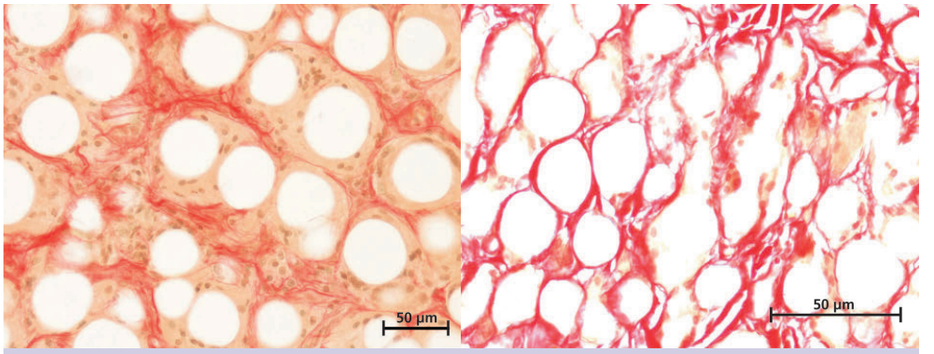


Figure 1.11
Collagen stimulation by Ellansé: Animal model[5]

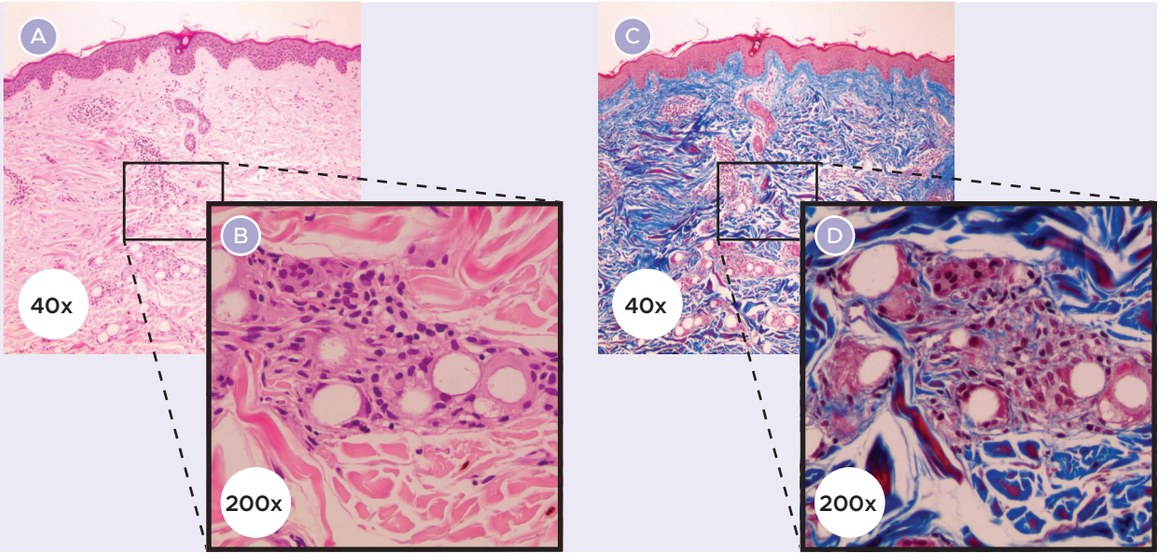


Figure 1.12
Collagen stimulation by Ellansé: Human model

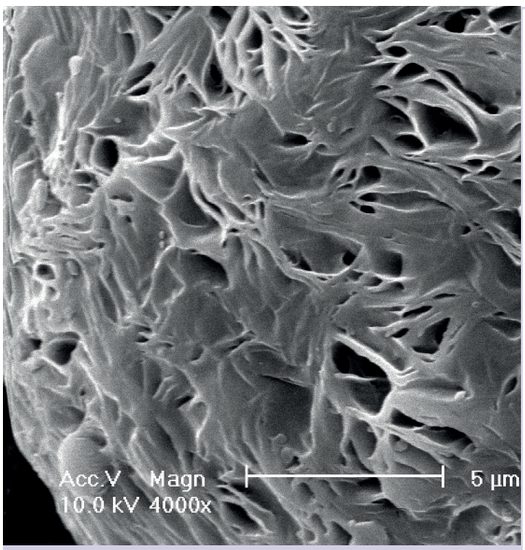
Microscopic images (13 months post-injection) show PCL microspheres surrounded with collagen deposition and a mild fibroblastic and histiocytic tissue response. Stainings were haematoxylin and eosin (A and B) and Martin's trichrome (C and D)[9]

Resorption of Ellansé

CMC is resorbed 2–3 months after injection[4]. PCL-filler degradation occurs via hydrolysis (Figure 1.13)[4] and is characterised by bulk degradation brought about by water penetrating the PCL microspheres, causing progressive internal hydrolysis of the ester bonds throughout the entire polymer matrix.

The length and the molecular weight of the polymer chains decrease over time, while the mass, volume and shape of the implant remain unchanged. Then, when hydrolysis has produced low-molecular-weight polymer chains, diffusion of the small polymer fragments occurs[4].

Longevity of the microspheres ultimately depends on the hydrolytic breakdown of PCL crystalline regions. The PCL chains of the M version of Ellansé are longer than those of the S version, and consequently take longer to degrade[4]. The difference in duration of the two Ellansé products (S and M) is due to the differing chain length (molecular weight) of the PCL chains within the microspheres[4].



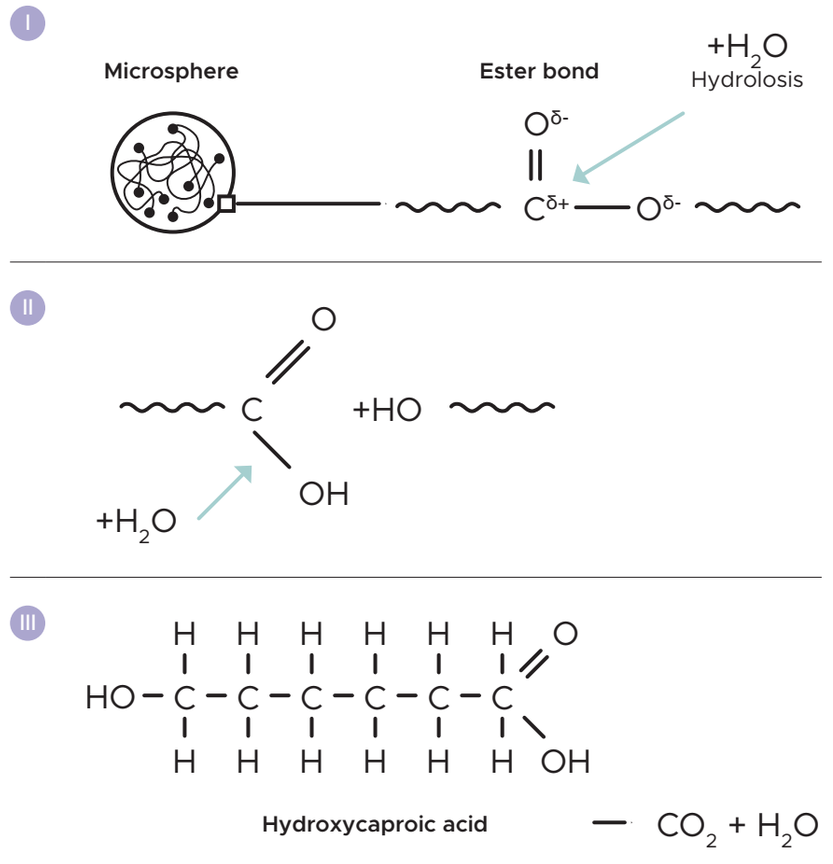


Figure 1.13
Hydrolysis and bulk degradation of polycaprolactone microspheres[4]

Clinical/aesthetic effect

Ellansé gel's elasticity is greater than that of volumising hyaluronic acid[1,11] (HA), meaning that projection and volumisation of the injected area are instantly visible. Because the collagen-stimulating PCL microspheres are maintained in the injection area, aesthetic improvement is also more long term than that seen with HAs[12]. Ellansé also has excellent rheological properties and combines high elasticity[4] with specifically designed viscosity that is suitable for subdermal injection[3].

In a randomised, prospective, blinded, split-face, single-centre study comparing Ellansé with HA in 40 patients, nasolabial folds (NLFs) treated with Ellansé showed statistically significant improvements on the Wrinkle Severity Rating Scale and greater improvements on the Global Aesthetic Improvement Scale (GAIS) compared with NLFs treated with an HA-based dermal filler[12].

Ellansé also improves skin quality, enhancing density, firmness, tonicity and texture from within.

A clinical trial was carried out to assess the effect of Ellansé on skin quality parameters in 24 patients up to 24 months post-treatment[11]. Although Ellansé was injected in the subdermis* of the midface, patient echographs clearly showed a substantial increase in tissue density in the dermis following treatment with Ellansé, compared with baseline[11]. This improvement was statistically significant at all time points during the 24-month study. Skin firmness, tonicity and smoothness were also statistically significantly improved with Ellansé, compared with baseline[11].

*Ellansé should not be placed intradermally. Please refer to Ellansé Instructions for Use for further Information.[3]

Model is not an actual patient.

Packaging and available options

As an injectable implant, Ellansé is considered a class III medical device.

Ellansé is available in two options that differ only in their duration of action. Packaging includes two ready-to-use syringes containing 1 ml of Ellansé and four 27G ¾" needles (Figure 1.14)[1]. The clinical and aesthetic improvements with Ellansé are immediate, long lasting and stable[4,9].

Ellansé L and E versions are no longer available.

- CE mark 2009
- Injectable implant
- Medical device: class III
- Ready-to-use syringes
- 2 x 1 ml syringe

ELLANSÉ S
18 months' longevity

ELLANSÉ M
24 months' longevity

Figure 1.14
Ellansé packaging and available options

Summary

The composition of Ellansé, **70% aqueous CMC-based gel carrier** and **30% PCL composition,** allows for an immediate filling effect caused by CMC, followed by stimulation of the body's own collagen (neocollagenesis).

CMC is resorbed 2 to 3 months post-injection and is progressively replaced by the patient's own collagen (predominantly type I) stimulated by PCL microspheres. The microspheres of PCL are also bioresorbable.

Ellansé has a number of attributes that make it an attractive option as a dermal filler:

1. Encapsulation of polymer microspheres, within approximately 1 month, and the associated collagen scaffold prevent further inflammatory reactions from occurring[13]
2. The enduring collagen type in the injected site is predominantly the 'mature' collagen scaffold of collagen type I[5]
   a) The reduction of collagen type III means no further stimulation of the inflammatory response
3. The degradation of Ellansé constituents is completed by hydrolysis, leaving just water and carbon dioxide
4. Because the final volume within the treated area is greater than the volume of Ellansé injected, there is no requirement to 'touch up' the treatment
   a) The final volume is greater than the volume injected by 20–30% due to formation of collagen type I fibres[11]
5. The availability of two versions of Ellansé with different durations of action means that the length of treatment effect can be tailored to a patient's requirements
   a) This is achieved by varying the length of the PCL chains, allowing for predictable, controlled and adjustable bioresorption
6. The treatment technique is the same regardless of the Ellansé product selected
   a) Same:
   - Rheological properties
   - Technique
   - Syringe
   - Needle/cannula

Sinclair Training

Sinclair delivers scientifically advanced, aesthetic products and services made exclusively for the most highly skilled clinicians worldwide. Our educational arm, Sinclair College, exists to harness the power of science with excellence as standard through collaboration and insight with worldwide experts. We provide a forward-thinking approach to linked-up education across the Sinclair portfolio for ongoing engagement and education.

Our Sinclair College educational platform provides you with a whole host of informative webinars, courses, filmed video demonstrations and programmes to help support your professional development in aesthetics. Additionally, our education team works to create a personalised learning journey that helps our trainers and key opinion leaders take clinicians through the portfolio, giving the best possible patient outcomes to those who use our products.

The Sinclair College website and My e-College App can be used anywhere, giving you free and flexible access to product and anatomy modules, and practice development insight.

You can access the Sinclair College e-learning website and app by scanning the below QR codes:

Sinclair College e-learning website

My e-College App

References

1. Sinclair. Ellansé training materials.
2. Sinclair. Ellansé 10-year anniversary brochure.
3. Sinclair. Ellansé instructions for use.
4. Christen MO, Vercesi F. Polycaprolactone: How a well-known and futuristic polymer has become an innovative collagen-stimulator in esthetics. Clin, cosmet investig dermatol. 2020;13:31–48.
5. Nicolau PJ, and Marijnissen-Hofsté J. Neocollagenesis after injection of a polycaprolactone based dermal filler in a rabbit. Eur J Aesth Med Dermatol. 2013;3:19–26.
6. Laeschke K. Biocompatibility of microparticles into soft tissue fillers. Semin Cutan Medic Surg. 2004;23:214–7.
7. Anderson JM. Mechanisms of inflammation and infection with implanted devices. Cardiovasc Pathol. 1993;2:33S–41S.
8. Nicolau JP. Long-lasting and permanent fillers: biomaterial influence over host tissue response. Plast Reconstr Surg. 2007;119: 2271–86.
9. Kim JA, Van Abel D. Neocollagenesis in human tissue injected with a polycaprolactone-based dermal filler. J Cosmet Laser Ther. 2015;17:99–101.
10. Moers-Capri MM, Sherwood S. Polycaprolactone for the correction of nasolabial folds: A 24-month, prospective, randomized, controlled clinical trial. Dermatol Surg. 2013;39:457–63.
11. Sinclair. Data on file.
12. Galadari H, van Abel D, Al Naumi K, Al Faresi F, Galadari I. A randomized, prospective, blinded, split-face, single-center study comparing polycaprolactone to hyaluronic acid for treatment of nasolabial folds. J Cosmet Dermatol. 2015;14:27–32.
13. Lemperle G, Morhenn VB, Pestonjamasp V, Gallo RL. Migration studies and histology of injectable microspheres of different sizes in mice. Plast Reconstr Surg. 2004;113:1380–90.